

Dexamethasone reduction or omission with NEPA and olanzapine for HEC: A phase III trial.

Jian Zhang, Yanchun Meng, Yingying Liu, Yiqun Du, Xiaojun Liu, Ling Yang, Yong Chen, Shaodong Tian, Qin Zhou, Xiaojie Zhuang, Zikang Li, Jinsong Liu, Shencun Fang, Weifei Fan, Yu Mao, Ling Zhang, Hao Wu, Fei Yan, Weng Jie, Jianhua Zhao; Fudan University Shanghai Cancer Center, Shanghai, China; XinYu People's Hospital, Xinyu, China; Xinsteel Center Hospital, Xinyu, China; HuNan University of Medicine General Hospital, Huaihua, China; The First People's Hospital of KunShan, Suzhou, China; Yichun People's Hospital, Yichun, China; Ya'an People's Hospital, Ya'an, China; XianTao First People's Hospital, Xiantao, China; Nanjing Brain Hospital, Nanjing, China; JiangSu Province Official Hospital, Nanjing, China; JiangShan People's Hospital, Quzhou, China; The First People's Hospital of JinTan, Changzhou, China; The People's Hospital of LiuYang, Changsha, China; Loudi Central Hospital, Loudi, China; Yueyang Central Hospital, Yueyang, China; The First People's Hospital of JingDeZhen, Jingdezhen, China

Background: Prolonged dexamethasone (DEX) in antiemetic regimens for highly emetogenic chemotherapy (HEC) may impair immunotherapy efficacy. We evaluated if DEX can be reduced or omitted when combined with NEPA (netupitant/palonosetron) and olanzapine without compromising control. **Methods:** In this open-label, multicenter, phase III non-inferiority trial, adults receiving HEC were randomized 1:1:1 to: Standard Regimen (NEPA day1, olanzapine days1-4, DEX 12mg day1/8mg days2-4); DEX-sparing Regimen (same, DEX 6mg day1 only); or DEX-free Regimen (same, no DEX). The primary endpoint was overall complete response (CR: no emesis/no rescue) 0-120h. A hierarchical testing sequence (DEX-sparing vs Standard, then DEX-free vs Standard) with a -12% non-inferiority margin controlled type I error (one-sided $\alpha=0.025$). **Results:** Among 644 randomized patients (median age 54.9 years; 66.9% female), the overall CR rates were 72.4% for Standard, 72.2% for DEX-sparing (rate difference [RD] -0.19%, 95% CI -8.77 to 8.38; P for non-inferiority = 0.004), and 70.1% for DEX-free (RD -2.24%, 95% CI -10.81 to 6.38; P for non-inferiority = 0.013). Both experimental regimens met the non-inferiority criterion. Acute-phase (0-24 h) CR rates were 81.5%, 82.6%, and 80.8% (intergroup comparison, $P > 0.05$), and delayed-phase (24-120 h) CR rates were 77.1%, 77.6%, and 73.9% ($P > 0.05$), respectively, with no significant differences. For complete nausea control, the DEX-free regimen was inferior beyond 24 hours, whereas the DEX-sparing regimen remained comparable to Standard throughout. Steroid-related adverse events, such as insomnia, were primarily reported in the Standard regimen group. **Conclusions:** NEPA plus olanzapine with single-day low-dose or no DEX is non-inferior to standard 4-day DEX for CINV prevention in HEC, supporting steroid-sparing strategies relevant for chemo-immunotherapy. Clinical trial information: NCT06331520. Research Sponsor: None.

Baseline patient characteristics and chemotherapy regimen.

	Total (N=644)	Standard Regimen (N=217)	DEX-sparing Regimen (N=213)	DEX-free Regimen (N=214)
Age, years	54.9 $\pm$ 12.0	54.2 $\pm$ 11.7	55.2 $\pm$ 12.0	55.3 $\pm$ 12.2
Male	219 (34.0)	73 (33.6)	74 (34.7)	72 (33.6)
Female	425 (66.0)	144 (66.4)	139 (65.2)	142 (66.4)
Breast cancer	280 (43.5)	101 (46.5)	92 (43.2)	87 (40.6)
Lung cancer	141 (21.9)	45 (20.7)	50 (23.5)	46 (21.5)
AC regimen	148 (23.0)	57 (26.3)	52 (24.4)	39 (18.2)
Platinum-based regimen	472 (73.3)	153 (70.5)	152 (71.4)	167 (78.0)

Gabapentin plus tramadol versus tramadol alone for chemoradiotherapy-induced oral mucositis pain in head and neck cancer: Results of a randomized phase III trial.

Minit Jalan Shah, Nandini Sharrel Menon, Vanita Noronha, Vijay Maruti Patil, Laxman Sahu, Ajay Upadhyay, Ashok Singhal, Anjali Shah, Aravind Padmanabhan, Ayman Shaikh, Harshada Arolkar, Sandhyarani Nishank, Gargi Patlekar, Yashashree Parida, Kavita Prakash Nawale, Harshal Munekar, Ashwini Budrukhar, Naveen Mummudi, Sarbani Ghosh-Laskar, Kumar Prabhash; Tata Memorial Hospital, Tata Memorial Centre, Homi Bhabha National Institute, Mumbai, Maharashtra, India; Hinduja Hospital, Mumbai, India; Tata Memorial Hospital, Mumbai, India; Tata Memorial Hospital, Mumbai, Maharashtra, India; Tata Memorial Centre, Mumbai, Maharashtra, India; Tata Memorial Centre, Mumbai, India; Tata Memorial Hospital, Homi Bhabha National Institute, Mumbai, India

The full, final text of this abstract will be available at meetings.asco.org on the day of presentation and in the online supplement to the June 10, 2026, issue of the *Journal of Clinical Oncology*.

Ramelteon for prevention of postoperative delirium in elderly cancer patients: A randomized, double-blind, placebo-controlled multicenter trial, JORTC-PON02/J-SUPPORT2103/NCCH2103.

Ryoichi Sadahiro, Masanori Enokido, Yoshinobu Matsuda, Takuhiro Yamaguchi, Keisuke Ariyoshi, Shunsuke Oyamada, Yosuke Uchitomi, Tatsuo Akechi, Kotaro Hatta, Kazuko Matsumoto, Takatoshi Hirayama, Rika Nakahara, Asao Ogawa, Hironobu Hashimoto, Makoto Maeda, Asuko Sekimoto, Tetsufumi Sato, Noboru Yamamoto, Eiko Saito, Hiromichi Matsuoka; National Cancer Center Japan, Tokyo, Japan; Tonan Hospital, Sapporo, Japan; NHO Kinki Chuo Chest Medical Center, Sakai, Osaka, Japan; Division of Biostatistics, Tohoku University Graduate School of Medicine, Sendai, Japan; Department of Data Management, Japanese Organisation for Research and Treatment of Cancer (JORTC) Data Center, Tokyo, Japan; Department of Biostatistics, Japanese Organisation for Research and Treatment of Cancer (JORTC) Data Center, Tokyo, Japan; Division of Survivorship Research, National Cancer Center Institute for Cancer Control, National Cancer Center, Tokyo, Japan; Department of Psychiatry and Cognitive-Behavioral Medicine, Nagoya City University, Graduate School of Medical Sciences, Nagoya, Japan; Department of Psychiatry, Juntendo University Nerima Hospital, Tokyo, Japan; Kokoro Support Clinic, Tokyo, Japan; Division of Psycho-Oncology, Exploratory Oncology Research and Clinical Trial Center, National Cancer Center, Kashiwa, Chiba, Japan; Department of Pharmacy, National Cancer Center Hospital, Japan, Chuo-Ku, Tokyo, Japan; Department of Pharmacy, National Cancer Center Hospital, Japan, Tokyo, Japan; National Cancer Center Hospital, Tokyo, Japan; Tokyo University, Tokyo, Japan

The full, final text of this abstract will be available at meetings.asco.org on the day of presentation and in the online supplement to the June 10, 2026, issue of the *Journal of Clinical Oncology*.

Nationwide randomized, phase III, placebo-controlled trial of bupropion for cancer-related fatigue: Primary outcome results.

Luke Joseph Peppone, Joseph John Guido, Chin-Shang Li, Hyo S. Han, Margarita Bobonis Babilonia, Michelle Christine Janelins, Ramya Varadarajan, Bryan Faller, Rizwan Danish, Aasha I. Hoogland, Lisa Michelle Danish, Julianne E. Bower, Steve W. Cole, Zeruesenay Desta, Karen Michelle Mustian, Gary R. Morrow, Heather S.L. Jim; University of Rochester Medical Center, Rochester, NY; University of Rochester Medical Center Department of Neurobiology and Anatomy, Rochester, NY; Department of Surgery, Division of Supportive Care in Cancer and URCC NCORP Research Base, University of Rochester Medical Center, Rochester, NY; Moffitt Cancer Center and Research Institute, Tampa, FL; Department of Veterans Affairs James Hailey Hospital, Associate Professor Department of Psychiatry and Behavioral Medicine, University of South Florida Morsani College of Medicine, Tampa, FL; James P. Wilmot Cancer Center, University of Rochester Medical Center, Rochester, NY; Christiana Care Oncology and Hematology, Newark, DE; Heartland NCORP/Missouri Baptist Medical Center, St. Louis, MO; Genesee Cancer and Blood Disease, Flint, MI; H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL; Department of Psychology, UCLA, Los Angeles, CA; Department of Psychiatry, David Geffen School of Medicine, University of California, Los Angeles, CA; Indiana University School of Medicine, Indianapolis

The full, final text of this abstract will be available at meetings.asco.org on the day of presentation and in the online supplement to the June 10, 2026, issue of the *Journal of Clinical Oncology*.

YOCAS yoga, mood disturbance, and insomnia: A URCC NCORP RB nationwide, phase III, randomized, controlled trial with cancer survivors.

Yuri Choi, Po-Ju Lin, Hongying Sun, Lindsey Jean Mattick, Alisha Chakrabarti, Marianne Melnik, Janet C. Ruzich, Carla Jorgensen, Marie Anne Flannery, Lauren Victoria Ghazal, AnnaLynn Williams, Karen Michelle Mustian; Department of Surgery, University of Rochester Medical Center, Rochester, NY; Wilmet Cancer Institute, University of Rochester Medical Center, Rochester, NY; Department of Surgery, Division of Supportive Care in Cancer, University of Rochester Medical Center, Rochester, NY; Cancer Research Consortium of West Michigan, Grand Rapids, MI; Providence Cancer Institute, Clackamas, OR; Prisma Health Cancer Institute, Greenville, SC; University of Rochester Medical Center, Rochester, NY; School of Nursing, University of Rochester, Rochester, NY; University of Rochester School of Medicine and Dentistry, Rochester, NY; Department of Surgery, Division of Supportive Care in Cancer and URCC NCORP Research Base, University of Rochester Medical Center, Rochester, NY

Background: Mood disturbance (MoD) and insomnia are two of the most pervasive and troubling side effects experienced by cancer survivors for years after completing adjuvant treatments. MoD and insomnia significantly interfere with survivors' ability to perform essential daily activities such as cleaning, grocery shopping, cooking, taking medications, driving, and communicating with others. We previously reported that Yoga for Cancer Survivors (YOCAS) is effective for treating insomnia. YOCAS may also alleviate MoD, and changes in MoD may mediate the influence of YOCAS on insomnia. **Methods:** We conducted a nationwide, multisite, phase III randomized, controlled trial to examine: 1) the effects of YOCAS on MoD (i.e., overall MoD, anxiety, and fatigue), and 2) whether changes in MoD mediate the association between YOCAS and changes in insomnia. Survivors were recruited via the University of Rochester Cancer Center NCI Community Oncology Research Program Research Base (URCC NCORP RB). Non-metastatic cancer survivors, between 2–24 months post adjuvant therapy, aged 21 or older, with moderate or greater sleep disruption, and with no participation in yoga during the prior 3 months, were randomized to two arms: 1) standard care and 2) standard care plus the 4-week YOCAS intervention (2x/week; 75 min/session). The YOCAS consists of breathing exercises, 18 gentle Hatha and Restorative yoga postures, and meditation. MoD and insomnia were assessed using the Profile of Mood States and Insomnia Severity Index, respectively, at pre- and post-intervention. **Results:** A total of 410 survivors, recruited from 12 community-based oncology practices across the USA, were randomized (mean age = 54.10.4 years; 96% female; 75% breast cancer survivors). ANCOVAs revealed YOCAS participants, compared to standard care participants, experienced significantly less overall MoD (Mean Difference [Standard Error] = -5.08 [1.36]), anxiety (MD [SE] = -0.72 [0.29]), and fatigue (MD [SE] = -1.49 [0.41]; all $p < 0.05$) at post-intervention. Additionally, YOCAS participants reported significant improvements from pre- to post-intervention on overall MoD, anxiety, and fatigue (all $p < 0.05$), whereas standard care participants did not. Causal mediation analyses revealed changes in overall MoD partially mediated (24.9%; 95% CI: 10.9%, 42.6%) the association between YOCAS and changes in insomnia. Changes in fatigue also partially mediated (24.6%; 95% CI: 11.3%, 43.9%) the association between YOCAS and changes in insomnia (all $p < 0.05$). **Conclusions:** YOCAS yoga is effective for treating overall MoD, anxiety, and fatigue among survivors. Additionally, improvements in insomnia stemming from YOCAS yoga may be mediated by changes in overall MoD and fatigue. Clinicians should consider recommending yoga for survivors who experience overall MoD, anxiety, fatigue, and insomnia. Clinical trial information: NCT00397930. Research Sponsor: National Cancer Institute; UG1CA189961; National Cancer Institute; UG1CA189860; National Cancer Institute; UG1CA189953; National Cancer Institute; UG1CA189972; National Cancer Institute; T32CA102618.

A phase III placebo controlled randomized controlled trial using combination therapy for treatment-related fatigue in patients with prostate cancer.

Sriram Yennu, Penny A. Stanton, Seungtaek Choi, Paul Gettys Corn, Lisa Thomas, Quynh Nguyen, Minxing Chen, Chad Tang, Sean Eric McGuire, Mary E. Cavanaugh, Amado J. Zurita, Ana Aparicio, Sumit Kumar Subudhi, Bilal Ahmed Siddiqui, Patrick Glen Pilié, Premjit Roy, Carol Harrison, Sanjay Shete, Karen Basen-Engquist, Eduardo Bruera; The University of Texas MD Anderson Cancer Center, Houston, TX; Department of Radiation Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX; Department of Genitourinary Medical Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX; Department of Palliative, Rehabilitation and Integrative Medicine, The University of Texas MD Anderson Cancer Center, Houston, TX

Background: To determine if the combination of exercise (EX) plus methylphenidate (MP) is superior to EX plus placebo (PL) for 12 weeks in the treatment of cancer-related-fatigue (CRF) in patients with prostate cancer receiving androgen deprivation therapy (ADT) and/or radiation therapy (RT). **Methods:** Using a phase III randomized double-blind placebo-controlled design, we assessed treatments combining either EX or its stretching (ST) control with either MP (5mg twice a day, with dose titrated up to 20mg a day) or placebo. Patients were eligible if they had prostate cancer patients who are receiving androgen deprivation therapy and/or radiation therapy and had CRF; Eligible patients were randomized into one of four arms, EX + MP, EX + PL, ST + MP, ST + PL (2:1:1:1). Primary outcome was assessed using linear mixed-effects model comparing the differences in Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) scores at Weeks 1, 2, 4, 8 and 12. **Results:** 161 eligible patients were randomly assigned to 4 arms EX+MP (n = 65), EX+PL(n = 34), ST+MP (n = 30), and ST+PL (n = 32). Demographics, including mean age (65-67 years) were similarly distributed between arms (all $p > 0.05$). Bone metastases (~25%), and treatment modality distributions (ADT alone, ADT + RT, or RT alone) were comparable among the arms. The baseline FACIT-F scores [mean (SD)] were 28.5(11.0), 28.7(8.9), 28.5(9.3), and 30.3(11.0) respectively in arms EX+MP, EX+PL, ST+MP, and ST+PL arms. All 4 arms showed CRF improvement over time. There was a non-significant improvement in CRF in the EX+MP intervention arm, compared with EX+PL arm [FACIT-F coefficient, 2.73(95% CI, -0.49 to 5.96); $P = 0.097$]. Methylphenidate-containing arms (EX+MP and ST+MP) significantly improved CRF compared with their placebo counterparts (EX+PL and ST+PL), [FACIT-F coefficient, 3.23 (95% CI 0.84 to 5.63), $P = 0.008$]. There were no significant differences in CTCAE v.5 grade ≥ 3 adverse events by arms ($P > 0.99$). **Conclusions:** EX+MP arm was not superior to EX+PL arm in improvement of CRF. Methylphenidate-containing arms significantly improved CRF compared with their placebo arms. All four treatment arms showed improvement of CRF overtime suggesting strong placebo response. Further methylphenidate-containing multimodal CRF studies are needed. Clinical trial information: NCT03772834. Research Sponsor: National Institute of Health (NCI).

A digital health intervention to enhance well-being among adolescent and young adult survivors of cancer: Results from the EMPOWER full factorial trial.

John M. Salsman, Karly M. Ingram, Elizabeth Addington, Janet Tooze, Beverly J. Levine, Vivian M. McAllister, Laurie McLouth, DerShung Yang, Stacy Sanford, Lynne I. Wagner, Stephanie C. Bunch, Abby R. Rosenberg, Carmina G. Valle, Brad J. Zebrack, Dianna Howard, Michael Roth, Judith T. Moskowitz; Atrium Health Wake Forest Baptist, Winston-Salem, NC; East Carolina University, Greenville, NC; Northwestern University Feinberg School of Medicine, Chicago, IL; Wake Forest University School of Medicine, Winston-Salem, NC; University of Kentucky College Department of Behavioral Health, Lexington, KY; BrightOutcome, Buffalo Grove, IL; Robert H. Lurie Comprehensive Cancer Center, Chicago, IL; The University of North Carolina at Chapel Hill, Winston-Salem, NC; Dana-Farber Cancer Institute, Boston, MA; The University of North Carolina at Chapel Hill, Chapel Hill, NC; University of Michigan School of Social Work, Ann Arbor, MI; Atrium Health Wake Forest Baptist Comprehensive Cancer Center, Winston-Salem, NC; The University of Texas MD Anderson Cancer Center, Houston, TX

Background: Adolescent and young adult (AYA) survivors of cancer are at significant risk of adverse psychological outcomes, yet scalable, efficacious interventions to address their needs are limited. We evaluated a self-guided digital health intervention with affective, behavioral, and cognitive skills, “Enhancing Management of Psychological Outcomes With Emotion Regulation” (EMPOWER), for improving psychological outcomes. **Methods:** We recruited AYAs ($n = 352$; 74% female, median age 33 years) from three comprehensive cancer centers between Dec 2021 and Sept 2024. AYAs were diagnosed at and currently aged 15 to 39 years, within 5 years post-curative treatment, and had internet access. In a full factorial design, AYAs were randomly assigned to 5 weekly components, either EMPOWER intervention or attention control ($2^5 = 32$ arms): 1. positive events, capitalizing & gratitude (vs. cognitive skills); 2. mindfulness (vs. financial literacy); 3. positive reappraisal (vs. nutrition); 4. personal strengths & goal-setting (vs. weight management); 5. acts of kindness (vs. sun protection). Didactic lessons and skills practices were delivered via a website designed specifically for the study. AYAs completed PROMIS measures for positive affect (primary outcome), and depression and anxiety (secondary outcomes) at pre-intervention, post-intervention, and two and four months post-intervention. Using the intent-to-treat principle and a mixed model with linear contrasts, we estimated average within-person changes over time by component (intervention/control) for AYAs and compared changes by component. **Results:** From pre to post-intervention, positive affect increased ($p < 0.05$) among those in 3 of the 5 EMPOWER and 4 of the 5 control components (mean change = 1.4 to 1.9) and anxiety decreased ($p < 0.05$) for those in 4 of 5 EMPOWER and 4 of 5 control components (mean change = -1.2 to -2.0). Further, anxiety was significantly lower ($p < 0.05$) for all EMPOWER and control components at two and four-months post intervention (mean change = -1.3 to -2.4). There was little change in depression for any group. We found no treatment effects for any outcome whereby AYAs who received intervention content had significantly greater improvements than those receiving attention control content. Instead, some EMPOWER (positive events, capitalizing, & gratitude; acts of kindness) and control components (nutrition) were associated with clinically meaningful changes in outcomes, based on PROMIS metrics. **Conclusions:** Our findings suggest a range of affective, behavioral, and cognitive strategies drawn from both positive psychology and health education domains are similarly effective in enhancing positive affect and mitigating post-treatment anxiety and highlight the potential benefit of low-touch, self-guided digital health strategies for AYA survivors of cancer. Clinical trial information: NCT04317417. Research Sponsor: National Institutes of Health, National Cancer Institute; CA242849.

Impact of electronic patient-reported outcome measure (ePROM)–triggered, collaborative care (CC)–based symptom intervention on depression and anxiety in young adults (YAs) with cancer.

Michael H. Storandt, Zhaohui Jin, Kathryn Jean Ruddy, Deirdre R. Pachman, Oudom Kour, Veronica Grzegorzczuk, Kurt Kroenke, Joan M. Griffin, Jessica Austin, Sandra A. Mitchell, Ashley Wilder Smith, Shawna L. Ehlers, Linda L. Chlan, Ewan Kemar Cobran, Jacob Ron Greenmyer, Ryan Christian Augustin, Wendy A. Allen-Rhoades, Qian Shi, Andrea L. Cheville; Mayo Clinic Rochester, Rochester, MN; Division of Oncology, Mayo Clinic Rochester, Rochester, MN; Department of Medical Oncology, Mayo Clinic Rochester, Rochester, MN; Division of Community Internal Medicine, Geriatrics, and Palliative Care, Mayo Clinic Rochester, Rochester, MN; Department of Physical Medicine and Rehabilitation Research, Mayo Clinic Rochester, Rochester, MN; Indiana University School of Medicine and Regenstrief Institute, Indianapolis, IN; Mayo Clinic Arizona, Scottsdale, AZ; National Cancer Institute, National Institutes of Health, Bethesda, MD; Department of Psychiatry and Psychology, Mayo Clinic Rochester, Rochester, MN; Mayo Clinic College of Medicine and Science, Scottsdale, AZ; Department of Physical Medicine and Rehabilitation, Mayo Clinic Rochester, Rochester, MN

Background: YAs with cancer, defined as those diagnosed prior to the age of 40, may experience greater symptom burden compared to those diagnosed at older ages. We evaluated the impact of an ePROM–triggered, CC–based, supportive care intervention on symptom burden in YAs with cancer. **Methods:** The Enhanced, Electronic Health Record–facilitated Cancer Symptom Control (E2C2) trial was a cluster–randomized, pragmatic trial (NCT03892967) that enrolled oncology patients seen at Mayo Clinic Rochester and within the Mayo Clinic Health System (sites in Minnesota and Wisconsin) between March 2019 and January 2023. Patients routinely reported the severity of six SPPADE symptoms (Sleep deficit, Pain, Physical function impairment, Anxiety, Depression, and Energy deficit/fatigue) on 11–point numerical rating scales. Symptom severity was classified as none to mild (0–3), moderate (4–6), or severe (7–10). Those with moderate or severe symptoms were offered symptom management education, while those with severe symptoms were also offered the option to work virtually with a symptom care manager. In this post hoc analysis, we examined the effects of the intervention on change in symptom scores among YAs and time to improvement to a mild/moderate level in those with at least one severe symptom. **Results:** Among 40,659 patients who responded to at least one survey, 2,598 were YAs and 38,061 were adults ≥ 40 years. Among YAs, 10.7%, 24.3%, and 65.1% were 18–24 years, 25–31 years, and 32–39 years, respectively. A greater proportion of YA patients were female (61.5% vs 57.0%), of a non–white race (12.4% vs 5.3%), living in an urban setting (65.7% vs 55.1%), single (36.4% vs 9.6%), on non–government insurance (78.1% vs 36.6%), employed (72.6% vs 37.4%), and had a Bachelor’s degree or greater (37.8% vs 28.3%, $p < 0.001$ for all). Fewer YA patients had metastatic disease compared to older patients (24.2% vs 35.2%, $p < 0.001$). Compared to a pre–intervention baseline, the mean change in symptom score for YA patients following the intervention demonstrated improvements in anxiety (-0.195) and depression (-0.168 , $p < 0.0001$ for both), while physical function impairment worsened over the intervention period (0.101 , $p = 0.014$). Compared to adults ≥ 40 years, YAs experienced greater intervention effects for management of depression ($p < 0.001$), fatigue ($p = 0.01$), pain ($p < 0.0001$), and physical function impairment ($p < 0.0001$). Among YAs with a severe symptom during the intervention period, median time to improvement to a mild/moderate level was longer for anxiety compared to those ≥ 40 years (3.5 vs 2.7 months, $p = 0.009$). **Conclusions:** Routine ePROM surveillance, coupled with CC–based symptom management, led to improvements in anxiety and depression among YAs with cancer, although, time to improvement was longer for anxiety compared to adults ≥ 40 years. Research Sponsor: NCI of the National Institutes of Health.

SUPPORT+ digital self-management and clinical support for advanced cancer: A randomized controlled trial.

Wing-Lok Chan, Inda Sung Soong, Mei Ying Lim, Winnie Wing Yan Tin, Steven Wai Kwan Siu, Jeffrey Ng, Carmen Leung, Alex Leung, Holly Hou, Kwok-keung Yuen, Dora LW Kwong, Rina Hui; Department of Clinical Oncology, The University of Hong Kong, Hong Kong, Hong Kong; Department of Clinical Oncology, Pamela Youde Nethersole Eastern Hospital, Hong Kong, Hong Kong; Department of Oncology, Princess Margaret Hospital, Hong Kong, Hong Kong; Department of Clinical Oncology, Tuen Mun Hospital, Hong Kong, Hong Kong; Department of Clinical Oncology, Queen Mary Hospital, Pokfulam, Hong Kong; Haven of Hope Hospital, Kowloon, Hong Kong; Queen Elizabeth Hospital, Kowloon, Hong Kong; Department of Clinical Oncology, Queen Elizabeth Hospital, Hong Kong, Hong Kong; The University of Hong Kong, Hong Kong, Hong Kong; Queen Mary Hospital, Hong Kong, Hong Kong; Department of Clinical Oncology, LKS Faculty of Medicine, The University of Hong Kong, Hong Kong, Hong Kong

The full, final text of this abstract will be available at meetings.asco.org on the day of presentation and in the online supplement to the June 10, 2026, issue of the *Journal of Clinical Oncology*.

Efficacy of YES, an mHealth intervention for adolescent and young adults (AYA) with breast cancer (BC), to address AYA survivorship concerns.

Shoshana M. Rosenberg, Noah Graham, Kate Dibble, Nabihah Tayob, Ella Johnson, Chloe M. Hery, Kayla Willams, Erik Harden, Ashley Pariser Davenport, Cecilia R. DeGraffinreid, Timiya Nolan, Magnolia Contreras, Noel Roma, Sandra A. Mitchell, Kimberly Sabelko, Deb Schrag, Dawn L. Hershman, Ann H. Partridge, Michelle Joy Naughton; Weill Cornell Medicine, New York, NY; Dana-Farber Cancer Institute, Boston, MA; The Ohio State University, Columbus, OH; The Ohio State University Comprehensive Cancer Center, Columbus, OH; Herbert Irving Comprehensive Cancer Center, Columbia University Medical Center, New York, NY; Division of Preventive Medicine, Heersink School of Medicine, O'Neal Comprehensive Cancer Center, Birmingham, AL; National Cancer Institute, National Institutes of Health, Bethesda, MD; Susan G. Komen, Dallas, TX; Memorial Sloan Kettering Cancer Center, New York, NY; Herbert Irving Comprehensive Cancer Center, Columbia University Irving Medical Center, New York, NY

Background: AYA BC survivors often have unmet concerns that are understudied and sub-optimally addressed. Primary results from the YES trial (NCT04906200) demonstrated that YES, an AYA-focused mHealth intervention, improved quality of life and reduced specific symptoms in AYA BC survivors at 6 months (mo) post-enrollment. Here we report a pre-specified secondary analysis of YES on reducing AYA survivorship concerns. **Methods:** We conducted a multicenter (Dana-Farber Cancer Institute, The Ohio State University, Columbia University Medical Center) RCT of YES, an mHealth intervention which provides tailored information, resources and support in response to monthly electronic patient-reported outcome monitoring, a journal platform, and a chat room. Participants age ≤ 39 at diagnosis (dx) of stage 0-3 BC, < 3 years post-dx were randomized 1:1 to YES or Usual Care (UC). Survivorship concerns were measured at baseline, 3, and 6 mo with AYA HOPE survey items; participants rated their level of concern across a range of domains. Generalized linear mixed effects models analyzed the binary endpoint of somewhat/very vs no/low concern for each issue. Odds of being somewhat/very concerned about a domain at 6 mo were compared between arms, adjusting for baseline concern. **Results:** From 6/2021-12/2024, 360 participants were randomized (YES:179; UC: 181) following baseline survey completion. Participant characteristics were balanced between arms. Median time from dx was 19 (IQR: 12-27) mo. Median age at dx was 34 (IQR: 31-37) yrs; 61% had stage 2 or 3 BC. Overall, a majority of participants endorsed high levels of concern at baseline related to: long-term side effects of treatment (67%), long-term health effects of cancer (70%), recurrence (79%), checking for signs of recurrence (57%), possibility of a new cancer (67%), exercise (60%), nutrition (58%), familial cancer risk (51%), and body image (56%). Other endorsed concerns included: fertility (43%), financial support for medical care (37%), financial concerns (38%), talking about cancer experience with family/friends (27%), having enough information about treatment (25%), meeting other AYAs (22%), alcohol and cancer (15%), and smoking cessation (3%). At 6 mo, adjusting for baseline concern, the YES group (vs UC) had lower odds of being somewhat/very concerned about finances (OR: 0.36, 95% CI: 0.13 - 0.98, $p = 0.05$), financial support for medical care (OR 0.35, 95% CI 0.13-0.96, $p = 0.04$), family cancer risk (OR 0.36, 95% CI 0.17-0.77, $p = 0.009$), and alcohol and cancer (OR 0.15, 95% CI 0.03-0.75, $p = 0.02$). **Conclusions:** Concerns across a range of survivorship domains are prevalent in AYA BC survivors. The YES mHealth intervention reduced concerns about several survivorship issues, supporting the potential for this highly scalable intervention to help manage these concerns as an adjunct to routine clinical care for AYA BC survivors. Clinical trial information: NCT04906200. Research Sponsor: National Cancer Institute; U01CA24,6648; Breast Cancer Research Foundation; Susan G. Komen; American Cancer Society.

Effect of a weight loss intervention (WLI) on quality of life (QOL) and symptoms in women with breast cancer: Results from the Breast Cancer Weight Loss (BWEL) trial.

Jennifer A. Ligibel, Dawn L. Hershman, Amylou C. Dueck, Linda Mackie McCall, Brenda F. Ginos, Pamela Jean Goodwin, Anna Weiss, Olwen Hahn, Patricia Spears, Electra D. Paskett, Judith O. Hopkins, Erica L. Mayer, Elizabeth S. Frank, Vanessa Bernstein, Vered Stearns, Julia R. White, Thomas Wadden, Eric P. Winer, Lisa A. Carey, Ann H. Partridge; Dana-Farber Cancer Institute, Boston, MA; Herbert Irving Comprehensive Cancer Center, Columbia University Irving Medical Center, New York, NY; Alliance Statistics and Data Management Center and Mayo Clinic Rochester, Rochester, MN; Alliance Statistics and Data Management Center, Duke University, Durham, NC; Mayo Clinic Arizona, Scottsdale, AZ; Mount Sinai Hospital-Breast Medical Oncology, Toronto, ON, Canada; Department of Surgery, University of Rochester, Rochester, NY; University of Chicago, Alliance for Clinical Trials in Oncology, Chicago, IL; UNC Patient Advocates for Research Council, Raleigh, NC; Department of Internal Medicine, The James Comprehensive Cancer Center, College of Medicine, The Ohio State University Wexner Medical Center, Columbus, OH; Novant Health Cancer Institute, Kernersville, NC; Medical Oncology, Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA; Dana-Farber Cancer Institute, Lexington, MA; BC Cancer Agency Vancouver Island Centre, Victoria, BC, Canada; Weill Cornell Medical Center, New York, NY; University of Kansas Medical Center Comprehensive Cancer Center, Kansas City, KS; University of Pennsylvania, Philadelphia, PA; Yale Cancer Center, New Haven, CT; Lineberger Comprehensive Cancer Center, The University of North Carolina School of Medicine, Chapel Hill, NC

Background: BWEL (Alliance A011401; NCT02750826) is a Phase III trial that randomizes patients (pts) with stage II-III breast cancer and body mass index (BMI) ≥ 27 kg/m² 1:1 to a 24-month (mo) lifestyle-based WLI + health education (HE) or HE alone. Here we report prespecified secondary outcomes of the impact of the WLI on patient-reported QOL and symptoms. **Methods:** The first 540 BWEL pts (randomized between 9/2016 and 7/2017) were included in this substudy that collected PROMIS 29 Profile 2.0 and Global Health scores at enrollment, 6 and 24 mos. Adjusting for baseline scores, mean physical function (predefined substudy primary outcome), global physical and mental health, fatigue and other scores were compared at 6 and 24 mos using analysis of covariance (ANCOVA). P-values <0.05 were considered significant. Positive differences in positive attributes (e.g., physical function) and negative differences in negative attributes (e.g., anxiety) represented better outcomes in the WLI arm. **Results:** At baseline, median BMI was 32.9 kg/m² (26.5 – 69.1), median age was 53 (25 – 78) years; 83.9% of pts were non-Hispanic White, 10.7% were Black and 5.9% were Hispanic. At 6 mos, the WLI (vs HE) arm had significantly better physical function (ANCOVA-based mean difference between arms 1.9 [95% CI 0.8, 3.0]; $p<0.001$), global physical health (2.0 [95% CI 0.9, 3.0]; $p<0.001$), global mental health (1.30 [95% CI 0.2, 2.4], $p=0.03$), social roles and activities (2.3 [95% CI 1.1, 3.6]; $p<0.001$), and fatigue (-1.7 [95% CI -3.1, -0.4], $p=0.01$) (Table). Improvements were generally maintained at 24 mos. Similar findings were seen in analyses using longitudinal mixed modeling. **Conclusions:** The BWEL WLI demonstrated QOL benefits for patients with breast cancer, resulting in significantly better physical function, global physical and mental health, and symptoms. Future analyses will evaluate which populations experienced the most benefit, as well as the relationships among QOL, symptoms, and weight loss. **Support:** U10CA180821, U10CA180882, UG1CA189823; U10CA180820; U10CA180868; U10CA180863, CCS 707213; U10CA180888; UG1CA189858; <https://acknowledgments.alliancefound.org>. Clinical trial information: NCT02750826. **Research Sponsor:** National Cancer Institute/U.S. National Institutes of Health; UG1CA189858; U10CA180821, U10CA180882, UG1CA189823; U10CA180820; U10CA180868; U10CA180863, CCS 707213; U10CA180888; U10CA180820; U10CA180868; U10CA180888; Susan G Komen Foundation; Breast Cancer Research Foundation; American Cancer Society.

Analysis of covariance-adjusted least squares means values at 6-mos adjusted for baseline scores.

QOL/Symptom Attributes	HE	WLI	Between arm difference (95% CI)*	P value
Physical Function	47.1	49.0	1.9 (0.8, 3.0)	<0.001
Global Physical Health	46.2	48.1	2.0 (0.9, 3.0)	<0.001
Global Mental Health	48.6	49.9	1.3 (0.2, 2.4)	0.03
Social Roles and Activities	52.7	55.0	2.3 (1.1, 3.6)	<0.001
Anxiety	50.2	50.0	-0.2 (-1.6, 1.2)	0.77
Depression	47.5	47.5	-0.0 (1.2, 1.2)	0.96
Fatigue	50.6	48.9	-1.7 (-3.1, -0.4)	0.01
Sleep Disturbance	51.0	51.1	0.1 (-0.6, 0.8)	0.80
Pain Interference	51.3	50.3	-1.0 (-2.4, 0.4)	0.15

*Positive differences in positive attributes and negative differences in negative attributes favor WLI arm.

Association of social isolation with overall survival in cancer patients.

Danlin Zeng, Alan Bates, Bonnie Leung, Cheryl Ho, Srinivas Raman, John-Jose Nunez; Faculty of Medicine, University of British Columbia, Vancouver, BC, Canada; BC Cancer, Vancouver, BC, Canada; Department of Medical Oncology, BC Cancer, Vancouver, BC, Canada; University of British Columbia, Vancouver, Vancouver, BC, Canada

Background: Social isolation has been associated with increased all-cause mortality, particularly in cardiovascular and mental health conditions. Prior studies show that larger social networks, greater perceived social support, and marital status are associated with improved survival. However, the impact of social isolation on cancer patients remains incompletely characterized. This study examines the association between social isolation and overall survival (OS) in a large cancer cohort. **Methods:** 47,562 adult cancer patients treated at British Columbia Cancer between April 1, 2011, and December 31, 2016, who completed the Psychosocial Screen for Cancer (PSSCAN-Revised) questionnaire at their initial visit were included. Patients with prior malignancies were excluded. OS was estimated using Kaplan-Meier methods and compared using log-rank tests. Multivariable Cox proportional hazards regression was used to identify independent associations with OS. **Results:** The mean age was 64.5 years (SD 13.9). 55.2% were female. At their initial visit, 67% had non-metastatic disease, 17% had metastatic disease, and metastatic status was unknown in 16%. Social isolation was prevalent: 24.7% lived alone, 14.1% had lost a partner, 11.6% lacked assistance with instrumental activities of daily living (IADLs), 4.7% lacked regular social contact, 6.9% lacked emotional support, and 29.3% had at least one domain of social isolation. Median OS was shorter across all five domains of social isolation: patients living alone (37 vs 58 months), those who lost a partner (34 vs 56 months), those without regular social contact (32 vs 52 months), those without IADL support (49 vs 53 months), and those lacking emotional support (45 vs 53 months; all $p < 0.05$). Anxiety (36.8%) and depression (25.6%) were also associated with worse survival ($p < 0.001$). In multivariable Cox regression, independent predictors of increased mortality included metastatic disease (HR 4.41), depression (HR 1.44), anxiety (HR 1.29), lack of regular social contact (HR 1.26), male sex (HR 1.22), living alone (HR 1.18), and older age at presentation (HR 1.04 per year; all $p < 0.001$). **Conclusions:** Multiple domains of social isolation were independently associated with shorter OS in cancer patients. These findings highlight social isolation as a clinically relevant prognostic factor and support the incorporation of psychosocial risk assessments into oncology care to inform risk stratification and supportive interventions. Research Sponsor: None.

Vitamin D insufficiency and risk of taxane-induced peripheral neuropathy: Results from SWOG S1714.

Nam Nguyen-Hoang, Joseph M. Unger, Amy Kristine Darke, Michael Jordan Fisch, Norah Lynn Henry, Dawn L. Hershman, Meghna S. Trivedi, Daniel Louis Hertz; University of Michigan, College of Pharmacy, Ann Arbor, MI; Fred Hutch Cancer Center, Seattle, WA; SWOG Statistics and Data Management Center, Fred Hutchinson Cancer Center, Seattle, WA; The University of Texas MD Anderson Cancer Center, Carelon Medical Benefits Management, Houston, TX; University of Michigan Rogel Cancer Center, Ann Arbor, MI; Herbert Irving Comprehensive Cancer Center, Columbia University Irving Medical Center, New York, NY; Herbert Irving Comprehensive Cancer Center, Columbia University Medical Center, New York, NY; University of Michigan College of Pharmacy, Ann Arbor, MI

Background: Taxane-induced peripheral neuropathy (TIPN) affects up to 70% of patients treated with taxanes and can lead to functional impairment, reduced quality of life, and treatment disruption. There are no proven TIPN preventive strategies. Vitamin D insufficiency is a modifiable factor that has been linked to increased TIPN risk in paclitaxel-treated patients with breast cancer. We analyzed the association between baseline vitamin D levels and TIPN among patients receiving taxane-based treatments in a large, multicenter, prospective cohort study (SWOG S1714). **Methods:** In a prespecified analysis, baseline vitamin D levels were quantified from plasma samples using liquid chromatography-tandem mass spectrometry. Vitamin D insufficiency was defined as total 25-hydroxyvitamin D ≤ 20 ng/mL. The primary endpoint was development of TIPN, defined as an increase of ≥ 8 points from baseline in the sensory subscale of the EORTC QLQ-CIPN20 (0-100 scale, with higher score indicating worse symptoms) by week 24. The secondary endpoint was the greatest worsening from baseline in the sensory subscale CIPN20 score. Multivariable Cox proportional hazards model was used to evaluate time to initial development of TIPN and linear regression was used for the secondary endpoint, both adjusting for age, cancer stage, race/ethnicity, comorbidities, taxane type, and planned treatment duration. Statistical significance was set at $\alpha = 0.05$. **Results:** Among 1278 evaluable patients, 610 had available serum samples for vitamin D analysis (mean age 54.8 years [standard deviation 11.9]; 98% female; 85% White; 90% breast cancer; 59% paclitaxel-treated). Of these, 134 (22%) were vitamin D insufficient at baseline, and 383 (63%) developed TIPN during 24 weeks of follow-up. At baseline, CIPN20 sensory score did not differ by vitamin D status ($p = 0.70$). Baseline vitamin D insufficiency was significantly associated with higher risk of TIPN (adjusted hazard ratio 1.35; 95% confidence interval [CI] 1.06-1.72; $p = 0.013$). Patients with vitamin D insufficiency had more severe worsening of neuropathy (greatest worsening in CIPN20 sensory score: mean 23.4 vs. 18.5 points; adjusted mean difference 4.7 points; 95% CI 1.0-8.4; $p = 0.013$). **Conclusions:** Baseline vitamin D insufficiency was associated with significantly increased risk and severity of TIPN in this prospective cohort of patients receiving taxane-based therapy across multiple cancer types. These findings highlight vitamin D status as a potentially modifiable biomarker for TIPN risk and support clinical trials of vitamin D supplementation as a TIPN prevention strategy. Research Sponsor: National Cancer Institute/ U.S. National Institutes of Health; R37CA277043, UG1CA189974.

An international phase III randomized, double-blind, double-dummy trial comparing duloxetine and pregabalin for opioid-refractory neuropathic cancer pain.

Hiromichi Matsuoka, Jessica Lee, Shunsuke Oyamada, Keisuke Ariyoshi, Charmain Strauss, Belinda Fazekas, Shota Kobayashi, Katherine Clark, Eriko Satomi, Hiroto Ishiki, Takaomi Kessoku, Hideaki Hasuo, Ryo Morita, Takahiro Higashibata, Yoshinobu Matsuda, Akira Inoue, Yoshihisa Matsumoto, Yasuhito Fujisaka, Meera Ruth Agar, David Christopher Currow; National Cancer Center Japan, Tokyo, Japan; Improving Palliative, Aged and Chronic Care through Clinical Research and Translation, University of Technology Sydney, Concord Centre for Palliative Care, Concord, Australia, Sydney, Australia; Department of Biostatistics, Japanese Organisation for Research and Treatment of Cancer (JORTC) Data Center, Tokyo, Japan; Department of Data Management, Japanese Organisation for Research and Treatment of Cancer (JORTC) Data Center, Tokyo, Japan; IMPACCT Trials Coordination Centre (ITCC) IMPACCT, Faculty of Health University of Technology Sydney, Sydney, Australia; Flinders University, Daw Park, Australia; JORTC Data Center, Tokyo, Japan; University of Notre Dame, Sydney, Australia; Department of Palliative Medicine, National Cancer Center Hospital, Tokyo, Japan; International University of Health and Welfare Narita Hospital, Narita, Japan; Kansai Medical University, Hirakata, Japan; Department of Respiratory Medicine, Akita Kousei Medical Center, Akita, Japan; University of Tsukuba, Tsukuba, Japan; NHO Kinki Chuo Chest Medical Center, Sakai, Osaka, Japan; Department of Palliative Medicine, Tohoku University School of Medicine, Sendai, Japan; The Cancer Institute Hospital of Japanese Foundation for Cancer Research, Tokyo, Japan; Osaka Medical and Pharmaceutical University Hospital, Osaka, Japan; University of Sydney and Sydney Cancer Centre, Ultimo, Australia; College of Medicine and Public Health, Flinders University, Bedford Park, SA, Australia

Background: Management of neuropathic cancer pain (NCP) refractory to standard-dose opioids remains a major clinical challenge, and direct comparative evidence between adjuvant analgesics is limited. This study aimed to compare the efficacy and safety of duloxetine and pregabalin in patients with opioid-refractory NCP. **Methods:** We conducted an international, multicenter, double-blind, randomized controlled trial. Adult cancer patients who continued to experience pain despite opioid analgesia were eligible to participate if they met the International Association for the Study of Pain criteria for neuropathic pain and had a Brief Pain Inventory (BPI) Item 3 (worst pain in the past 24 hours) score of ≥ 4 . Inpatients and outpatients from Japan and Australia were randomized at a ratio of 1:1 to the duloxetine group (D group) or the pregabalin group (P group). The study drugs were titrated up to duloxetine 60mg daily or pregabalin 150mg twice daily until day 14 (D14). The primary endpoint was BPI item 3 at D14. Secondary endpoints included the change in BPI item 3 from baseline at D14, and the proportion of patients achieving ≥ 1 points, ≥ 2 points, $\geq 30\%$ and $\geq 50\%$ pain reduction. The primary endpoint was analyzed using a two-sided Student's T-test ($\alpha=0.05$) under the intention-to-treat principle. A sample size of 64 patients per group was estimated to detect a mean difference of 1.0 (SD 2.0) with 80% power. **Results:** Between February 2020 and June 2025, 147 patients were enrolled across 18 institutions. Baseline BPI item 3 scores were similar between the D and P groups (7.23 vs 7.04). At D14, mean scores were 5.62 and 5.45, with no significant difference ($P=0.70$), corresponding to mean reductions of 1.57 and 1.55, respectively. Rates of pain reduction (≥ 1 point, ≥ 2 points, $\geq 30\%$, $\geq 50\%$) were similar between groups (D: 53/45/36/25% vs P: 50/36/26/19%). Grade ≥ 2 adverse events included decreased appetite (29%), nausea (21%), fatigue (20%), in the D group, and constipation (23%), decreased appetite (16%), dizziness/fatigue (12%), in the P group. **Conclusions:** No significant difference in analgesic efficacy was observed between duloxetine and pregabalin in patients with opioid-refractory NCP. The magnitude of pain reduction exceeded the mean NRS change typically associated with placebo (approximately 0.5–1.0 points), and the response rates for $\geq 50\%$ pain reduction were substantially higher than the $\approx 3\%$ reported for placebo in a prior NCP study. The estimated numbers needed to treat were low (4.6 for duloxetine and 6.3 for pregabalin) and were smaller than those reported in non-cancer neuropathic pain, suggesting comparable or potentially greater efficacy. However, given the relatively high incidence of adverse events and the distinct adverse event profiles of each drug, careful and individualized treatment selection balancing efficacy and tolerability is warranted. Clinical trial information: jRCTs051190097. Research Sponsor: Japan Agency for Medical Research and Development (AMED).

A URCC NCORP Research Base nationwide phase II randomized controlled trial (RCT) investigating the effect of exercise on chemotherapy-induced peripheral neurotoxicity (CIPN).

Ian Kleckner, Po-Ju Lin, Hongying Sun, Chin-Shang Li, Umang Gada, Dee Murray, Thushini Manuweera, Amber Kleckner, Aruna C. Gowda, Natalya Greyz, Seema Harichand-Herd, Arshin Sheybani, Nimish Mohile, Bryan A. Faller, Karen Michelle Mustian; University of Maryland Baltimore, Baltimore, MD; Department of Surgery, Division of Supportive Care in Cancer, University of Rochester Medical Center, Rochester, NY; Department of Surgery, Division of Supportive Care in Cancer and URCC NCORP Research Base, University of Rochester Medical Center, Rochester, NY; Wilmot Cancer Institute, University of Rochester Medical Center, Rochester, NY; University of Maryland, Baltimore, MD; Oncology Hematology Consult, New Albany, OH; The Permanente Medical Group, San Rafael, CA; Iowa-Wide Oncology Research Coalition NCORP (IWORC), Des Moines, IA; IWORC NCORP, Des Moines, IA; University of Rochester Medical Center, Rochester, NY; Missouri Baptist Medical Center, Saint Louis, MO

Background: Over 60% of patients with cancer receiving taxane, platinum, or other neurotoxic agents experience CIPN, which presents as numbness, tingling, and sometimes pain in the hands and feet. CIPN reduces quality of life and can increase mortality by limiting chemotherapy dose. With extremely limited treatments for CIPN, exercise has emerged as one of the most promising yet unproven treatments with no Phase III RCTs to date. **Methods:** This phase II RCT examines the effect of exercise on CIPN in the University of Rochester Cancer Center (URCC) NCI Community Oncology Research Program (NCORP) Research Base network, recruiting 111 patients across 37 community oncology practices spanning 11 states in the US. Key eligibility include receiving neurotoxic chemotherapy (taxane, platinum, vinca alkaloid, etc.) in the past 9 months and reporting symptoms of CIPN (≥ 4 of 10 at its worst in the past 2 weeks). Participants were randomized 1:1 to 6 weeks of usual care (UC) or virtually delivered Exercise for Cancer Patients (vEXCAP). vEXCAP is a virtually delivered, standardized, individualized, moderate-intensity, home-based, progressive walking and resistance exercise program. We assessed CIPN both pre- and post-intervention using patient-reported CIPN-20 (0-100 scale) and tactile sensitivity in the finger and toe using monofilaments. Each night, participants rated numbness/tingling in the hands/feet on a 0-10 scale. The primary outcome was CIPN-20 total score with CIPN-20 sensory and motor subscales as exploratory. **Results:** The 111 patients were 59.5 ± 10.5 yrs, 76% female, 83% White, 37% breast cancer, 36% gastrointestinal cancer. Exercise yielded statistically and clinically meaningful improvements in CIPN sensory symptoms compared to UC ($\Delta\text{CIPN-20} = -4.7$ [MCID = 4], effect size [ES] = -0.27, $p = 0.049$). Exercise had a weak effect on CIPN motor symptoms ($\Delta\text{CIPN-20} = 1.5$, ES = 0.08, $p = 0.936$) and the CIPN-20 total score ($\Delta\text{CIPN-20} = -1.2$, ES = -0.07, $p = 0.393$). Tactile sensitivity was negatively correlated with CIPN sensory symptoms, as expected (finger: $\rho = -0.21$, $p = 0.043$, toe: $\rho = -0.18$, $p = 0.092$). Effects of exercise on tactile sensitivity were beneficial yet small and not statistically significant (ES = 0.04 and 0.07, both $p > 0.682$). Daily symptom ratings suggest that possible benefits of exercise emerge after 24 days (0.75 ± 0.46 unit reduction, $p = 0.104$), with clear benefits after 30 days (0.93 ± 0.46 unit reduction, $p = 0.045$) that grow further through study completion. **Conclusions:** Six weeks of walking and resistance exercise may reduce CIPN sensory symptoms for patients with CIPN. A future phase III RCT is needed to definitively test for replication and inform clinical practice. Funded by NCI: UG1CA189961, UG1CA189804, UG1CA189822, UG1CA189819, UG1CA189830, R21CA256154, and K07CA221931. Clinical trial: NCT04888988. Clinical trial information: NCT04888988. Research Sponsor: National Cancer Institute (USA).

A multicenter randomized phase II trial of topical betamethasone ointment for preventing severe chemoradiotherapy-induced oral mucositis in head and neck cancer.

Sakiko Soutome, Takumi Hasegawa, Mika Nishii, Yasumasa Kakei, Daisuke Takeda, Shunsuke Sawada, Yuka Kojima, Madoka Funahara, Hiroshi Kurita, Kenichiro Ishibashi, Hirokazu Nakahara, Masaya Akashi, Koichiro Irie, Tomohiro Yamada, Masahiro Umeda; Center for Clinical and Translational Research, Toyama University Hospital, Toyama, Japan; Department of Oral and Maxillofacial Surgery, Kobe University School of Medicine, Kobe-Shi, Hyogo, Japan; Department of Medical Technology, Division of Dentistry and Rehabilitation, Kob University Hospital, Kobe-Shi, Japan; Clinical and Translational Research Center, Kobe University Hospital, Kobe, Japan; Department of Oral and Maxillofacial Surgery, Kobe University Graduate School of Medicine, Kobe-Shi, Japan; Department of Oral and Maxillofacial Surgery, Kansai Medical University, Hirakata, Japan; Department of Oral and Maxillofacial Surgery, Kansai Medical University, Hirakata-Shi, Japan; School of Oral Health Sciences, Kyushu Dental University, Kitakyushu, Japan; Department of Oral and Maxillofacial Surgery, Shinshu University School of Medicine, Matsumoto, Japan; Department of Oral and Maxillofacial Surgery, Nagoya City University Graduate School of Medical Sciences, Nagoya, Japan; Department of Oral Pathology, Faculty of Dentistry, Asahi University, Gifu, Japan; Department of Oral and Maxillofacial Surgery, Kobe University Graduate School of Medicine, Kobe, Japan; Department of Oral Health, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan; Department of Oral and Maxillofacial Surgery, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan; Division of Research and Treatment for Oral and Maxillofacial Congenital Anomalies, Aichi Gakuin University, Nagoya, Japan

Background: Severe oral mucositis (OM) is a major unmet clinical problem during cisplatin-based chemoradiotherapy (CRT) for head and neck cancer, with no established preventive strategy. Although topical dexamethasone has shown benefit during radiotherapy alone, its efficacy during CRT is limited. This study represents the first randomized trial evaluating a potent topical corticosteroid, betamethasone ointment, for preventing severe OM during cisplatin-based CRT. **Methods:** Patients with head and neck cancer receiving CRT with the oral cavity included in the radiation field were enrolled at six institutions in Japan. Upon development of grade 1 OM (CTCAE v5.0), patients were randomized to standard oral care alone (control) or standard oral care plus topical betamethasone ointment applied three times daily (intervention). Treatment continued until completion of radiotherapy or onset of grade 3 OM. The primary endpoint was time to grade 3 OM, analyzed using multivariable Cox proportional hazards models. Secondary endpoints included time to grade 2/3 OM and incidence of oral candidiasis. **Results:** A total of 68 patients were analyzed (intervention n=35; control n=33). The cumulative incidence of grade 3 OM was significantly lower in the intervention group (14.3%) than in the control group (48.5%). Topical betamethasone significantly reduced the risk of grade 3 OM (HR 0.246, 95% CI 0.081–0.749). Betamethasone also delayed the onset of grade 2/3 OM. Non-use of a spacer was independently associated with grade 2 OM. Betamethasone did not increase oral candidiasis, whereas denture use was a significant risk factor. **Conclusions:** Topical betamethasone ointment substantially reduced the incidence of severe OM during cisplatin-based CRT without increasing oral candidiasis. This simple, low-cost, and widely accessible intervention could be rapidly implemented in routine clinical practice to mitigate CRT-induced toxicity. To our knowledge, this is the first randomized trial demonstrating the efficacy of a potent topical corticosteroid for preventing severe OM during cisplatin-based CRT. Clinical trial information: jRCTs071200013. Research Sponsor: None.

The efficacy and safety of add-on ruxolitinib for patients with severe checkpoint inhibitor pneumonitis management with corticosteroids: A multicenter, open-label, randomised phase 2 trial.

Yan Xu, Xiaoxing Gao, Chen Wei, Zhimin Zeng, Junzhen Gao, Xiaoling Yang, Xiao-Yan Liu, Qing Zhou, Ruxuan Chen, Xiaoyan Si, Hanping Wang, Jing Zhao, Minjiang Chen, Wei Zhong, Junping Zhang, Anwen Liu, Hui Huang, Mengzhao Wang; Peking Union Medical College Hospital, Beijing, China; Department of Respiratory and Critical Care Medicine, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing, China; Center for Health Policy and Health Economics, National Infrastructures for Translational Medicine, Institute of Clinical Medicine, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China; Department of Oncology, the second affiliated hospital of Nanchang University, Nanchang, Jiangxi, China; Affiliated Hospital of Inner Mongolia Medical University, Hohhot, China; Shanxi Bethune Hospital, Shanxi Academy of Medical Sciences, Tongji Shanxi Hospital, Third Hospital of Shanxi Medical University, Taiyuan, China; Department of Respiratory and Critical Care Medicine, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China; Department of Respiratory Medicine, Peking Union Medical College Hospital, Chinese Academy of Medical Science, Beijing, China; Department of Thoracic Oncology, Cancer Center, Shanxi Bethune Hospital, Shanxi Academy of Medical Sciences, Tongji Shanxi Hospital, Third Hospital of Shanxi Medical University, Taiyuan, China; Oncology Department, The Second Affiliated Hospital of Nanchang University, Nanchang, Jiangxi, China; Department of Respiratory and Critical Care Medicine, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China

Background: Checkpoint inhibitor pneumonitis (CIP) stands out as a remarkable complication during ICIs therapy. Severe CIP represents a potentially life-threatening immune-related adverse event (irAE) with limited evidence from clinical trials that guides therapeutic interventions. Ruxolitinib, a selective JAK1/2 inhibitor, effectively attenuates cytokine-release syndrome and show significant anti-fibrotic in mouse lung with BLM model. We conducted a multicenter, investigator-initiated, open-label, phase 2 randomized controlled trial to evaluate the efficacy and safety of add-on ruxolitinib for patients with severe CIP management with corticosteroids.

Methods: Patients with malignant who were suffered from CTCAE grade (G) 3 or G4 CIP after ICIs therapy were screened. Enrolled CIP patients were randomly assigned 1:1 to control group (only glucocorticoids) or ruxolitinib group (glucocorticoids plus ruxolitinib). Initiated dosage of glucocorticoids was no less than prednisone 1 mg/kg/day (or same steroid equivalent dose) with subsequent tapering off. In ruxolitinib group, enrolled patients were add-on ruxolitinib (5 mg twice daily for 2 weeks, followed with 5 mg daily for 2 weeks). The primary end point was the proportion of patients with a prednisone daily dosage of no more than 10mg and improvement to G1 CIP at week 8. Continuous variables were analyzed using a mixed-effects model for repeated measures with treatment group, study visit and treatment-by-visit interaction.

Results: From April 2023 to November 2025, a total of 60 eligible patients were recruited and randomly assigned to control group and ruxolitinib group. There were 52 cases of G3 CIP and 8 cases of G4 CIP. There were more patients in the ruxolitinib group improved to G1 CIP and received $\leq$ prednisone 10mg daily at 8th week than in the controlled group (20cases/66.7% vs 11cases/36.7%, $p = 0.0379$). This effect was more significant in the 2nd and 4th week. Two patients in ruxolitinib group and 4 patients in the control group died within eight weeks. The repeated measures analysis using a generalized linear mixed model demonstrated a significant overall treatment effect, ie. add-on ruxolitinib was associated with significantly higher odds of clinical improvement (adjusted OR = 5.12, 95% CI 1.06 - 24.64; $p = 0.04$). A total of 13 G3 or higher treatment-related AEs (TRAEs) occurred (7 cases in control group and 6 cases in ruxolitinib group), including 9 cases of infectious diseases. **Conclusions:** Add-on ruxolitinib for malignant patients with severe CIP management with glucocorticoids show with higher resolution rates and earlier response trends than only glucocorticoids treatment. And there were no different adverse events between them. Add-on ruxolitinib with glucocorticoids might be a promising proposed treatment for patients with severe CIP. Clinical trial information: NCT05899725. Research Sponsor: National High Level Hospital Clinical Research Funding; 2022-PUMCH-C-054.

A randomized phase III trial of dexamethasone mouthwash to prevent chemotherapy-induced oral mucositis in patients with breast cancer.

Sayaka Kuba, Yasuhiro Hagiwara, Nobuhiro Shibata, Takafumi Sangai, Ryoichi Matsunuma, Uhi Toh, Kenichi Watanabe, Takayuki Iwamoto, Kosho Yamanouchi, Michiko Harao, Miki Yamaguchi, Masahiko Suzuki, Shigeto Maeda, Noriko Maeda, Akiko Ebata, Nobutaka Iwakuma, Sakiko Soutome, Takeshi Yamaguchi, Yuichiro Kikawa, Hirofumi Mukai; Nagasaki University Hospital, Nagasaki, Japan; Department of Biostatistics, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan; Department of Clinical Oncology, Kansai Medical University Hospital, Hirakata, Japan; Department of Breast and Thyroid Surgery, Kitasato University School of Medicine, Sagami-hara, Japan; Shizuoka Kenritsu Sogo Byoin, Shizuoka, Japan; Department of Surgery, School of Medicine, Kurume University, Kurume-Shi, Japan; NHO Hokkaido Cancer Center, Sapporo, Japan; Breast and Thyroid Surgery, Kawasaki Medical School Hospital, Kurashiki, Japan; Nagasaki Harbor Medical Center, Nagasaki, Japan; Department of Breast Oncology, Jichi Medical University Hospital, Shimotsuke-Shi, Japan; JCHO Kurume General Hospital, Kurume, Japan; Kitamurayama Hospital, Higashine-Shi, Japan; Nagasaki Rosai Hospital, Sasebo, Japan; Department of Gastroenterological Breast and Endocrine of Surgery, Yamaguchi University Graduate School of Medicine, Ube, Japan; Department of Breast and Endocrine Surgical Oncology, Graduate School of Medicine, Tohoku University, Sendai, Miyagi, Japan; Breast Center, Department of Breast Surgery, NHO Kyushu Medical Center, Fukuoka, Japan; Center for Clinical and Translational Research, Toyama University Hospital, Toyama, Japan; Department of Medical Oncology, Toranomon Hospital, Tokyo, Japan; Department of Breast Surgery, Kansai Medical University Hospital, Hirakata, Japan; National Cancer Centre Hospital East, Kashiwa, Japan

Background: Oral mucositis is a common adverse event in patients undergoing chemotherapy for breast cancer. A previous randomized phase II trial showed that a dexamethasone-based mouthwash significantly reduced the incidence and severity of chemotherapy-induced oral mucositis. The SMASH-BC trial was designed to confirm the efficacy and safety of dexamethasone-based mouthwash for preventing chemotherapy-induced oral mucositis in patients with breast cancer. **Methods:** This multicenter, open-label, randomized phase III trial was conducted in Japan. Patients with early breast cancer scheduled to receive standard adjuvant or neoadjuvant chemotherapy (AC, EC, dose-dense AC/EC, TC, or pembrolizumab-containing regimens) were randomized 1:1 to receive either a dexamethasone-based mouthwash (10 mL of dexamethasone elixir 0.01%) or tap-water mouthwash as a control. The mouthwash was swished for 2 min and spit, four times daily for 8 weeks, starting on day 1 of chemotherapy. Randomization was stratified by chemotherapy regimen, smoking status, and institution. The primary endpoint was the incidence of all-grade oral mucositis at 8 weeks, assessed using electronic patient-reported outcomes (ePRO). Assuming an all-grade oral mucositis incidence of 55% in the control group and 35% in the intervention group, 212 patients were required to provide 80% power with a two-sided α of 0.05. The planned sample size was 230, allowing for 10% attrition. **Results:** Overall, 230 patients were randomized (intervention, $n = 117$; control, $n = 113$), and 220 patients (intervention, $n = 114$; control, $n = 106$) were included in the analysis. The incidence of ePRO-assessed all-grade oral mucositis at 8 weeks was 58.8% and 63.2% in the intervention and control groups, respectively (risk ratio [RR], 0.93; 95% confidence interval [CI], 0.75–1.15; $P = 0.59$). The incidence of ePRO-assessed moderate-to-very severe oral mucositis was 13.2% and 18.9% in the intervention and control groups, respectively (RR, 0.70; 95% CI, 0.38–1.29). During the 56-day study period, mucositis reported by ePRO on a median of 2 and 6 days in the intervention and control groups, respectively (median difference -4 days; 95% CI, -5.3 to 8.3 days). The incidence of physician-assessed oral mucositis was 31.9% vs. 41.5% in the intervention and control groups, respectively (RR, 0.77; 95% CI, 0.54–1.09). The incidence of grade ≥ 3 adverse events was 6.2% and 6.6% in the intervention and control groups, respectively (RR, 0.94; 95% CI, 0.34–2.58). However, the incidence of oral candidiasis was higher in the intervention group (5.4% vs 0%). **Conclusions:** Prophylactic dexamethasone mouthwash did not significantly reduce all-grade oral mucositis at 8 weeks. Overall safety was comparable between groups; however, the incidence of oral candidiasis was higher in the intervention group. Clinical trial information: jRCTs071240036. Research Sponsor: Japan Agency for Medical Research and Development.

Cardiovascular disease incidence in women with early-onset breast cancer.

Vidhya Nair, Sayan Dasgupta, Jennifer M. Specht, Richard Cheng, Kerryn Reding, Cecile Laurent, Janise M. Roh, Marilyn L. Kwan, Heather Greenlee; University of Washington, Seattle, WA; Fred Hutch Cancer Center, Seattle, WA; University of Washington School of Medicine, Seattle, WA; University of Washington School of Nursing, Seattle, WA; Kaiser Permanente Northern California, Pleasanton, CA; Fred Hutchinson Cancer Research Center, Seattle, WA

Background: Early-onset breast cancer (BC) before age 40 is generally associated with advanced stage at diagnosis and worse outcomes. Improvements in detection and treatment have led to reduction in BC mortality. Cardiovascular disease (CVD) is the leading cause of non-BC death in women with BC, but younger women are traditionally considered to be at lower risk for CVD. Given the limited data on CVD in early-onset BC, this study evaluates incident CVD in women younger than age 40 in the Pathways Heart Study. **Methods:** The Pathways Heart Study (R01/U01CA214057) is an ongoing, prospective cohort study including 14,402 women diagnosed with BC at KPNC from 2005–2013 and followed through 2021. In this study, eligible BC cases were women age 18–39 years at time of stage I–III BC diagnosis without pre-existing CVD. Cases were matched 1:5 to controls without BC on age at diagnosis and race/ethnicity. Cancer treatment, CVD (ischemic heart disease, heart failure, cardiomyopathy, stroke) and cardiometabolic risk factors (hypertension, diabetes, hyperlipidemia) were extracted from electronic health records. Cumulative incidence rates (CIR) were calculated as number of incident CVD events divided by total person-time at risk and expressed per 1,000 person-years. **Results:** A total of 535 women with early-onset BC were matched to 2,651 controls. Mean age was 35.1 years with mean follow up of 7.8 years. Overall, cases had a higher CIR of CVD (3.40 per 1,000 person-years (PY)) than controls (1.37/1000 PY). CIRs of hypertension, dyslipidemia, and diabetes were higher in cases compared to controls (14.89, 12.14, and 9.74/1000 PY, respectively). Among BC types and stage, women with hormone receptor-positive HER2-positive and stage III BC had the highest CVD CIRs (7.14 and 5.65/1000 PY, respectively). Women who received chemotherapy with anthracyclines and those who received endocrine therapy had higher CVD CIRs compared with those who did not, while there were no differences by receipt of radiation therapy (Table 1). **Conclusions:** Although the absolute incidence of CVD was low in BC patients younger than 40 years, these patients experienced a >2 fold higher CVD rate compared with matched controls. Patients treated with anthracyclines and endocrine therapy had higher CIR of CVD compared with those not treated. Future analyses will include formal comparison through survival and regression models of incident CVD and cardiometabolic disease in women with early-onset BC, accounting for confounders, including treatments received, education, income, and comorbidities. Research Sponsor: National Cancer Institute.

Cumulative incidence rates (CIR) of cardiovascular disease (CVD) in women age <40 years in the Pathways Heart Study.

	CIR of CVD per 1,000 person-years (95% CI)
Chemotherapy	
With Anthracycline	4.15 (2.07, 7.43)
Without Anthracycline	3.39 (0.70, 9.89)
None	0.00 (0.00, 6.31)
Endocrine Therapy	
Yes	3.77 (1.88, 6.74)
No	2.50 (0.51, 7.29)
Radiation Therapy	
Yes	3.40 (1.55, 6.45)
No	3.40 (1.10, 7.93)

Machine learning (ML)-based prediction of fatal immune checkpoint inhibitor (ICI)-associated myocarditis (MC) with multi-cohort validation.

Hassan M. Abushukair, Eman Alghamdi, Keila Ostos-Mendoza, John Wells, Romina Barrios-Oneeglio, Sagal Pannu, Woncheol Jung, Aik-Choon Tan, Noha Abdel-Wahab, Zain Asad, Amin Nassar, Steven M. Blum, Douglas Buckner Johnson, Nicolas Palaskas, Fawaz F. Al-Harbi, Tae Gyu Oh, Abdul Rafeh Naqash; Stephenson Cancer Center, Oklahoma City, OK; Saudi Food and Drug Authority, Pharmacovigilance Department, Riyadh, Saudi Arabia; Department of Cardiology, The University of Texas MD Anderson Cancer Center, Houston, TX; Department of Medicine, Cardiology Division Vanderbilt University Medical Center, Nashville, TN; Stephenson Cancer Center at The University of Oklahoma Health Sciences Center, Oklahoma City, OK; University of Oklahoma, Oklahoma City, OK; University of Utah, Salt Lake City, UT; The University of Texas MD Anderson Cancer Center, Houston, TX; Department of Medicine, University of Oklahoma Health Sciences Center, Oklahoma City, OK; Yale Cancer Center, New Haven, CT; Krantz Family Center for Cancer Research, Massachusetts General Brigham Cancer Institute, Boston, MA; Vanderbilt-Ingram Cancer Center, Vanderbilt University Medical Center, Nashville, TN; Saudi Food and Drug Authority, Pharmacovigilance Division, Riyadh, Saudi Arabia; University of Oklahoma Health Science Center, Oklahoma City, OK

Background: ICI-associated MC is a rare but highly fatal immune-related adverse event (irAE). Identifying clinical predictors of MC-specific fatality remains an unmet need. Herein, we develop and externally validate an ML model to predict ICI-MC fatality using clinical and laboratory features. **Methods:** The WHO Vigibase database was queried through December 22, 2024, to identify cases of ICI-MC with complete clinical data, including age, sex, cancer and ICI type, co-occurring irAEs, overlap status with myositis (MS) and/or myasthenia gravis (MG), MC timing from ICI start, and MC-specific fatality. Multivariable logistic regression was used to assess correlates of MC-specific fatality. An XGBoost ML model using all collected clinical data was trained to predict MC-specific fatality using an 80/20 split of data for training and testing. We augmented our clinical ML model with troponin (T or I) values at the time of ICI-MC diagnosis from two institutions (n = 37: OU n = 13, MGH n = 24), normalized to institutional upper limits of normal. Two additional external cohorts (n = 68: VUMC n = 18, MDACC n = 50) were used to validate our final clinical and augmented models. **Results:** We identified 822 cases from Vigibase with ICI-MC, with a median age of 69 years (IQR: 60–76), 59.1% (n = 486) were males. Pts with lung cancer had the highest proportion of cases (23.7%, n = 195). Most patients received ICI monotherapy (59%, n = 485). Median time to MC onset was 30.4 days (IQR: 21–91.3). MC occurred alone in 588 cases (71.5%) and with MS and/or MG in the remainder. MC-specific fatality occurred in 147 cases (17.9%). After multivariable adjustments, MC onset within the first month of ICI start was associated with higher MC-fatality odds vs. later onset (vs 1–3 months: ROR = 0.38 [0.21–0.67], vs 3–12 months: ROR = 0.5 [0.25–0.95]). Co-occurring non-MC major cardiac adverse events (ROR: 0.27 [0.17 – 0.44]) and pneumobronchitis (ROR: 0.29 [0.11 – 0.78]) were also associated with increased MC-specific fatality. The optimized MC-fatality clinical ML model achieved AUCs of 0.76 (training) and 0.73 (testing), with early MC onset as the most contributing feature. External validation (n = 37) of our clinical model yielded an AUC of 0.74. Augmenting our clinical ML model with baseline troponin (n = 37) significantly improved performance (AUC: 0.79, likelihood-ratio p = 0.046), with a further external validation (n = 68) AUC of our augmented ML model of 0.67. Our ML model is available online for use through: https://ohbiolab.shinyapps.io/ici-mc_fatality_predictor/. **Conclusions:** ICI-MC timing and co-occurring cardio-pulmonary reactions are key determinants of MC-specific fatality. Our findings highlight the potential promise for early risk stratification to identify high-risk pts with ICI-MC who could benefit from closer monitoring or more tailored immunosuppressive interventions at ICI-MC diagnosis. Research Sponsor: None.

Artificial intelligence surrogate models to predict long-term cardiovascular effects of immune checkpoint inhibitor therapies using electrocardiograms.

Frances Dean, Joshua Barrios, Geoffrey Tison, Javid J. Moslehi, Ahmed Alaa; University of California, San Francisco, San Francisco, CA; Section of Cardio-Oncology and Immunology, University of California, San Francisco, San Francisco, CA; University of California, Berkeley, Berkeley, CA

Background: Immune checkpoint inhibitors (ICI) revolutionized the treatment landscape for many cancers, with close to 50% of cancer patients now ICI eligible. Acutely, ICI are associated with myocarditis. Long term cardiovascular effects of ICI are less clear. We built artificial intelligence (AI) models as surrogates for predicting long-term cardiovascular disease (CVD) after ICI using electrocardiograms (ECG). **Methods:** Using data from over 80,000 cancer patients treated from 1986 to 2021 at the University of California, San Francisco, we develop two ECG AI models as surrogates for risk over time of CVD. First, we built a model of observed CVD using true outcomes in a time to event framework. This model is a surrogate for prevalence under the current standard of care. Second, we build a model for causal outcomes using before-and-after data and estimate risk from ECGs for causal analyses. We hold out patients (N=15,277), including all those treated with anthracyclines (N= 3,681), trastuzumab (N=751), or ICI (N= 3,572), for evaluation. Causal effects are estimated with paired pre and post treatment ECGs within three years. **Results:** Models have average AUC across CVDs and years of 0.78 and 0.77. The observed model estimates ICI treated patients compared to those with any other cancer treatment have higher average 10-year risk of ischemic heart disease (IHD) by 10% (95% CI: 2-18%), venous thromboembolism (VTE) by 10% (1-20%), and critical ventricular arrhythmias (CVA) by 10% (3-19%), largely due to high baseline risk. Anthracycline and trastuzumab treated patients did not have higher 10-year heart failure (HF) risk relative to other treatments in aggregate. The causal framework estimates anthracyclines increased average 10-year risk of HF by 45% and trastuzumab by 46%. Anthracyclines and trastuzumab significantly increased risk of atrial fibrillation, IHD, ischemic stroke, CVA, VTE, and conduction disorders as well. ICI increased risk of each of these significantly by smaller amounts. Notably, after ICI, average 10-year risk of HF increased by 32% and IHD by 17%. **Conclusions:** Our study demonstrates potential long-term CVD effects of ICI as estimated from ECGs. This framework can be used to evaluate effects of new therapies in the future. Research Sponsor: U.S. National Science Foundation; DGE 2146752.

10-year pre/post treatment relative risks.

CVD	Anthracycline	Trastuzumab	ICI
Atrial fibrillation	1.34 [1.29, 1.39]	1.30 [1.24, 1.36]	1.25 [1.21, 1.28]
Ischemic heart disease	1.25 [1.21, 1.28]	1.28 [1.23, 1.32]	1.17 [1.14, 1.19]
Heart failure	1.45 [1.39, 1.52]	1.46 [1.38, 1.55]	1.32 [1.27, 1.36]
Ischemic stroke	1.41 [1.32, 1.50]	1.31 [1.22, 1.41]	1.28 [1.21, 1.35]
Critical ventricular arrhythmia	1.18 [1.15, 1.22]	1.14 [1.09, 1.19]	1.10 [1.07, 1.13]
Venous thromboembolism	1.29 [1.24, 1.33]	1.26 [1.21, 1.31]	1.26 [1.21, 1.30]
Conduction disorder	1.19 [1.17, 1.21]	1.19 [1.16, 1.21]	1.15 [1.13, 1.17]

The impact of body composition on cardiac function in women with early breast cancer taking cardiotoxic chemotherapy.

Gabriel Aleixo, Wei-Ting Hwang, Ramy Sedhom, Rakesh Sharma, Wonyoung Jung, Congying Xia, Walter Witschey, Bonnie Ky; University of Pennsylvania, Philadelphia, PA; Department of Biostatistics, Epidemiology, and Informatics, University of Pennsylvania, Philadelphia, PA; Penn Center for Cancer Care Innovation, University of Pennsylvania, Philadelphia, PA; Hospital of the University of Pennsylvania, Philadelphia, PA

Background: Anthracyclines and HER2-directed therapies have improved survival in early breast cancer (EBC), but cardiotoxicity remains a concern for long-term survivors. Cardiovascular disease may ultimately exceed breast cancer as a cause of death, highlighting the need for better understanding of therapy-related cardiac dysfunction. Body composition abnormalities are linked to adverse cardiovascular outcomes but are not well captured by body mass index and are understudied. We evaluated longitudinal associations between baseline CT-derived body composition and echocardiography measures of cardiac structure and function. **Methods:** This is a retrospective analysis of women with stage I–III EBC treated with anthracyclines and/or trastuzumab at the University of Pennsylvania. Eligible patients had a pre-treatment and ≥ 1 follow-up echocardiogram and pre-treatment abdominal CT or PET-CT imaging for body composition assessment. L3-based segmentation quantified skeletal muscle mass, muscle density (SMD), subcutaneous and visceral adiposity (SAT, VAT), and adipose tissue density (SATD, VATD). Core-lab echocardiographic outcomes included systolic function (LVEF, GLS) and diastolic function (E/e'). Using multivariable-adjusted generalized estimating equations (GEE) models, we evaluated longitudinal associations between baseline body composition (per 1-SD increase) and two complementary outcomes for each metric: (1) absolute values over time (overall burden) and (2) change from baseline (within-participant worsening). **Results:** Across 182 participants, the median age was 49.5 years (Q1–Q3 41–60), HER2-positive disease was present in 64 (35.4%), estrogen receptor-positive disease in 114 (62.6%), and triple-negative disease in 37 (20.4%). Anthracycline-based therapy was administered to 150 (82.4%), radiation therapy to 140 (76.9%), and mastectomy was performed in 106 (58.6%). Baseline hypertension, hyperlipidemia, and diabetes were present in 56 (30.8%), 43 (23.6%), and 12 (6.6%), respectively. In multivariable-adjusted GEE models, higher baseline VAT was associated with a greater decline in LVEF over time (-2.1 LVEF points per 1-SD increase; 95% CI -4.1 to -0.1 ; $p=0.04$). We next evaluated diastolic function, where higher baseline VAT was associated with a greater increase in E/e' over time (β 0.38 per 1-SD increase; 95% CI, 0.01 to 0.74; $p=0.04$). In models evaluating absolute E/e' over time, higher VAT (β 0.51; 95% CI, 0.11 to 0.91) and SAT (β 0.37; 95% CI, 0.06 to 0.59), and lower SMD (β -0.34 ; 95% CI, -0.66 to -0.02) and VAT density (β -0.36 ; 95% CI, -0.67 to -0.05) were associated with higher E/e' . No adjusted associations were observed for longitudinal change in GLS (all $p>0.05$). **Conclusions:** Baseline visceral adiposity was associated with worsening in longitudinal changes in systolic and diastolic function during cardiotoxic breast cancer therapy. Research Sponsor: None.

Exercise and cardiovascular risk among breast cancer patients.

Erika Libiar Estrada, Aileen Baecker, Jose Pio, Bhumi B. Bhakta, David K. Yi, Aniket A. Kawatkar; Kaiser Permanente Southern California, Research and Evaluation Department, Pasadena, CA

Background: Breast cancer is the most common cancer among U.S. females, accounting for 15% of new diagnoses. As survivorship increases, cardiovascular disease (CVD) has become a major cause of long-term morbidity and mortality. Survivors remain at elevated risk for CVD due to treatment-related cardiotoxicity and underlying risk factors. Despite this growing burden, evidence on whether exercise mitigates cardiac dysfunction remains limited and inconsistent. This study examines the association between physical activity and subsequent CVD and mortality outcomes among breast cancer patients with documented Exercise Vital Sign (EVS) data.

Methods: A retrospective cohort study was conducted within the Kaiser Permanente Southern California (KPSC) health system. Adult members (≥ 18 years) with primary breast cancer diagnosed from 2011–2019 were identified through the KPSC cancer registry. Eligible patients had ≥ 12 months of continuous enrollment and at least two encounters (separated by ≥ 1 month) with EVS data in the year prior to diagnosis. Physical activity was defined using median exercise volume: completely inactive (0 min/week; reference), insufficiently active (IA; $> 0 - < 149$ min/week), and sufficiently active (SA; ≥ 150 min/week). Outcomes included all-cause, cancer-specific, and CVD mortality; congestive heart failure (CHF); cardiomyopathy; and major adverse cardiovascular events (MACE). Cox proportional hazards models adjusted for demographic factors, lifestyle characteristics, tumor features, insurance type, and pre-existing cardiovascular comorbidities. **Results:** Among the cohort ($N = 12,481$), compared with the completely inactive group, SA was associated with lower risk of CHF (HR 0.74; 95% CI 0.59–0.89). For MACE, both IA (HR 0.78; 95% CI 0.71–0.86) and SA (HR 0.66; 95% CI 0.59–0.74) demonstrated decreased risk. Similar reductions were observed for all-cause mortality (IA HR 0.75; 95% CI 0.68–0.83; SA HR 0.62; 95% CI 0.54–0.70), cancer-specific mortality (IA HR 0.82; 95% CI 0.71–0.96; SA HR 0.69; 95% CI 0.57–0.83), and CVD mortality (IA HR 0.68; 95% CI 0.58–0.79; SA HR 0.53; 95% CI 0.43–0.65). Physical activity was not associated with reduced cardiomyopathy risk. **Conclusions:** Physical activity appears to reduce cardiovascular and mortality risk among breast cancer survivors in a dose-responsive manner, with SA patients experiencing the greatest benefit. Even insufficient activity was associated with improved prognosis compared with complete inactivity, supporting the incorporation of exercise promotion into survivorship care. Regular physical activity may reduce CVD and mortality risk among breast cancer survivors, supporting routine EVS screening and referral to exercise or cardio-oncology programs in survivorship care. These findings also reinforce the need for institutional and payer policies that prioritize exercise assessment and counseling as standard components of cancer survivorship care. Research Sponsor: The National Heart, Lung, and Blood Institute; 5R01HL151665.

Time-resolved cardiovascular risk after immune checkpoint inhibitors: A large real-world cancer cohort study.

Yibin Jia, Chenwei Xu, Bingyin Zhang, Zhentao Fu, Xiaolei Guo, Jianbo Wang; Qilu Hospital of Shandong University, Jinan, China; Shandong Provincial Center for Disease Control and Prevention, Jinan, China

Background: With expanding use of immune checkpoint inhibitors (ICIs), immune-related toxicities increasingly influence outcomes beyond tumor control. Cardiovascular events are among the most consequential yet potentially preventable complications. Given the low incidence of major adverse cardiovascular events (MACE) and their relatively narrow post-initiation window, reliable time-resolved risk estimation requires very large cohorts, which remain scarce, limiting evidence to guide surveillance and prevention. **Methods:** We conducted a pan-cancer retrospective cohort study (N = 269,257; mean follow-up 4.5 years) using a large real-world cancer registry from Shandong Provincial Center for Disease Control and Prevention. Patients receiving ICIs after their broad clinical implementation were compared with patients treated in the pre-ICI era without immunotherapy, a design chosen to mitigate indication-related differences observed in the contemporary setting. Propensity scores derived from elastic net regularization were used to construct overlap weights for balancing covariates across cohorts. We evaluated MACE, AMI (acute myocardial infarction), and stroke across four prespecified intervals (0–90, 91–180, 181–270, and 271–365 days) using interval-stratified weighted Cox models. Absolute risk differences were further characterized using weighted incidence density differences and restricted mean survival time. **Results:** All covariates achieved excellent balance (maximum |SMD| = 0.004) after weighting. ICI exposure was associated with higher 1-year MACE risk (HR, 1.17; 95% CI, 1.12–1.23; $P < 0.001$), corresponding to a weighted incidence density difference of 10.90 per 1,000 person-years (95% CI 8.73–13.06). The largest absolute risk increase was observed during 0–90 days after ICI initiation (weighted incidence density difference, 17.83 per 1000 person-years; 95% CI, 12.43 to 23.24). The risk of AMI peaked early, with a statistically significant association observed only during 0–90 days (HR, 1.86; 95% CI, 1.54–2.24; $P < 0.001$). In contrast, stroke risk peaked during days 91–180 (HR, 1.27; 95% CI, 1.11–1.44; $P < 0.001$) and remained significantly elevated through 181–270 days (HR, 1.25; 95% CI, 1.08–1.44; $P = 0.003$). Stroke accounted for 51% (95% CI: 19% to 83%), 63% (95% CI: 37% to 89%), 66% (95% CI: 43% to 90%), and 67% (95% CI: 45% to 88%) of the total weighted incidence density difference for MACE during days 0–90, 0–180, 0–270, and 0–365, respectively. **Conclusions:** ICI exposure was associated with temporally heterogeneous cardiovascular risk, with AMI concentrated in the first 90 days and stroke risk remaining elevated thereafter. These results suggest a time-tailored approach to cardio-oncology care, characterized by intensified early monitoring for AMI and sustained attention to stroke prevention in subsequent months. Research Sponsor: National Natural Science Foundation of China; the Fund of Taishan Young Scholar Project for Jianbo Wang; the Natural Science Foundation of Shandong Province.

The genetic polymorphism underlying immune checkpoint inhibitor–induced endocrine toxicity.

Ming-Hua Cong, Meng Tang; National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China; National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Beijing, China

Background: Immune checkpoint inhibitors (ICIs) have transformed cancer therapy by enhancing T cell–mediated anti-tumor immunity; however, immune-related adverse events (irAEs)—particularly endocrine toxicities (e.g., thyroiditis, hypophysitis, adrenal insufficiency; incidence 5–15%)—pose significant clinical risks, including lifelong hormonal dependency. Although germline genetic factors, especially human leukocyte antigen (HLA) variants, are implicated in irAE susceptibility, prior studies lack granularity in toxicity subtyping and comprehensive genetic characterization across diverse clinical contexts. **Methods:** We integrated high-resolution HLA genotyping with precise phenotypic annotation of endocrine irAEs (subclassified by organ specificity, onset, severity per CTCAE v5.0) in multi-center retrospective and prospective cohorts. A hypothesis-free genome-wide approach identified novel HLA loci, followed by functional validation of candidate variants. Machine learning models were trained to predict toxicity risk by integrating HLA markers with clinical covariates (ICI type, cancer diagnosis, baseline characteristics). **Results:** Subtype-specific HLA associations were identified (e.g., distinct *HLA-DRB1* alleles linked to thyroiditis versus hypophysitis). Collinearity analysis revealed significant positive correlations between non-endocrine irAE pairs (e.g., capillary hyperpermeability and gastrointestinal ulcers; $P < 0.01$), suggesting shared immunopathogenic pathways. The integrated risk model demonstrated robust stratification performance for endocrine toxicity susceptibility. Cohort demographics reflected real-world ICI utilization patterns (predominantly lung cancer), while clinical response data underscored challenges in achieving durable remission (notable progression rates). **Conclusions:** This study delineates the HLA-driven genetic architecture underlying endocrine irAEs and elucidates interdependencies among irAE subtypes. Integration of genetic risk profiling with clinical parameters enables personalized toxicity risk assessment, advocating for proactive, multidisciplinary monitoring protocols. These findings advance precision immunotherapy by informing biomarker-guided patient selection, optimizing safety, and refining clinical decision-making frameworks for ICI administration. Clinical trial information: MR-11-25-020518. Research Sponsor: None.

Cardiac safety of L-annamycin at high cumulative anthracycline exposure: Pooled analysis.

Robert C. Shepard, Erikson Wasyl, Patrick Collier, Ziad Zalaquett, Stuart Waymack; Molculin Biotech, Houston, TX; Cleveland Clinic, Cleveland, OH; Virginia Tech, Falls Church, VA

Background: Anthracyclines are widely used chemotherapeutic agents but limited by dose-dependent cardiotoxicity and lifetime cumulative dose restrictions. L-Annamycin is a next-generation anthracycline designed to eliminate cardiotoxicity and overcome multidrug resistance. In a Phase 1b/2 study in patients with acute myeloid leukemia (AML), L-Annamycin administered in combination with cytarabine as second-line therapy achieved a 50% complete remission (CR) rate and a 60% composite CR (CRc) rate with a median overall survival of 12.39 months (95% CI, 2.07–13.96) in the intent-to-treat population. We evaluated the cardiac safety of L-Annamycin in multiple clinical trials to assess its ability to support sustained anthracycline exposure in patients with AML and soft tissue sarcoma. **Methods:** Cardiac safety was evaluated across sponsor- and investigator-initiated clinical trials of L-Annamycin. Assessments included serial 12-lead electrocardiograms (ECGs), cardiac biomarkers (troponin I and T), and transthoracic echocardiography with centralized evaluation of left ventricular ejection fraction (LVEF) and global longitudinal strain (GLS), where available. Cardiac data were reviewed independently by a reviewer in the Division of Cardiovascular Medicine at the Cleveland Clinic. Changes in LVEF from baseline to final assessment were analyzed in relation to cumulative L-Annamycin dose and patient age. **Results:** An independent cardiac safety review was conducted for 90 patients who were treated with L-Annamycin across five completed clinical trials; 78 of these patients now have source-verified pre- and post-treatment left ventricular ejection fraction (LVEF) assessments. The median cumulative L-Annamycin dose among these patients was 660 mg/m² (95% CI, 645–690; range, 210–2,970 mg/m²), with most of the cumulative doses exceeding conventional lifetime anthracycline limits. Analysis of the change in LVEF from baseline to final assessment demonstrated no statistically significant difference (mean difference, –0.12%; 95% CI, –1.34 to 1.09; p = 0.84). Linear regression analysis documented no correlation between cumulative L-Annamycin dose and change in LVEF (p = 0.12), nor between patient age and change in LVEF (p = 0.73). Independent review of serial ECGs, cardiac biomarkers, cardiac adverse events, and available global longitudinal strain measurements also demonstrated no evidence of drug-induced cardiotoxicity. **Conclusions:** L-Annamycin was not associated with any detectable cardiotoxicity despite high cumulative anthracycline exposure. These findings suggest that L-Annamycin represents a next-generation anthracycline capable of delivering effective anthracycline therapy without traditional cumulative dose limitations, thus further supporting its ongoing pivotal Phase 2b/3 trial in AML patients. Research Sponsor: Molculin Biotech.

The association between cardiovascular disease risk and breast arterial calcifications identified on screening mammography: A retrospective study.

Tae Hoon Kim, Richard E. Shaw, Kariann Abbate, Eleonora Teplinsky; Valley Health System, Paramus, NJ; Valley Health System, Ridgewood, NJ

Background: Screening mammography enables early breast cancer detection and improves outcomes. Breast cancer and cardiovascular disease (CVD) share several overlapping risk factors in women. Breast arterial calcifications (BACs) are non-occlusive calcifications of the medial layer of small to medium-sized arteries in the breast that can be identified on mammography. Prior studies have demonstrated an association between BACs and increased cardiovascular risk with growing evidence suggesting that BACs may serve as a non-invasive, low-cost screening tool for CVD. Currently, routine screening for BACs is not uniformly performed. This study aimed to evaluate the prevalence of BACs in screening mammograms, and to characterize associated atherosclerotic cardiovascular disease (ASCVD) risk scores and cardiovascular risk factors among individuals with BACs. **Methods:** We performed a retrospective analysis of 650 individuals undergoing screening mammography at our institution from 2023 to 2025. Data collected included patient demographics, medical and social history, and cardiovascular risk factors, including blood pressure, diabetes mellitus, and lipid profiles. ASCVD risk scores were calculated for each individual. Statistical analyses, including chi-square test and T-test, were performed to evaluate associations between the presence of BACs, cardiovascular risk factors, and ASCVD scores. **Results:** Among the 650 women who underwent screening mammography, n = 641 had BI-RADS 1 (negative) or 2 (benign) results, while n = 9 had an abnormal mammogram that subsequently led to a breast cancer diagnosis. BACs were identified in 15.1% of the participants (n = 98). BAC prevalence increased significantly with age: 2.3% among women aged 40–49 years, 8% in those aged 50–59 years, 18.4% in those aged 60–69 years, and 42.2% among women aged 70 years and older ($p < 0.001$). Among participants with available ASCVD risk data (n = 429), BAC-positive patients had a significantly higher mean 10-year ASCVD risk when compared with BAC-negative patients (14.0% vs 5.23%, $p < 0.001$). Among the BAC-positive patients, 61.2% were categorized as ASCVD intermediate or high risk versus 20.8% of BAC-negative patients ($p < 0.001$). BAC-positive patients also exhibited higher mean systolic blood pressure (123.76 vs 120.66 mm Hg, $p = 0.042$). Hemoglobin A1c, total cholesterol, diastolic blood pressure, and smoking status did not differ significantly between the two groups. **Conclusions:** Breast arterial calcifications identified on screening mammograms were significantly associated with less favorable cardiovascular risk profiles. Implementation of routine BAC reporting may enable opportunistic CV risk detection during breast cancer screening, potentially leading to earlier preventive interventions. Research Sponsor: None.

Differences in the receipt of recommended cardiovascular assessment among cancer survivors in the United States by atherosclerotic cardiovascular disease status.

Reed Mszar, Ash Blythe Alpert, Eunata Gallardo-Vara, Esther Kang, Kerry Conlin, Ana Barac, Sarah Hull, Lauren Baldassarre, Michaela Ann Dinan, Melinda Irwin, Leah M. Ferrucci; Yale School of Public Health, New Haven, CT; Yale Cancer Center, New Haven, CT; Yale School of Medicine, New Haven, CT; Inova Schar Heart and Vascular, Inova Schar Cancer, Falls Church, VA; Yale University, New Haven, CT

Background: Cardio-oncology guidelines recommend annual cardiovascular (CV) assessment among cancer survivors, particularly those with pre-existing atherosclerotic cardiovascular disease (ASCVD). Despite this, little is known regarding the proportion of cancer survivors receiving comprehensive CV assessment and whether certain subgroups experience suboptimal uptake. We investigated the prevalence and predictors of receiving recommended comprehensive CV assessment (i.e., cholesterol, blood pressure, blood glucose) among cancer survivors in the United States. **Methods:** We used self-reported, cross-sectional data from the National Health Interview Survey (2012–2018), an annual, weighted survey that uses multistage sampling and interviews to produce nationally representative estimates of the noninstitutionalized U.S. population. Adults with cancer and complete information on ASCVD status (defined as a history of myocardial infarction, stroke, coronary heart disease, or angina) were included. To examine the association between sociodemographic characteristics and lack of recommended CV assessment within the past year, adjusted odds ratios (aOR) and 95% confidence intervals (CI) were calculated using multivariable logistic regression stratified by ASCVD status. **Results:** Among 16,420 cancer survivors (median age: 65.4 years; 20.1% with ASCVD), representing approximately 15.4 million survivors annually, 38.2% did not receive recommended CV assessment in the past year. Approximately 3.7% of cancer survivors (representing 566,043 individuals annually) received none of the CV assessments. Among cancer survivors with ASCVD, factors associated with increased odds of not receiving recommended CV assessment included lower (vs higher) level of education (aOR, 1.30 [95% CI, 1.01–1.65]). In cancer survivors without ASCVD, these factors included age 18–44 years (vs ≥ 75 years) (aOR, 1.82 [95% CI, 1.39–2.39]), low/lowest (vs high/middle) income (aOR, 1.23 [95% CI, 1.06–1.44]), uninsured (vs insured) status (aOR, 1.94 [95% CI, 1.37–2.74]), South (vs Northeast) region (aOR, 1.31 [95% CI, 1.05–1.62]), and no (vs yes) usual source of care (aOR, 2.42 [95% CI, 1.66–3.53]). Among all cancer survivors, there was a stepwise increase in receipt of CV assessment with increasing age at initial cancer diagnosis ranging from 52.7% among those aged 18–44 years at diagnosis to 68.5% among those aged 65–74 years at diagnosis ($p < 0.001$). **Conclusions:** More than 1 in 3 cancer survivors did not receive recommended annual CV assessment with several subgroups having even lower screening rates, including by age, socioeconomic status, and access to care. Improving awareness of contemporary cardio-oncology guidelines and targeting interventions during cancer survivorship are needed to increase uptake of optimal CV assessment. Research Sponsor: None.

Efficacy of primary cardioprotection with perindopril, bisoprolol, and trimetazidine in high-risk patients with breast and gastric cancer receiving anthracycline- and trastuzumab-containing therapy.

Evgenia Khatkova, Evgenia Novosel, Elizaveta Lukashova, Elena Stauver, Elena Shupenina, Yury Vasyuk, Lyudmila Zhukova; Moscow Clinical Scientific Center Named After A.S. Loginov, Moscow, Russian Federation; Department of Hospital Therapy №1, N. A. Semashko National Medical Research Center for Clinical Medicine, Russian University of Medicine, Moscow, Russian Federation

Background: Anthracyclines and trastuzumab are the most common antitumor agents associated with a substantial risk of cardiotoxicity (CTX). Patients with high or very high cardiovascular risk represent a vulnerable population where even subclinical myocardial injury can translate into clinically significant cardiac dysfunction. The present study is aimed to evaluate the efficacy of primary cardioprotective therapy (CPT) in preventing both subclinical and overt CTX in high-risk patients undergoing anthracycline (A)- and/or trastuzumab (T)-containing treatment. **Methods:** This single-center prospective observational study included 92 cancer patients (pts) with high or very high risk of CTX according to the Mayo Clinic risk score. The study population consisted of 7 men (8%) and 85 women (92%), with a mean age of 60.6 ± 11.8 years. Breast cancer (BC) was the most common diagnosis ($n = 84$; 91%), while gastric cancer (GC) accounted for 8 cases (9%). 17 (33.3%) pts in the intervention group and 16 (39%) pts in the control group had a history of congestive heart failure. AC (doxorubicin/cyclophosphamide) regimen was administered in 54 BC patients, AC followed by T in 30 BC pts, T – in 8 GC pts. The intervention group ($n = 51$) received primary CPT with perindopril and bisoprolol; trimetazidine was added in patients at very high cardiovascular risk or with established coronary artery disease. The control group ($n = 41$) did not receive CPT due to intolerance or refusal. Echo-cardiography with left ventricular ejection fraction (LVEF) and global longitudinal strain (GLS), 24-hour blood pressure monitoring, and multibiomarker assessment (troponin I, NT-proBNP, MPO, sST2) were performed at baseline and at 1, 3, 6, 9, and 12 months. **Results:** The control group showed a significant increase in indexed left atrial volume and indexed left ventricular end-diastolic volume at 6 and 9 months, respectively, indicating cardiac remodeling, which represents one of the earliest manifestations of subclinical cardiotoxicity. GLS reduction $\geq 18\%$ occurred in 21.2% of control pts vs. 7.1% in the intervention group ($p < 0.05$). Clinically significant cardiotoxicity with LVEF decline developed in 6 control pts vs. 1 in the intervention group. Cardiovascular complications were 2.5 times more frequent in the control group (70.1% vs. 24.8%). All-cause mortality at 12 months was significantly higher in the control group (11.7% vs. 5.1%, $p = 0.04$). **Conclusions:** In high-risk pts with BC and GC receiving anthracycline- and trastuzumab-containing therapy, primary CPT with perindopril, bisoprolol, and trimetazidine effectively prevents adverse cardiac remodeling, preserves myocardial systolic function, reduces the incidence of cardiovascular complications, and is associated with a significant reduction in one-year all-cause mortality. Research Sponsor: None.

Lipid-lowering therapy use among cancer survivors undergoing lung cancer screening: A cross-sectional analysis.

Sri Gopalsamy Ramaswamy, Eyerusalem Zewde, Akila Anandarajah, Busayo Akinloye, Benjamin Bowe, Thomas A. Odeny, Beryne Odeny; School of Public Health at Washington University in St. Louis, Saint Louis, MO; School of Public Health at Washington University in St. Louis, St. Louis, MO; Washington University School of Medicine, St. Louis, MO; Washington University in St. Louis, School of Medicine, St. Louis, MO

Background: Cardiovascular disease (CVD) causes 56% of non-cancer deaths among cancer survivors, yet lipid-lowering therapy (LLT) remains underutilized. Moreover, lung cancer screening (LCS) populations exhibit a dual high-risk profile, characterized by heavy smoking exposure and a history of cancer. We sought to examine the utilization of LLT among cancer survivors undergoing LCS and to identify disparities based on demographics, clinical factors, and social determinants of health. **Methods:** We conducted a cross-sectional study of 7,778 cancer survivors aged 50–80 years who underwent LCS through Barnes-Jewish Healthcare's LCS program between 2015 and 2023. The primary outcome measured was LLT use, specifically statins or statin substitutes, as documented in electronic health records. We assessed for associations with demographics (age, sex, race), clinical factors (prior ASCVD, cancer type), healthcare access (insurance status, rurality via Rural-Urban Commuting Area codes), and the Area Deprivation Index (ADI). The data were analyzed using multivariable logistic regression, adjusted for demographics, insurance status, smoking, indication, and provider, with results stratified by race and sex. **Results:** Overall, 65.8% of cancer survivors undergoing LCS used LLT. Compared with lung cancer, prostate (AOR = 1.35; 95% CI 1.08–1.71), hematologic (AOR = 1.35; 95% CI 1.03–1.76), and other solid cancers (AOR = 1.23; 95% CI 1.07–1.42) were associated with higher LLT use. When stratified by race, among White patients, male sex was associated with higher LLT use (AOR = 1.13; $p = 0.036$) and rural residence was associated with lower LLT use (AOR = 0.81; $p = 0.005$); these were not significant factors in Black patients. Prior ASCVD was the strongest associated factor (AOR = 2.54, $p < 0.001$), followed by age ≥ 65 years (AOR = 1.41, $p < 0.001$). Rural residence was associated with 29% lower odds of LLT use (AOR = 0.71, $p < 0.001$) even after adjusting for all other factors. Insurance status, and neighborhood deprivation were not associated with LLT use. **Conclusions:** LLT remains underused among cancer survivors at high cardiovascular risk, even during routine LCS. Rural patients were less likely to receive therapy, underscoring persistent geographic gaps in preventive care. The strong association of prior ASCVD with LLT use suggests that therapy is still primarily utilized reactively rather than preventively. Improving follow-up and care coordination during screening could help close prevention gaps and reduce heart disease deaths in cancer survivors. Research Sponsor: National Cancer Institute; Alvin J. Siteman Cancer Center at Washington University School of Medicine.

Predicting fluoropyrimidine cardiotoxicity using a focus beyond routine cardiovascular risk assessment.

Aminat Maaz Yusupova, Elena Shavarova, Aminat Khamzatkhonova, Denis Andreev, Maria Poltavskaya, Vsevolod Galkin; Moscow Cardio-Oncology Center of S.S.Yudin City Clinical Hospital, Moscow, Russian Federation; Moscow Cardio-Oncology Center of the SS.Yudin City Clinical Hospital, Moscow, Russian Federation; Department of Cardiology, Functional and Ultrasound Diagnostics of NV Sklifosovsky Institute for Clinical Medicine, IM Sechenov First Moscow State Medical University (Sechenov University), Moscow, Russian Federation; IDepartment of Cardiology, Functional and Ultrasound Diagnostics of NV Sklifosovsky Institute for Clinical Medicine, IM Sechenov First Moscow State Medical University (Sechenov University), Moscow, Russian Federation

Background: Fluoropyrimidines remain backbone of systemic therapy for colorectal cancer (CRC) but are associated with diverse cardiovascular (CV) toxicities ranging from hypertension to heart failure. Current CV risk stratification tools have uncertain predictive value in cancer populations. We aimed to identify clinically actionable predictors of CV complications during fluoropyrimidine-based therapy. **Methods:** Prospective single-center observational registry included 171 consecutive stage I-IV CRC patients initiating fluoropyrimidine-based chemotherapy between (median follow-up 6.5 months, IQR 3.0-8.0). All patients underwent structured baseline cardio-oncology assessment including CV risk stratification per ESC guidelines, 12-lead ECG, transthoracic echocardiography with global longitudinal strain measurement, and serum biomarkers (NT-proBNP, high-sensitivity troponin I). Primary endpoint was incidence of ≥ 1 prespecified CV complication. Missing data ($< 5\%$ for laboratory parameters) were addressed via complete-case analysis. Statistical analysis included χ^2 tests, Mann-Whitney U tests, and multivariable logistic regression with backward elimination (SPSS v28.0, significance $p < 0.05$). **Results:** Overall CV complication incidence was 33%. Event spectrum: Blood pressure destabilization (9%), thromboembolism (pulmonary embolism 5%, deep vein thrombosis 3%), arrhythmias 4.3%, coronary ischemia (angina 2.3%), ischemic stroke 0.6%, left ventricular systolic dysfunction (asymptomatic EF decline 1.8%, symptomatic heart failure 0.6%), moderate hydropericardium (2.3%), and isolated biomarker elevation (2.3%). Univariate analysis identified significant associations with CV complications for: diabetes mellitus (DM) (26.8% vs 10.4%, $p = 0.006$, OR 3.2), obesity (41.1% vs 26.1%, $p = 0.047$, OR 2.0), age (median 66.3 vs 63.1 years, $p = 0.041$), and high/very-high baseline CV risk (37.5% vs 14.3%, $p = 0.009$, OR 3.6). In multivariable analysis adjusting for age, sex, obesity, hypertension, and baseline CV risk category, only DM retained independent predictive value (adjusted OR 3.14, 95% CI 1.35-7.28, $p = 0.008$). Baseline NT-proBNP elevation correlated with increased all-cause mortality (58.3% vs 22.0%, $p = 0.010$) despite absence of CV deaths (all 12 deaths from cancer progression). **Conclusions:** Diabetes mellitus is the strongest independent predictor of CV toxicity in CRC patients receiving fluoropyrimidine chemotherapy, associated with 3-fold increased risk. While baseline CV risk stratification showed univariate association, it lost significance in adjusted analysis, highlighting DM's primacy. Systematic cardio-oncology monitoring appears effective given zero CV mortality. These data support prioritizing diabetic patients for intensified CV surveillance during fluoropyrimidine therapy. Research Sponsor: None.

Cost-effectiveness of post-discharge home care for reducing potentially avoidable readmissions in stage IV cancer.

Amal AlJuhani, Vanessa Huels, Michelle B. Nadler, Eitan Amir, Beate Sander, Uri Bender, Karine Ronan, Jacqueline Savill, Melanie Penner; Princess Margaret Cancer Centre, University Health Network, Toronto, ON, Canada; Institute of Health Policy, Management and Evaluation, Dalla Lana School of Public Health, University of Toronto, Toronto, Canada; Division of Medical Oncology & Hematology, Department of Medicine, Princess Margaret Cancer Centre and University of Toronto, Toronto, ON, Canada; Princess Margaret - University Health Network, Toronto, ON, Canada; University Health Network, Toronto, ON, Canada; The Princess Margaret Cancer Centre, Toronto, ON, Canada; The Princess Margaret Cancer Centre, Toronto, Canada; University of Toronto, Institute of Health Policy, Management and Evaluation, Toronto, ON, Canada

Background: Approximately 39% of hospital readmissions among stage IV cancer patients are potentially avoidable. These readmissions increase healthcare costs, reduce quality of life, and increase mortality. Home-based care may reduce avoidable readmissions through symptom management and care coordination, but cost-effectiveness in this population remains unknown. **Objective:** To evaluate the cost-effectiveness of home with care versus home without care for stage IV solid tumors patients post-discharge, from an Ontario public payer perspective. **Methods:** A four-state Markov model (Care, Readmission, Discharged, Death) was developed with week-long cycles with a 180 day horizon. Weekly potentially avoidable readmission rates were 1.8% (home with care) versus 5.4% (home without care). Utilities (0.65 vs 0.55) and costs (home care \$100/day; readmission \$994/day) were from Canadian sources. Primary outcome was incremental cost-effectiveness ratio (ICER) per quality-adjusted life-year (QALY). One-way, two-way, and probabilistic sensitivity analyses (1,000 simulations) were conducted. Value of information analysis quantified decision uncertainty. Costs and QALYs were discounted at 1.5% annually. **Results:** Home with care produced 0.166 QALYs at \$12,251 versus 0.105 QALYs at \$7,386, yielding 0.061 incremental QALYs (22 quality-adjusted days) at \$4,865 incremental cost (ICER: \$79,955/QALY). Home care cost was the most influential cost parameter with a threshold of \$115/day. Probabilistic analysis showed 60% probability of cost-effectiveness at willingness-to-pay (WTP) \$100,000/QALY, with acceptability curves crossing at \$80,000/QALY. Expected value of perfect information peaked at \$1,500/patient. **Conclusions:** Home with care may represent a cost-effective option for stage IV cancer patients at or below the commonly accepted Canadian WTP threshold of \$100,000/QALY, with robust findings across sensitivity analyses. Program costs are the primary value determinant, supporting policy consideration for post-discharge support services. Research Sponsor: None.

Cost-effectiveness results: Home with care versus home without care.			
Outcome	Home with Care	Home without Care	Difference
Total cost	\$12,251	\$7,386	+\$4,865
Total QALYs	0.166	0.105	+0.061
Quality-adjusted days	60.6	38.3	+22.3
ICER	—	—	\$79,955/QALY
Probability cost-effective at WTP \$100,000/QALY	60%	40%	—

QALY = quality-adjusted life-year; ICER = incremental cost-effectiveness ratio; WTP = willingness-to-pay. Costs in 2024 Canadian dollars.

County-level palliative care physician density and socioeconomic determinants of place of cancer death in the United States, 2021-2023.

Ruoxi Teng, Xuesong Han, Changchuan Jiang, Dio Kavalieratos, Robin Yabroff, Xin Hu; Department of Biostatistics, Yale University, New Haven, CT; American Cancer Society, Atlanta, GA; UT Southwestern Medical Center, Dallas, TX; Emory University, Atlanta, GA; Emory University School of Medicine, Atlanta, GA

Background: Palliative care, a specialized approach focused on care for individuals with serious illness including cancer, has been shown to improve end-of-life outcomes, including higher rates of death in preferred settings. However, access to palliative care remains inequitable due to significant geographic disparities in workforce distribution. This study examines the association between county-level palliative care physician density and place of death among US decedents died from cancer. **Methods:** We conducted a retrospective cohort study using CDC WONDER multiple cause of death data (2021-2023) linked with palliative care physician supply data from the American Medical Association (AMA) Physician Masterfile. The primary exposure was county-level palliative care physician density, categorized as zero, below-median, or above-median (among non-zero counties). The primary outcome was the county-level percentage of cancer deaths (ICD: C00-C97) occurring in non-hospital settings (home, hospice, long-term care, or nursing home). Covariates include county sociodemographic characteristics (race/ethnicity, median income, region, metropolitan status) and hospice facility availability. Multivariable regression models estimated associations between physician density and place of death, adjusting for other covariates. All models incorporated county population weighting and state-level clustering. **Results:** Most U.S. counties ($n = 2056$, 66.27%) had no palliative care physicians in 2020. Counties with palliative care physicians showed higher median household incomes, more hospice facilities and metropolitan status, and were concentrated in the Northeast and West (all $p < 0.001$). The average percentage of non-hospital facility deaths across all counties was 56.6% (SD = 7.1) for all causes, 60.5% (SD = 8.1) for heart disease, and 70.7% (SD = 8.0) for malignant neoplasms. Multivariable regression models revealed a dose-response relationship: counties with non-zero below median and above-median palliative care physician density showed 0.9 percentage points (ppts, $p < 0.05$) and 1.1 ppts ($p < 0.05$) higher proportions of cancer death at non-hospital facility-based facilities than counties without palliative care physicians. In addition, Metropolitan and Micropolitan counties had 2.5 ppts ($p < 0.001$) and 2.1 ppts ($p < 0.001$) higher proportions of cancer death at non-hospital facility-based facilities than non-metropolitan counties respectively. **Conclusions:** Higher county-level palliative care physician density is associated with increased non-hospital facility-based deaths for cancer, demonstrating a clear dose-response relationship. These findings suggest that ensuring access to palliative care, through workforce expansion or care delivery model innovation may facilitate end-of-life care planning aligned with patient preferences. Research Sponsor: None.

Palliative care involvement at the end of life in advanced cancer.

Rhea Sehgal, Tiana L. Clemons, Charles S. Day, Aditi Prabhu, Parita Patel, Carinne Jarvis, Ahmad Yousef; School of Medicine, Wayne State University, Detroit; Henry Ford Health, Royal Oak, MI; Henry Ford Hospital, Royal Oak, MI; Michigan State University College of Human Medicine, Grand Rapids, MI; Wayne State University School of Medicine, Detroit, MI

Background: High-intensity end-of-life (EoL) care in advanced cancer is common, costly, and often misaligned with patient goals, despite limited survival benefits. Value-based oncology emphasizes high-quality, goal-concordant care while reducing non-beneficial interventions. Palliative care is central to this model, yet its impact on overall spending versus patterns of care intensity near death remains unclear. We evaluated whether palliative care involvement in the final 30 days of life was associated with differences in total expenditures and healthcare resource allocation in patients with advanced cancer. **Methods:** We conducted a retrospective cohort study of adults with advanced cancer who died within an integrated health system between 2022 and 2025. Palliative care exposure was defined as ≥ 1 palliative encounter within 30 days of death. Financial data were obtained from enterprise cost-accounting systems; clinical and utilization data were derived from the electronic health record and institutional cancer registry. Outcomes included total 30-day healthcare charges and proportional spending across major service categories reflecting care intensity. Median charges were compared using Wilcoxon rank-sum tests, and spending distributions were analyzed via chi-square tests. **Results:** Among 1,635 decedents, 195 received palliative care within 30 days of death, a period associated with the highest concentration of EoL healthcare use. Median total 30-day charges did not differ significantly between patients who received palliative care and those who did not (\$14,610 vs \$17,100; $p = 0.054$). However, palliative care involvement was associated with a significant shift in spending patterns. Compared with patients without palliative care, those receiving palliative care had a lower proportion of spending on inpatient, procedural, diagnostic, and therapeutic services and a higher proportion on pharmacy, invasive therapeutic, home health, and hospice services. Overall spending distribution differed significantly between groups ($p = 0.046$). Across the cohort, inpatient and observation services accounted for the largest share of expenditures, followed by pharmacy, procedural, and invasive therapeutic services, with hospice representing a minority of total spending. **Conclusions:** EoL palliative care involvement was not associated with significant reductions in total healthcare spending but was linked to differences in care intensity, reflected by a redistribution of expenditures from inpatient and procedural services to pharmacy, invasive therapeutic, and home health care. The value of palliative care in oncology lies not in cost savings but in promoting high-quality EoL care that aligns with patient goals and oncology care priorities. Future analyses will include patient-reported outcomes to examine how shifts in care intensity and spending relate to EoL symptom burden, quality of life, and goal-concordant care. Research Sponsor: None.

End-of-life anti-cancer treatment (Rx) patterns in patients (pts) with the six most common cancers in the USA.

Umang Swami, Yeonjung Jo, Varun Nandakumar, Zeynep Irem Ozay, Georges Gebrael, Edwin Lin, Ethan Murdock, Gabriel Hooper, Richard Tanner Hardy, Tejita Agarwal, Rachel Revillo, Krishnam Goel, Ayana Srivastava, Benjamin L. Maughan, Vinay Mathew Thomas, Haoran Li, Sumanta Kumar Pal, Rana R. McKay, Neeraj Agarwal; Department of Medicine, Huntsman Cancer Institute, University of Utah, Salt Lake City, UT; Huntsman Cancer Institute at The University of Utah, Salt Lake City, UT; University of Utah, Salt Lake City, UT; Huntsman Cancer Institute, Salt Lake City, UT; University of Kansas, Lawrence, KS; City of Hope Comprehensive Cancer Center, Duarte, CA; UC San Diego Moores Cancer Center, La Jolla, CA; Huntsman Cancer Institute (NCI-CCC), University of Utah, Salt Lake City, UT

Background: Pts with ≤ 6 months of life expectancy qualify for hospice. However, most pts with advanced/metastatic (a/m) cancer continue to receive Rx up to weeks prior to death. Data describing end-of-life Rx patterns in these pts remain limited but are essential to improve clinical care delivery. Herein, we evaluated real-world Rx patterns in relation to the time of death across 6 most common a/m solid tumors: advanced non-small cell lung cancer (aNSCLC), metastatic breast cancer (mBC), metastatic prostate cancer (mPC), advanced colorectal cancer (aCRC), metastatic pancreatic cancer (mPanC), and advanced urothelial carcinoma (aUC).

Methods: This study used the US-based, electronic health record-derived deidentified Flatiron Health Research Database. Eligibility: diagnosis of aNSCLC, mBC, mPC, aCRC, mPanC and aUC, had a recorded date of death, and information on initiation of first-line (1L) Rx. The data cutoff date was 6/30/2025. Pts were categorized as treatment-free if no systemic Rx was administered within the final 1 or 3 months of life, or on-treatment if systemic Rx was received within 1 or 3 months before death. Demographic and clinical variables at the last line of Rx initiation, including age, race, socioeconomic status, practice type, and insurance, were summarized using medians (IQR) or proportions. **Results:** Of 111,337 pts with aNSCLC, 82,339 had a recorded date of death, of whom 59,777 initiated 1L Rx. Of 43,218 pts with mBC, 26,572 had a recorded date of death, of whom 23,055 initiated 1L Rx. Of 27,979 pts with mPC, 14,793 had a recorded date of death, of whom 9,667 initiated 1L Rx. Of 45,013 pts with aCRC, 29,749 had a recorded date of death, of whom 24,219 initiated 1L Rx. Of 18,942 pts with mPanC, 15,690 had a recorded date of death, of whom 11,528 initiated 1L Rx. Of 15,236 pts with aUC, 10,872 had a recorded date of death, of whom 7,815 initiated 1L Rx. The proportion of pts receiving systemic Rx within 1 month or 3 months before death for each cancer type is summarized in Table. Baseline characteristics, Rx patterns and trends by cancer type will be presented at the meeting. **Conclusions:** Across six most common cancers in the US, systemic Rx use remained common near the end of life, with up to one-third of pts treated in the final month. These findings suggest the need for greater emphasis on early involvement of palliative care teams and timely transition of pts with terminal cancers to comfort care. Research Sponsor: None.

Proportion of pts with a/m cancer receiving systemic Rx within 1 month or 3 months before death.

Cancer type	Eligible pts	Rx within 1 month of death, n (%)	Rx within 3 months of death, n (%)
aNSCLC	59,777	19,268 (32.2)	38,227 (63.9)
mBC	23,055	8,416 (36.5)	15,972 (69.3)
mPC	9,667	2,438 (25.2)	5,762 (59.6)
aCRC	24,219	7,172 (29.6)	15,386 (63.5)
mPanC	11,528	4,191 (36.3)	9,184 (79.7)
aUC	7,815	2,358 (30.2)	5,170 (66.1)

Temporal trends and sociodemographic disparities in place of death among adults with pancreatic cancer in the United States (1999–2023).

Ali Mushtaq, Darshan Shivanne Gowda, Jibran Ikram, Abdul Qadeer, Afthab Salam Kannian, Rishi Chowdhary, Mohanad Baroudi, Moaath Ali Mustafa; Cleveland Clinic Foundation, Cleveland, OH; Hassan Institute of Medical Sciences, Hassan, Karnataka, India; Department of Cardiovascular Medicine, Heart, Vascular, and Thoracic Institute, Cleveland Clinic, Cleveland, OH; University of Texas Medical Branch, Galveston, TX; Department of Medicine, Government Medical College, Kozhikode, India; Metrohealth Medical Center, Cleveland, OH; Department of Hematology and Medical Oncology, Cleveland Clinic Taussig Cancer Institute, Cleveland, OH

Background: Location of death is a critical quality metric for pancreatic cancer due to its rapid trajectory and high symptom burden. While home-based hospice is promoted, it is unclear if shifts from hospital death have been equitable. We analyzed 25-year national trends and independent predictors of place of death. **Methods:** We analyzed CDC WONDER death certificate data (1999–2023) for pancreatic cancer decedents aged ≥20 years (ICD-10 C25.x). Place of death categories: Home, Hospice/Nursing Facility, Inpatient, or Outpatient/ER. We calculated annual trends and used multinomial logistic regression to estimate adjusted odds ratios (aOR) with 95% confidence intervals (CI), adjusting for age, sex, race/ethnicity, urbanization, and year. Inpatient death served as the reference category. **Results:** Of 899,332 deaths, acute care hospital deaths declined (34.0% to 21.0%) while home (48.6% to 56.1%) and hospice/nursing facility deaths (15.7% to 21.3%) increased. However, significant disparities persisted. Compared to Non-Hispanic Whites, Black patients were less likely to die at home (aOR 0.55; 95% CI, 0.54–0.56) or in hospice/nursing facilities (aOR 0.63; 95% CI, 0.62–0.65) and significantly more likely to die in Outpatient/ER settings (aOR 1.57; 95% CI, 1.51–1.64). Hispanics were less likely to die in hospice/nursing facilities (aOR 0.57; 95% CI, 0.55–0.58). Rural residents had lower odds of hospice/nursing facility death (aOR 0.89; 95% CI, 0.87–0.91) vs. large metro. Younger age (20–64) was associated with hospital death. **Conclusions:** Despite substantial shifts from hospital to home settings, Black and Hispanic patients remain significantly less likely to access hospice and more likely to die in emergency settings. These findings highlight structural inequities requiring targeted interventions to ensure high-quality end-of-life care for minority populations. Research Sponsor: None.

Multivariable adjusted odds ratios (aOR) for place of death in pancreatic cancer.			
Predictor Comparison	Decedent's Home (aOR)	Hospice/Nursing Facility (aOR)	Outpatient or ER (aOR)
Black vs. White	0.55 (0.54–0.56)	0.63 (0.62–0.65)	1.57 (1.51–1.64)
Asian vs. White	0.74 (0.72–0.76)	0.51 (0.49–0.53)	0.85 (0.77–0.95)
Hispanic vs. Non-Hispanic	0.92 (0.90–0.94)	0.57 (0.55–0.58)	1.01 (0.94–1.08)
Rural vs. Large Metro	1.08 (1.06–1.10)	0.89 (0.87–0.91)	0.92 (0.88–0.97)
Male vs. Female	0.90 (0.89–0.91)	0.78 (0.77–0.79)	1.09 (1.05–1.13)
Age 85+ vs. 20–64	1.79 (1.75–1.82)	3.69 (3.61–3.76)	0.66 (0.62–0.71)
Age 75–84 vs. 20–64	1.39 (1.37–1.41)	1.91 (1.88–1.94)	0.81 (0.78–0.85)
Age 65–74 vs. 20–64	1.18 (1.17–1.20)	1.33 (1.31–1.36)	0.89 (0.85–0.92)

Abbreviations: aOR, adjusted Odds Ratio; CI, Confidence Interval; ER, Emergency Room; Ref, Reference Group.

Impact of social vulnerability on end-of-life care in hematologic malignancies.

Jude O. Ossai, Yazmin Reategui-Almonacid, Oladayo Oyebanji, Lemchukwu Amaeshi, Albert Owusu-Ansah, Zaheer Qureshi, Angimar Uriepetro-Palma, Ayodeji David Johnson; Rutgers/Newark Beth Israel Medical Center, Newark, NJ; Department of Internal Medicine, University Hospitals Cleveland Medical Center, Cleveland, OH; Montefiore Medical Center, Moses Campus, Department of Medicine, Bronx, NY; Rowan-Virtua School of Osteopathic Medicine, Teaneck, NJ; Jefferson Einstein Philadelphia Hospital, Philadelphia, PA; Boston Medical Center - Brighton, Boston, MA

Background: Patients with hematologic malignancies frequently receive intensive inpatient care near the end of life. While disparities in end-of-life (EOL) care are well described in oncology, how cumulative social vulnerability shapes treatment intensity and palliative care involvement among hospitalized patients with hematologic cancers remains unclear. We examined the association between social vulnerability burden and inpatient EOL care patterns using a nationally representative database. **Methods:** We performed a retrospective cohort study using the 2021–2022 National Inpatient Sample of adult hospitalizations with hematologic malignancies. A composite hematologic social vulnerability index (cSVI-Heme) was constructed using validated proxies available in NIS: minoritized race/ethnicity, Medicaid or uninsured status, and lowest ZIP-code income quartile. Hospitalizations were classified as low (0), moderate (1), or high (≥ 2) vulnerability. The primary outcome was high-intensity EOL care (invasive mechanical ventilation, cardiopulmonary resuscitation, or acute dialysis). Secondary outcomes included palliative care utilization and in-hospital mortality. Associations were assessed using multivariable logistic regression and inverse probability of treatment weighting, adjusting for demographics, comorbidity burden, acute organ failure, sepsis, malignancy subtype, and hospital characteristics. **Results:** The cohort included 202,802 hospitalizations, of which 54.2% were low, 31.0% moderate, and 14.8% high vulnerability. Overall, 5.9% involved high-intensity EOL care, increasing stepwise across vulnerability tiers (5.1% vs 6.5% vs 7.9%; $p < 0.001$). After adjustment, compared with low vulnerability hospitalizations, moderate vulnerability was associated with higher odds of high-intensity EOL care (aOR 1.25, 95% CI 1.19–1.30), and high vulnerability with substantially higher odds (aOR 1.50, 95% CI 1.42–1.58), demonstrating a clear dose–response relationship. Findings were confirmed in propensity-weighted analyses. This gradient was driven primarily by acute dialysis (3.1% vs 4.6% vs 6.2%; $p < 0.001$), while rates of mechanical ventilation and CPR were similar. High vulnerability was independently associated with higher in-hospital mortality (aOR 1.20, 95% CI 1.12–1.28), whereas palliative care utilization did not increase after adjustment. **Conclusions:** Among hospitalized patients with hematologic malignancies, greater social vulnerability is associated with higher-intensity end-of-life care and increased mortality, with a clear dose–response relationship. These differences are not accompanied by greater palliative care involvement, highlighting a mismatch between treatment intensity and supportive care. Integrating social vulnerability into inpatient hematologic oncology care may support earlier goals-of-care discussions and more equitable EOL care. Research Sponsor: None.

Effects of tai chi qigong on gene expression profiles in older male cancer survivors with fatigue.

Anita Kinney, Samuel Tunddealao, Yong Lin, Biren Saraiya, Shou-En Lu, Cindy K. Blair, Dolores D. Guest, Emily Heidt, Evelyn Arana-Chicas, Elizabeth A. Handorf, Antoinette Stroup, Yibin Kang, Wadih Arap, Steve W. Cole, Michael R. Irwin; Department of Biostatistics and Epidemiology, Rutgers School of Public Health, Piscataway, NJ; Rutgers Cancer Institute, New Brunswick, NJ; Department of Biostatistics and Epidemiology, Rutgers School of Public Health, New Brunswick, NJ; University of New Mexico Comprehensive Cancer Center, Albuquerque, NM; Department of Molecular Biology, Princeton University, Princeton, NJ; Department of Psychiatry, David Geffen School of Medicine, University of California, Los Angeles, CA

Background: The HERO trial showed that Tai Chi Qigong (TCQ) reduced fatigue (primary endpoint) in male cancer survivors. Fatigue-related biological pathways influenced by mind-body therapies, such as TCQ, remain poorly defined. This trial hypothesized that TCQ, compared to an exercise-intensity matched (EIM) intervention and usual care (UC), would have a more favorable effect on the regulation of two major fatigue-associated functional gene clusters: a) inflammation-vasodilation-metabolite sensing and b) energy and adrenergic activation among older male cancer survivors with fatigue. **Methods:** In this three-arm randomized trial (NCT 03345563), 113 male cancer survivors aged ≥ 55 years with fatigue were randomized to 12 weeks of TCQ ($n = 45$), EIM ($n = 43$), or UC ($n = 25$), delivered twice weekly with recommended home practice. Gene expression profiles were assessed at baseline and at 1 week and 3 months post-intervention using genome-wide transcriptional profiling of blood samples. A key secondary endpoint was changes in gene expression at the 3-month follow-up. A minimum of 8 subjects per study arm is required to achieve 80% power (two-sided $\alpha = 0.05$) to detect a 2.0-fold change in gene expression. Intervention effects were evaluated using an intention-to-treat approach and general mixed linear models, with baseline adjustment and time of sample collection included as time-varying covariates. Multiple comparisons were controlled for using the false discovery rate (FDR). Upregulation of DBI, IL-10, ADRB2, VIPR2, OXTR, ASIC3, P2RX4, P2RX7, ATP5E, NDUFS5 genes and downregulation of TNF, NR3C1, P2RY1, HSPA2 genes were deemed as favorable effects. Mean difference (MD), 95% CI, and FDR corrected p-values were reported. **Results:** TCQ favorably regulated the expression of genes associated with inflammation (TNF: MD = -1.25; CI: -1.97 - -0.53; $p = 0.001$ and IL-10: MD = 0.51; CI: 0.02 - 1.00; $p = 0.043$), metabolite-sensing (P2RX4: MD = 0.45; CI: 0.04 - 0.85; $p = 0.032$), and energy activation (P2RY1: MD = -0.43; CI: -0.95 - -0.08; $p = 0.037$, ATP5E: MD = 0.15; CI: 0.05 - 0.30; $p = 0.035$, and NDUFS5: MD = 0.14; CI: 0.02 - 0.28; $p = 0.042$) at 3 months post-intervention. EIM favorably regulated genes associated with vasodilation (OXTR: MD = 0.89; CI: 0.36 - 1.42; $p = 0.001$) and inflammation (NR3C1: MD = -0.24; CI: -0.47 - -0.01; $p = 0.043$). Compared with EIM, TCQ produced greater increases in ADRB2, an adrenergic activator (MD: 0.81; CI: 0.26 - 1.35; $p = 0.003$) and P2RX4 (MD: 0.56; CI: 0.12 - 1.01; $p = 0.013$) and favorably decreased the expression of P2RY1 (MD: -0.93; CI: -1.51 - -0.35; $p = 0.002$). **Conclusions:** TCQ produced meaningful changes in inflammatory, adrenergic, energy, and metabolic pathways, supporting potential biological mechanisms through which TCQ may reduce fatigue in older male cancer survivors. Larger trials with a broader representation of participants are needed to confirm these pathway-level effects. Clinical trial information: NCT03345563. Research Sponsor: National Cancer Institute; R01CA203939.

Digital prehabilitation and functional performance signals in older adults undergoing hepatobiliary cancer surgery: A pilot study.

Mohammed Al-Jumayli, Alice Yu, Marina Sehovic, Lizz .Altenhofen, Amalia Stefanou, Rebecca Grillo, Morgan Bean, MartTheodore DeVera, Rachel Carmella, Martine Extermann, Daniel AnayaSaenz, Nathan Parker; H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL

Background: Older adults undergoing hepatobiliary cancer surgery often have limited functional reserve and face barriers to accessing structured preoperative conditioning. Technology-enabled, home-based prehabilitation may offer a scalable approach to support surgical readiness while generating early signals of functional change. **Methods:** Adults aged ≥ 65 years scheduled for hepatobiliary tumor resection with ≥ 4 weeks before surgery were enrolled in a multimodal, digitally supported prehabilitation program. The intervention combined wearable-monitored aerobic activity (≥ 90 minutes/week) with twice-weekly, live video-supervised progressive resistance training delivered by certified exercise trainers. Functional performance was assessed using the 30-second chair stand and arm curl tests, and health status was measured with the SF-12 survey at baseline and preoperative follow-up. Implementation and engagement metrics were captured to contextualize delivery in a geographically dispersed population. Analyses of functional outcomes were exploratory and intended to estimate effect sizes and inform future, adequately powered studies. **Results:** Twenty-one participants (median age 78 years; range 66–88) completed baseline and preoperative assessments over a median intervention duration of 4.5 weeks. Participants resided a median of 127 km from the cancer center, supporting remote delivery of the intervention. Improvements were observed in lower extremity function (30-second chair stand: 12.0 ± 3.2 to 13.8 ± 4.6 repetitions; $p = 0.04$) and upper extremity strength (30-second arm curl: 17.7 ± 5.4 to 22.2 ± 7.1 repetitions; $p < 0.001$). Patient-reported physical and mental health scores demonstrated favorable, though not statistically significant, trends. Engagement with wearable-monitored aerobic activity exceeded recommended weekly targets, and completion of tele-supervised resistance sessions remained high across the intervention period. **Conclusions:** In this pilot cohort of older adults preparing for hepatobiliary cancer surgery, a digitally supported, home-based prehabilitation model was associated with favorable short-term functional performance signals and high levels of engagement across a geographically dispersed population. These findings are hypothesis-generating and support further evaluation of tele-prehabilitation in trials powered to assess perioperative and clinical outcomes. Research Sponsor: None.

Real-world feasibility and efficacy of a tailored exercise program in patients with cancer.

Alice Avancini, Anita Borsati, Gloria Adamoli, Christian Ciurnelli, Andrea Trevisan, Lorenzo Belluomini, Ilaria Trestini, Daniela Tregnago, Marco Sposito, Jessica Insolda, Alessandra Auriemma, Elena Fiorio, Federico Schena, Michele Milella, Sara Pilotto, Emilio Bria; University of Verona, Verona, Italy; Azienda Ospedaliera Universitaria Integrata Verona, Verona, Italy; Azienda ospedaliera Universitaria Integrata Verona, Verona, Italy; Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Italy

Background: Exercise (EX) is associated with improved survival, symptom control, and management of treatment-related side effects in patients (pts) with cancer. However, evidence from large, real-world cohorts including unselected pts across different phases of the disease trajectory remains limited. This study aimed to evaluate the feasibility and effectiveness of a tailored EX program implemented in routine clinical practice. **Methods:** A three-month, bi-weekly supervised EX program was offered to consecutive cancer pts referred at the University Hospital of Verona, regardless of treatment status. The program included moderate-intensity aerobic exercise (10–30 minutes/session) and resistance training (2–3 sets of 8–12 repetitions; six exercises). The primary endpoint was feasibility, assessed by recruitment rate, adherence, and dropout. Secondary endpoints included cardiorespiratory fitness (six-minute walking test, 6MWT), muscular strength (handgrip strength test, HST), waist-hip ratio (WHR), and quality of life (QoL), measured using the EORTC QLQ-C30. Pre- and post-intervention outcomes were analyzed using descriptive statistics and paired Student's t-tests. **Results:** A total of 2276 pts were recruited (92% recruitment rate) with a median age of 57 ± 12 years. The most frequent tumor types were upper gastrointestinal cancers (34%) and breast cancer (31,8%). 84% of patients were receiving systemic treatments, and 47% had metastatic disease. Overall, 156 pts completed the intervention (dropout rate 31%, mainly due to disease progression), with an adherence rate of 84%. Significant improvements were observed in WHR (-1.2% , $p = 0.03$), 6MWT ($+25$ m, $p < 0.001$), and HST ($+1.9$ kg, $p < 0.01$). QoL significantly improved in physical, role, emotional, and social functioning (all $p < 0.01$), along with reductions in fatigue, nausea/vomiting, pain, dyspnea, insomnia, appetite loss, and diarrhea. Global QoL and financial difficulties also significantly improved. **Conclusions:** In a real-world, unselected cohort of cancer pts across different treatment phases, a tailored EX program is feasible and associated with meaningful improvements in physical function and QoL. These findings support the integration of structured exercise programs into routine oncology care beyond controlled clinical trial settings. Clinical trial information: NCT04226508. Research Sponsor: None.

Dyadic exercise intervention for LGBTQ+ cancer survivors: Associations with health-related quality of life, fatigue, and inflammation biomarkers.

Hala Awad, Charles Stewart Kamen; University of Rochester Medical Center, Rochester, NY

Background: Mixed training (aerobic/resistance) exercise is a key adjuvant therapy in exercise oncology; it decreases cancer mortality and improves patients' quality of life, in part by modulating the tumor microenvironment, regulating the HPA axis, and inflammatory pathways. LGBTQ cancer survivors and their partners frequently experience excessive fatigue, insomnia, impaired health-related quality of life (HRQOL), and relationship stress, yet remain underrepresented in exercise oncology research. **Methods:** We conducted an RCT with 70 LGBTQ+ cancer survivor-partner dyads ($N = 140$) to compare a 6-week home-based dyadic exercise program (EXCAP-PA) against a survivor-only intervention. Analyses focused on changes from baseline to post-intervention. Primary outcomes included the Survivor Profile of Mood States (POMS) Fatigue and PROMIS global health change to assess HRQOL. ANCOVA-style linear models regressed change scores on treatment arm and baseline values. Mediation analyses assessed whether changes in dyadic support, cortisol, and C-reactive protein (CRP) mediated the effect of treatment on fatigue and HRQOL. **Results:** Among 56 survivor-partner dyads with analyzable data, delivery of EXCAP-PA was feasible in this LGBTQ+ population. Both survivors and partners in each arm demonstrated improved HRQOL; however, the treatment arm did not significantly predict changes in PROMIS global health for survivors (survivors: $B = 0.10$, $SE = 0.39$, $p = 0.80$; partners: $B = 0.03$, $SE = 0.41$, $p = 0.94$). Baseline symptom burden strongly influenced outcomes: higher baseline fatigue was associated with greater reductions in POMS Fatigue-Inertia ($B = -0.55$, $SE = 0.15$, $p < 0.001$), indicating that participants with the highest fatigue experienced the largest improvements. In the CRP model ($n \approx 44$), higher baseline CRP was significantly associated with greater subsequent decreases in log-transformed CRP ($B = -0.37$, $SE = 0.17$, $p = 0.04$). The model relating fatigue change to baseline fatigue, baseline CRP, and CRP change explained a substantial proportion of variance ($R^2 = 0.29$; $F(3,40) = 5.42$, $p = 0.003$), whereas baseline cortisol was not significantly related to fatigue change. Although mediation analyses using changes in dyadic support, log-transformed CRP, or log-transformed cortisol as mediators of treatment arm effects on fatigue or HRQOL yielded small, non-significant indirect effects, the outcomes are consistent with a beneficial effect in which dyadic processes and reduced inflammation improve symptoms and HRQOL. **Conclusions:** Dyadic EXCAP-PA proved feasible for LGBTQ+ survivor-partner dyads. Although this pilot is underpowered to detect significant effects on global health, fatigue, or inflammation, the findings highlight high-symptom/high-CRP survivors as a priority subgroup for future, larger dyadic exercise trials. Research Sponsor: National Cancer Institute; NCI K07 CA190529.

Circulating heat shock protein 90 alpha (Hsp90α) as a biomarker for cancer cachexia.

Syed Hasan Raza Jafri, Edson Alves de Lima Junior, Julie Haewon Rowe, Amirali Tahanan, Putao Cen, Neha Maithel, Anneliese Gonzalez, Jessica Trevino Jones, Betty Arceneaux, Minjae Lee, Mohammad Hossein Rahbar, Hyun Ho Choi, Hongyu Wu, Yi-Ping Li; University of Texas, Houston, TX; UT Health, Houston, TX; The University of Texas Health Science Center at Houston (UTHealth Houston) McGovern Medical School, Houston, TX; The University of Texas Health Science Center at Houston, Houston, TX; University of Texas at Houston Health Science Center, McGovern Medical School, Houston, TX; University of Texas Medical School at Houston, Houston, TX; UT Physicians, Houston, TX; (UT Health Houston) McGovern Medical School, Houston, TX; UT Health McGovern School of Medicine, Houston, TX

Background: Cancer cachexia is defined clinically by a consensus definition of ≥5% unintentional weight loss in cancer patients over previous 6 months. There is a need to develop blood-based biomarkers for more accurately identifying patients with cancer cachexia. Tumor-cell derived Hsp90α has been shown to be a key driver for muscle wasting and systemic inflammation in pre-clinical models of cancer cachexia. **Methods:** We conducted a prospective case control study between April 2020 and February 2025 to identify biomarkers of cancer cachexia. Cases were newly diagnosed patients with stage III/IV cancers with ≥5% unintentional weight loss and serum albumin of < 3.5g/dl (Cachexia group). Controls were newly diagnosed patients with stage I-III cancers without weight loss and serum albumin of ≥3.5g/dl (non- cachexia group). We collected 5ml of blood at first visit and analyzed plasma Hsp90α levels using Enzyme linked immunosorbent assay (ELISA). We performed univariable comparisons of geometric means of Hsp90α between the groups using two sample t-test . To evaluate the classification performance of Hsp90α for identifying cancer cachexia, we used receiver operating characteristic (ROC) analysis with area under the curve (AUC). **Results:** A total of 200 patients were consented and 171 were included in final analysis. There were 110 cases and 61 controls. Mean age of cases was 68 years and of controls 62 years (p=0.003). 64% of cases were males as opposed to 30% in controls (p <0.001). There was no significant difference in race between the groups. Cancer types included lung, gastro-intestinal, breast and other cancers in both cases and controls. Mean plasma Hsp90α at diagnosis was significantly higher in cases 40.60 ng/mL than in controls 32.47 ng/mL (p < 0.001). On up to one year follow up (6 visits total) the mean Hsp90α remained significantly elevated in cases as compared to controls (p <0.001). Mean Hsp90α levels among cases was highest in patients with GI cancers (49.98 ng/mL) followed by Lung cancer (40.67 ng/mL) and other cancer types (27.92 ng/mL), p <0.001. Based on ROC analysis, Hsp90α level of ≥35 ng/mL has AUC of 94% for differentiating cancer patient with cachexia from those without cachexia. When stratified by sex, Hsp90α ≥35 ng/mL remained significantly higher in cases than in controls for both men and women (p<0.001). **Conclusions:** Hsp90α is a blood-based biomarker that is significantly elevated in cancer patients with cachexia as opposed to those without cachexia. Plasma Hsp90α ≥35 ng/mL accurately identifies cancer patients with cachexia and represents a promising biomarker for cancer cachexia both in clinical care and research. Research Sponsor: U.S. National Institutes of Health; National Center for Advancing Translational Sciences (NCATS); Biostatistics/ Epidemiology/ Research Design (BERD) component of the Center for Clinical and Translational Sciences (CCTS) awarded to the University of Texas Health Science Center at Houston, Texas.

Distribution of Hsp90α amongst case-control based on optimal cutoff (≥35 ng/mL).			
Variable	Study group	Cutoff category	Number of patients
Hsp90	Case	< 35	20
Hsp90	Case	≥ 35	90
Hsp90	Control	< 35	61
Hsp90	Control	≥ 35	0

Tele-nutritional collaborative care in patients with stage IV gastrointestinal cancer receiving chemotherapy: A randomized clinical trial.

Shihong Xu, Jitao Zhou, Tingting Dai, Fu Ming; Department of Biotherapy, Cancer Center, West China Hospital, Chengdu, China; Division of Abdominal Tumor Multimodality Treatment, Department of Radiation Oncology, State Key Laboratory of Biotherapy and Cancer Center, West China Hospital, Sichuan University, Chengdu, Sichuan, China; Department of Clinical Nutrition, West China Hospital, Sichuan University, Chengdu, China

Background: Cancer cachexia is characterized by systemic inflammation and progressive muscle loss, fundamentally compromising quality of life (QOL) and overall survival. While early nutritional intervention is imperative, patients in resource-constrained regions like Western China often lack timely access. We conducted the tele-nutrition collaborative care (T-NICE) trial to evaluate the efficacy of a hybrid remote care delivery model for patients with stage IV gastrointestinal cancer undergoing chemotherapy. **Methods:** This randomized clinical trial was conducted at West China Hospital. Patients with histologically confirmed stage IV gastrointestinal cancer (esophageal, gastric, or colorectal) were randomly assigned (1:1) to the T-NICE intervention versus Standard Nutrition Care (SNC). The T-NICE group received a collaborative hybrid telecare model involving a lean team (dietitian and social worker), comprising an initial in person education followed by app-based monitoring and adaptive telephone counseling. **Primary Endpoint:** The incidence of cancer cachexia (defined as involuntary weight loss $>5\%$, or $>2\%$ if BMI <20 kg/m²) over 6 months. **Secondary Endpoints:** Longitudinal changes in nutritional status (PG-SGA, NRS 2002) and body weight. **Exploratory end points** included the QOL (using the EORTC QLQ-C30), psychology characteristics (using DT, PHQ-9 and HADS) and caregiver burden (using ZBI). Assessments were conducted at monthly intervals through the six months endpoint. **Results:** A total of 160 patients were enrolled (80 to T-NICE, 80 to SNC). Cachexia incidence was significantly lower in T-NICE vs. SNC (22.4% VS. 60.8%; adjusted odds ratio [aOR], 0.18; 95%CI, 0.09–0.37; $P < .001$). After six months, weight stabilized in T-NICE group compared to loss in SNC (mean change, +0.86kg [95% CI, -0.20–1.93] VS -3.61 kg [95% CI, -4.70 to -2.52]), resulting in a mean difference of -4.56 kg (95% CI, -5.73 to -3.39; $P < .001$). The T-NICE group also had lower PG-SGA scores (5.10 [95%CI, 4.14–6.06] VS 6.50 [95%CI, 5.54–7.46]; $P = .015$). T-NICE participants had higher EORTC QLQ-C30 Global Health scores (74.42 vs. 66.67; $P = .004$) and improved various functional status. Psychological benefits and reduced caregiver burden were also observed. **Conclusions:** The T-NICE trial demonstrated that an integrated tele-nutrition model significantly reduced cachexia incidence, improved QOL, nutritional status, psychology status and alleviated caregiver burden. Key strengths included the model's scalability and low staffing requirements, maximizing resource efficiency while delivering substantial clinical benefits. Clinical trial information: NCT06332664. Research Sponsor: None.

A mediation analysis of neurocognitive deficits and patient-reported mood among patients with lung cancer with brain metastases.

Mary Catherine Boulanger, Stephen Lo, Daniel Chiu, Kelcie Willis, Lindsey Hofflander, Deborah Anne Forst, Nancy Wang, Florence Keane, Joseph Greer, Jennifer S. Temel, Laura A. Petrillo; Massachusetts General Hospital, Boston, MA; Department of Psychiatry, Mass General Brigham; Harvard Medical School, Boston, MA; Division of Hematology and Oncology, Department of Medicine, Massachusetts General Hospital; Harvard Medical School, Boston, MA

Background: Advances in lung cancer therapeutics have led to a growing population of patients with lung cancer who are facing the challenges of living with the sequela of brain metastases and the therapies used to treat them. Patients experience neurocognitive deficits, difficulties with functioning, and mood symptoms. However, the mechanisms by which neurocognitive deficits contribute to mood symptoms in this patient population remain to be fully elucidated. In this study, we aimed to evaluate patient-reported functioning as a mediator between neurocognitive deficits and mood symptoms. **Methods:** Using a prospectively collected single-site registry, we conducted an exploratory cross-sectional study among patients with lung cancer with brain metastases at the time of evaluation for stereotactic radiosurgery. The registry included data on patient demographic and clinical characteristics, neurocognitive deficits per clinician exam (visual impairment, cranial nerve deficit, sensory deficit, motor deficit, gait impairment/incoordination, decline in ability to concentrate, decline in memory), and patient-reported functioning (self-care, usual activities, mobility) and mood symptoms (anxiety/depression) from the European Quality of Life 5-Dimensions 3-Level Version. First, we selected functional domains significantly associated with mood symptoms in a logistic regression analysis to test as potential mediators. Then, we used a regression-based path analysis to test the selected functional domain as a mediator between neurocognitive deficits and mood symptoms. The mediation model adjusted for age, performance status, tobacco use, extracranial disease status, prior brain surgery, and prior brain radiation. **Results:** Of 463 patients, 33.9% demonstrated any neurocognitive deficit, 38.7% self-reported any functional difficulty (self-care, usual activities, or mobility), and 15.3% reported mood symptoms. Difficulty with usual activities was associated with increased mood symptoms (OR=1.65, 95% CI=1.36, 1.97), which we then tested as a mediator. Motor deficits (OR=1.66, 95% CI=1.30, 2.38) and gait impairment/incoordination (OR=1.50, 95% CI=1.19, 2.09) had positive indirect effects on mood symptoms (i.e. increased mood symptoms) through difficulties with usual activities. No other neurocognitive deficits showed significant effects on mood symptoms. **Conclusions:** Among patients with lung cancer with brain metastases, the associations of motor deficits and gait impairment/incoordination with worsened mood are mediated by difficulties with engaging in usual activities. These findings underscore the potential for tailored supportive care, utilizing strategies from cognitive rehabilitation, palliative care and psychology, to improve patients' mood by helping them adapt to and cope with difficulties in engaging in their usual activities. Research Sponsor: None.

ASTRON (OGSG 2401): A multicenter prospective trial of ferric carboxymaltose without erythropoiesis-stimulating agents for iron deficiency anemia in patients with gastric/colorectal cancer receiving chemotherapy.

Ryohei Kawabata, Hiroki Yukami, Toshifumi Yamaguchi, Hisashi Hara, Chiaki Inagaki, Seiichiro Mitani, Masahiro Tanemura, Haruna Furukawa, Toshihiko Matsumoto, Keiji Sugimura, Hiroaki Sawai, Kiyoshi Maeda, Masaaki Motoori, Yusuke Kurioka, Shunji Endo, Shogen Boku, Yukinori Kurokawa, Toshimasa Tsujinaka, Toshio Shimokawa, Taroh Satoh; Sakai City Medical Center/Osaka Cancer Institute Center, Osaka, Japan; Cancer Chemotherapy Center, Osaka Medical and Pharmaceutical University Hospital, Takatsuki, Japan; Sakai City Medical Center, Sakai, Osaka, Japan; Kindai University, Sakai, Japan; Kindai University, Faculty of Medicine Department of Medical Oncology, Sakai, Osaka, Japan; Department of Surgery, Rinku General Medical Center, Izumisano, Osaka, Japan; Rinku General Medical Center, Izumisano, Osaka, Japan; Department of Medical Oncology, Ichinoimiya-Nishi Hospital, Aichi, Japan; Department of Gastroenterological Surgery, Kansai Rosai Hospital, Amagasaki, Hyogo, Japan; Department of Gastroenterology, Takatsuki General Hospital, Taroh, Japan; Department of Gastroenterological Surgery, Osaka Metropolitan University Graduate School of Medicine, Osaka, Japan; Department of Gastroenterological Surgery, Osaka General Medical Center, Osaka, Japan; Kochi Medical School, Nankoku, Japan; Department of Digestive Surgery, Kawasaki Medical School, Kurashiki, Kurashiki, Japan; Department of Medical Oncology, Kansai Medical University Hospital, Hirakata, Japan; Department of Gastroenterological Surgery, Osaka University Graduate School of Medicine, Suita, Japan; Izumi City General Hospital, Izumi, Japan; Department of Biostatistics, Faculty of Medicine, Wakayama Medical University, Wakayama, Japan; Center for Cancer Genomics and Precision Medicine, The University of Osaka Hospital, Suita, Japan

Background: Iron deficiency anemia (IDA) during chemotherapy for patients with gastrointestinal cancer worsens quality of life (QoL) and may compromise treatment continuity. Ferric carboxymaltose (FCM) enables high-dose intravenous iron supplementation; however, prospective data without concomitant erythropoiesis-stimulating agents (ESAs) remain limited. We conducted a multicenter prospective trial to evaluate intravenous FCM without concomitant ESAs or red blood cell (RBC) transfusion support. **Methods:** This was a multicenter prospective single-arm study. Key eligibility criteria included unresectable or recurrent gastric or colorectal cancer, ongoing chemotherapy, hemoglobin (Hb) <10.0 g/dL, and transferrin saturation (TSAT) $<20\%$. FCM was administered as three 500 mg doses at ≥ 7 -day intervals (total 1500 mg), with all doses completed within 29 days of the first infusion (Day 1). The primary endpoint was Hb improvement rate at week 8, defined as an Hb increase ≥ 1.0 g/dL from baseline without RBC transfusion. The improvement rate was tested against a threshold of 18% using a one-sided exact binomial test ($\alpha=0.05$). QoL (FACT-An and EQ-5D-5L) was analyzed using linear mixed-effects models. **Results:** Fifty-two patients were enrolled; 51 received FCM. Median age was 72 years (range 45–90). Primary tumors were gastric (71.2%) and colorectal (28.8%); ECOG PS 0/1/2 was 50.0%/46.2%/3.8%. Disease status was unresectable in 55.8% and postoperative recurrence in 44.2%. The primary tumor was present in 40.4%. Most patients (90.4%) were receiving cytotoxic chemotherapy. Baseline median Hb was 9.15 g/dL (IQR 8.50–9.50), TSAT 8.55% (IQR 5.77–12.80), and ferritin 37.6 ng/mL (IQR 17.1–179.0). The week-8 Hb improvement rate was 72.5% (37/51; 95% CI 58.3–84.1; $p<0.001$). Hb improvement rates at weeks 4 and 12 were 58.8% (30/51) and 76.5% (39/51), respectively. FACT-An total score improved at week 8 (mixed-model estimate +4.93; 95% CI 0.23–9.62; $p=0.040$). EQ-5D also improved at week 8 (estimate +6.72; 95% CI 0.98–12.46; $p=0.022$). Planned protocol treatment was completed in 49/52 patients (94.2%). No treatment-related serious adverse events or deaths were observed. **Conclusions:** FCM achieved an Hb improvement rate of 72.5% and improved QoL in patients with gastric or colorectal cancer and IDA receiving chemotherapy, with high protocol completing and no treatment-related serious adverse events. These findings support FCM as an effective and feasible option for managing IDA during chemotherapy without ESAs. Clinical trial information: jRCTs051240288. Research Sponsor: Zeria Pharmaceutical Co., Ltd.

Correlation of University of Texas Cancer Cachexia Staging (UTCCS) with clinical variables of systemic inflammation, nutritional status, and physical function in patients with cancer cachexia.

Harshit Khosla, Syed Hasan Raza Jafri, Julie Haewon Rowe, Putao Cen, Jessica Trevino Jones, Anneliese Gonzalez, Neha Maithel, Rabab Jafry, Betty Arceneaux, Shahroz Aziz, Mina Hanna, Amirali Tahanan, Yi-Ping Li, Mohammad Hossein Rahbar; University of Texas Health Science Center at Houston, Houston, TX; University of Texas, Houston, TX; The University of Texas Health Science Center at Houston (UTHealth Houston) McGovern Medical School, Houston, TX; UT San Antonio, San Antonio, TX; University of Texas Medical School at Houston, Houston, TX; University of Texas at Houston Health Science Center, McGovern Medical School, Houston, TX; Aga Khan University Hospital, Karachi, Pakistan; UT Health, Houston, TX; The University of Texas Health Science Center at Houston, Houston, TX; University of Texas Graduate School of Biomedical Sciences at Houston, Houston, TX

Background: Cancer cachexia is a heterogenous syndrome characterized by ongoing loss of skeletal mass with or without adipose tissue, that is not entirely reversible. University of Texas Cancer Cachexia Staging (UTCCS) is a recently described novel model for staging cachexia using simple clinical parameters such as body mass index (BMI), serum albumin (alb), neutrophil to lymphocyte ratio (NLR) and resting heart rate (RHR). The validity of this model to correlate with functional status, nutrition and overall survival in patients with advanced or metastatic cancer has been assessed in current study. **Methods:** In a prospective study of newly diagnosed cancer patients with stage III/IV cancers, >5% body weight loss and serum albumin < 3.5g/dL biomarkers of cachexia were identified. UTCCS was developed using 4 clinical variables namely (BMI), (Alb), (NLR) and (RHR) using quartile as cut off. Based on these variable patients were categorized into stage I, stage II or stage III cancer cachexia. Blood biomarkers, dietary assessment and functional status were estimated. Kaplan-Meier survival curves were generated for patients in each stage. **Results:** Cancer distribution amongst 110 patients included lung cancer (n=50), GI cancers (n=42) and other cancers (n= 18). Cachexia stage distribution in patients was assessed (stage I= 45%, stage II =36% and stage III=18%). Patients with stage III cachexia had statistically significantly lower ECOG performance status (p=0.006), higher inflammatory state as measured by advanced lung cancer inflammation index (p<0.001), lower simplified nutritional appetite questionnaire (SNAQ score) (p=0.01), lower skeletal muscle index (p=0.03) and 30 seconds chair rise time (p<0.001). Median overall survival (OS) for stage I was 12.7 months, stage II 7.1 months and stage III 3.5 months (p=0.047). **Conclusions:** UTCCS system is a novel way of estimating the severity of cancer cachexia and correlates with inflammatory, dietary and functional parameters expected in patients with increasing severity of cancer cachexia. Research Sponsor: None.

A retrospective cohort studying integrative palliative care in a community oncology practice: Impact and outcomes.

Summiya Nasim, Molly Jain, Madeline Ku, Peyton Clouse, Joseph William McCollom; Parkview Hospital Randallia, Fort Wayne, IN; Indiana University School of Medicine, Fort Wayne, IN; Parkview Cancer Institute, Fort Wayne, IN

Background: Embedding palliative care within oncology practice supports symptom management and shared decision-making; however, its impact on real-world healthcare utilization and end-of-life planning is less well characterized. In 2018, a dedicated palliative oncology service was implemented at a Midwestern community cancer institute. We evaluated whether this integrated model was associated with differences in healthcare utilization, hospice referral, and advance care planning (ACP) compared with standard oncology care prior to implementation. **Methods:** We conducted an IRB-approved retrospective cohort study of adults with cancer treated at a single institution. Two age-, stage-, and histology-matched cohorts were identified: patients treated after implementation of the embedded palliative oncology service (2018–2021; Cohort A, n=300) and patients treated prior to implementation (2012–2017; Cohort B, n=300). Clinical data were extracted from the electronic medical record. Outcomes included emergency department (ED) visits, inpatient and ICU admissions, inpatient and ICU length of stay, hospice referral, and documented ACP. Continuous variables were compared using two-sample t-tests and categorical variables using χ^2 tests ($\alpha=0.05$). Post-hoc power analyses were performed for outcomes demonstrating between-group differences. **Results:** Both cohorts were predominantly White (88% in Cohort A vs 93% in Cohort B) with a slight difference in mean age (70.8 vs 75.0 years). Cohort A included a higher proportion of patients with stage III–IV disease (74% vs 53%, $p\leq 0.05$). Compared with standard oncology care, the integrated palliative oncology model was associated with a higher mean number of ED visits (4.1 vs 3.0, $p<0.05$). There were no significant differences in inpatient admissions, ICU admissions, or inpatient length of stay between groups. Hospice referral and ACP documentation occurred significantly more frequently in Cohort A (both $p<0.05$). Post-hoc analyses demonstrated adequate power (>80%) to detect observed differences in ED utilization, hospice referral, and ACP documentation. **Conclusions:** Implementation of an integrated palliative oncology service was associated with increased ED utilization alongside substantially higher rates of hospice referral and ACP documentation, without an accompanying increase in hospital or ICU admissions or length of stay. These findings suggest that embedded palliative oncology may promote earlier end-of-life planning while maintaining stable inpatient utilization. Prospective studies are needed to better understand drivers of ED use and to further refine integrated palliative oncology care models. Research Sponsor: None.

Behavioral predictors of pain control among adult cancer survivors: Examining the impact of smoking, physical activity, and alcohol consumption.

Clifford A. Atuari, Danny Hadidi, Fatemeh Alibeiki, Joseph George Sokhn; St. Luke's Hospital, Chesterfield, MO

Background: Cancer-related pain remains a prevalent and debilitating symptom among adult cancer survivors, substantially impairing quality of life. While pharmacologic therapies are central to pain management, growing evidence suggests that modifiable lifestyle behaviors may influence pain outcomes. This study examined the association between smoking status, alcohol consumption, physical activity, and pain control among adult cancer survivors in the United States. **Methods:** We conducted a cross-sectional analysis using data from the 2022 Behavioral Risk Factor Surveillance System (BRFSS), a nationally representative survey of U.S. adults. The study population included adults aged ≥ 18 years with a history of cancer who reported physical pain attributable to cancer or its treatment. The primary outcome was self-reported pain control (controlled vs uncontrolled). Primary predictors included smoking status (current, former, never), heavy alcohol consumption (men >14 drinks/week; women >7 drinks/week), and physical activity in the past 30 days outside of regular employment. Multivariable logistic regression models were used to estimate odds ratios (ORs) with adjustment for age, sex, race/ethnicity, educational attainment, and household income. Sampling weights were applied to account for the complex survey design. **Results:** A total of 1,380 cancer survivors with cancer-associated pain were included. Most participants were aged ≥ 60 years (62.4%), female (63%), and non-Hispanic White (78.9%). Overall, 76% reported controlled pain, while 24% reported uncontrolled pain. Compared to current smokers, participants who had never smoked had significantly lower odds of having uncontrolled pain (OR=0.45; 95% CI 0.25 – 0.81, $p=0.001$). Former smokers had a 41% lower odds of having uncontrolled pain than current smokers (OR=0.59; 95% CI 0.33 – 0.94, $p=0.04$). Heavy alcohol consumption was not significantly associated with pain control (OR=1.03, 95% CI 0.48 – 2.21, $p=0.94$). Physical inactivity was significantly associated with poorer pain outcomes; participants who were inactive in the past 30 days had 72% higher odds of uncontrolled pain compared with those who engaged in physical activity (OR=1.72, 95% CI 1.11 – 2.67, $p=0.01$). **Conclusions:** Smoking and physical inactivity are significantly associated with poor pain control among adult cancer survivors. Incorporating smoking cessation and exercise promotion into survivorship care plans may enhance pain management and overall quality of life among cancer survivors. Research Sponsor: None.

Utilisation of the Henry score in malignant bowel obstruction and characterisation of management approaches and outcomes: Experience from a New Zealand regional centre.

Nicole Lundon; Velindre Cancer Centre, Cardiff, United Kingdom

Background: Malignant Bowel Obstruction (MBO) is a common, life-threatening complication of advanced malignancy associated with a high symptom burden and poor prognosis. Henry et al developed the Henry Score to predict 30-day mortality in MBO patients. It has not been routinely used to guide clinical decision-making regarding the management of MBO or validated in populations outside the United States of America. This study was designed to assess the utility of the Henry Score in predicting 30-day mortality in palliative patients presenting to hospital with malignant bowel obstruction in a New Zealand regional centre and to characterise the management approaches and outcomes of surgical versus non-surgical interventions. **Methods:** Retrospective cohort study of 235 patients admitted with MBO to Palmerston North Hospital (2010–2024). The Henry Score (0–5) incorporating five clinical and laboratory factors was calculated for each patient. Management approaches and survival outcomes were analysed. **Results:** Complete Henry Score data was available for 82.1% of patients. Sixty-four underwent surgical management, 171 non-surgical interventions. Median overall survival was 82.5 days (surgical: 130.5 days; non-surgical: 52 days; $p=0.005$). The 30-day mortality rate was 33.2%. The Henry Score demonstrated prognostic discrimination, with 30-day mortality of 28.0% for low scores (0–2) vs 43.0% for high scores (3–5) ($p=0.034$), and corresponding median survivals of 83 vs 39 days. Cox analysis identified hypoalbuminemia as the only factor significantly associated with mortality risk (HR 1.67, $p=0.001$). Māori patients had higher Henry Scores (68.2% vs 41.9% with scores ≥ 3 , $p=0.025$) and shorter median survival (37 vs 97.5 days) than New Zealand European patients. **Conclusions:** The Henry Score effectively predicts 30-day mortality in MBO patients in New Zealand. Higher scores were associated with increased 30-day mortality, supporting the potential use of this measure for prognostication and advanced care planning. Hypoalbuminemia was the strongest predictor of mortality. Future prospective studies are needed to determine if clinical implementation of the Henry Score improves patient outcomes. Research Sponsor: None.

Genetic associations with chemotherapy-induced nausea and vomiting: A genome-wide association study.

Aasha I. Hoogland, Martine Extermann, Arshiya Mariam, Daniel Miller Rotroff, Taylor Welniak, Oanh Nguyen, Yvelise Rodriguez, Xiaoyin Li, Brent Small, Stacy Fischer, Kristen Carpenter, Daneng Li, Anita Kinney, Donna L. Berry, Heather S.L. Jim; H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL; Cleveland Clinic Lerner Research Institute, Cleveland, OH; Cleveland Clinic, Cleveland, OH; The University of North Carolina at Chapel Hill, Chapel Hill, NC; University of Colorado Anschutz, Aurora, CO; The Ohio State University, Columbus, OH; City of Hope National Comprehensive Cancer Center, Duarte, CA; Rutgers Cancer Institute, New Brunswick, NJ; University of Washington School of Nursing, Seattle, WA; Department of Health Outcomes and Behavior, H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL

Background: Nausea and vomiting affect up to 80% of patients treated with chemotherapy, and the costs of healthcare utilization due to chemotherapy-induced nausea are estimated to cost over \$6 billion each year in the United States. Existing antiemetic regimens targeting 5-HT₃ and NK₁ antagonists are suboptimal, as up to 40% of continue to report nausea despite antiemetic treatment. Further, existing risk prediction algorithms have poor discrimination.

Methods: In this original research study, we conducted a genome-wide association study of genetic factors associated with patient- and clinician-reported nausea and vomiting at 24 hours after infusion (acute) and 5 days after infusion (delayed) in patients treated with moderately- or highly-emetogenic chemotherapy. Participants were recruited from five ORIEN centers: City of Hope, Moffitt Cancer Center, Ohio State University, Rutgers University, and University of Colorado-Denver. Patient-reported CINV was assessed using the MASCC Anti-emesis Tool and clinician-reported CINV was assessed using Common Terminology Criteria for Adverse Events (CTCAE) ratings. The study cohort was divided into a training set (70% of the sample) and a test set (30% of the sample). Machine learning was used to evaluate the predictive performance of a polygenic score along with clinical variables, over and above models with clinical variables only. Areas under the curve (AUC) were used to compare the accuracy of each predictive model. **Results:** Participants (n=1,271) were 58 years of age on average (SD=13), and most were female (74%), White (97%), with breast cancer (41%). Half of participants (50%) had early stage cancer and most were treated with a guideline-concordant prophylactic regimen (70%). Any acute and delayed self-reported nausea was reported by 42% and 70% of participants, respectively. For acute nausea, one gene, *C12orf50*, met the threshold for suggestive significance ($P = 4.58 \times 10^{-6}$). For vomiting, the presence of the G allele at rs9712639 (nearest gene: *OR7E23P*) was linked to an increased likelihood of clinician-reported acute vomiting ($P = 1.83 \times 10^{-8}$). A further 11 SNPs reached the threshold for suggestive significance and were associated with both acute and delayed vomiting reported by clinicians; these were mapped to the *FTLP18* gene. Polygenic scores did not improve predictive risk models based on clinical factors only. **Conclusions:** Results of our GWAS indicate that there are different genetic associations for acute and delayed nausea and vomiting, suggesting potentially distinct genetic factors underlying each outcome. However, regardless of outcome, genetic information did not significantly improve models predicting the development and intensity of CINV. Research Sponsor: National Cancer Institute; R01CA219389.

Early outpatient palliative care for patients with multiple myeloma: A randomized pilot study.

Breffni Hannon, Samantha Lo, Criselda Isabel Cenizal, Timo Carpen, Lisa W. Le, Vanessa Shao, Dior Caruso, Sita Bhella, Vishal Kukreti, Guido Lancman, Keith Stewart, Suzanne Trudel, Chloe Yang, Nicolas Chin-Yee, Christine Chen, Camilla Zimmermann; Princess Margaret Cancer Centre, Toronto, ON, Canada; Princess Margaret Cancer Centre, University Health Network, Toronto, ON, Canada; Princess Margaret Hospital, Toronto, ON, Canada; Princess Margaret Cancer Centre, UHN, Toronto, ON, Canada; Division of Medical Oncology & Hematology, Princess Margaret Cancer Centre, Toronto, ON, Canada; Princess Margaret Cancer Centre, University of Toronto, Toronto, ON, Canada

Background: Early palliative care is recommended for patients with advanced or incurable cancer. Despite these recommendations, patients with multiple myeloma are often referred late to palliative care, or not at all. We assessed the feasibility of an early outpatient palliative care intervention for patients with multiple myeloma. **Methods:** English-speaking adults (≥ 18 years) with newly-diagnosed or relapsed multiple myeloma and at least one symptom scored $\geq 3/10$ on the revised version of the Edmonton Symptom Assessment System (with constipation and sleep added, ESAS-rCS) were recruited from multiple myeloma outpatient clinics at the Princess Margaret Cancer Centre, Toronto, Canada. Participants were randomized to routine outpatient care from their multiple myeloma team (usual care arm), or to monthly in-person or virtual interdisciplinary outpatient palliative care clinic visits for 3 months alongside usual multiple myeloma care (intervention arm). The primary outcome was feasibility (recruitment of 40 patients/12 months; $\geq 60\%$ completion of patient-reported outcome measures monthly for 3 months; $\geq 60\%$ of those randomized to the intervention arm attending ≥ 1 palliative care clinic visit). Exploratory efficacy outcomes were measured at 1-, 2- and 3-months (primary endpoint), including quality of life (FACIT-Pal, primary efficacy outcome), symptom burden (ESAS-rCS), mood (PHQ-9) and satisfaction with care (FAMCARE-P16). **Results:** Of 40 patients recruited within 12 months (median age 66.5 years [range 33–92]; 17 [42.5%] female), 21 were randomized to the intervention arm and 19 to usual care. The 1-, 2- and 3-month completion rates among all participants for all measures were 37/39 (94.9%), 36/39 (92.3%), and 33/38 (86.8%), respectively; one intervention arm participant withdrew and one died during the study period. In the intervention arm, 17/21 (80.9%) attended at least one palliative care clinic visit; in the usual care arm, 3/19 (15.8%) were referred to the palliative care clinic during the study period. The mean difference (B) in change in the FACIT-Pal total score at 3-months from baseline between the intervention and usual care arm was 15.5 (standard error [SE] 8.8, $p=0.09$) after adjusting for baseline scores. The change in ESAS-rCS total distress scores at 3-months was improved in the intervention arm compared with usual care (adj. B = -13.7 [SE 5.4], $p=0.02$), as were individual symptom scores for drowsiness (adj. B = -2.1 [SE 0.9], $p=0.02$), constipation (adj. B = -2.1 [SE 1.0], $p=0.03$) and sleep (adj. B = -3.6 [SE 0.8], $p=0.0002$). Changes in PHQ-9 and FAMCARE-P16 total scores at 3-months did not differ between study arms. **Conclusions:** This pilot trial demonstrated that a larger randomized controlled trial of early palliative care versus usual care for patients with multiple myeloma is feasible. Preliminary results are encouraging for improvements in symptom burden and quality of life. Clinical trial information: NCT06485076. Research Sponsor: Helga and Antonio De Gasperis Grand Challenges Clinical Trials in Myeloma.

Using IPOS to trigger advance care planning in outpatient palliative oncology: A multicenter real-world study.

Sarah Ananda Gomes, Flavia Santos Dumont Sorice, Renata Ferrari, Pamela Carvalho Muniz, Maria Helena Cruz Rangel da Silva, Mariana Laloni, Carlos Gil Moreira Ferreira, Bruno Lemos Ferrari, Cristiane Decat Bergerot; Oncoclinicas & Co - Medica Scientia Innovation Research (MEDSIR), Sao Paulo, Brazil; Oncoclinicas&Co - Medica Scientia Innovation Research (MEDSIR), Sao Paulo, Brazil; Oncoclinicas, São Paulo, Brazil; Oncoclinicas & Co - Medica Scientia Innovation Research (MEDSIR), São Paulo, Brazil

Background: Advance care planning (ACP) is central to high-quality palliative oncology care; however, in Brazil, ACP is not routinely integrated into clinical practice, making timely patient identification challenging. Patient-reported outcomes, such as the Integrated Palliative Outcome Scale (IPOS), may support earlier and more structured ACP discussions. This study evaluated whether IPOS, alone or combined with functional status and follow-up time, can identify patients undergoing ACP in outpatient palliative oncology. **Methods:** This multicenter, observational study used real-world data from a national Brazilian program across eight states. Adult patients with cancer who completed the IPOS at program entry were included. Functional status was assessed using the Palliative Performance Scale (PPS). ACP was defined as documented initiation during follow-up. Logistic regression models evaluated associations between IPOS domains, PPS, and ACP, adjusting for follow-up time. Discrimination was assessed using receiver operating characteristic (ROC) curves based on predicted probabilities from the final model. **Results:** A total of 1,301 patients were included (median age 68 years; SD 15.4), of whom 61.4% were female. The most common cancer types were gastrointestinal (30.3%), breast (16.6%), genitourinary (12.3%), and lung (11.9%). ACP was initiated in 32.1% of patients during follow-up. Median baseline IPOS total score was 22 (SD 10.1) and median PPS at entry was 70 (SD 15.7). Median follow-up time was 11.3 weeks (SD 20.2). Baseline IPOS total score did not discriminate ACP initiation (AUC 0.48), while functional status showed modest inverse discrimination (AUC 0.59). Time in palliative care demonstrated higher standalone discrimination (AUC 0.64). A multivariable model combining functional status, selected IPOS symptom and psychosocial domains, and follow-up time significantly improved discrimination for ACP (AUC 0.66; 95% CI 0.63–0.69). **Conclusions:** IPOS total score alone does not function as a screening tool for ACP initiation. However, when combined with functional status and longitudinal exposure to palliative care, IPOS symptom and psychosocial domains meaningfully improve identification of patients undergoing ACP. These findings support the use of IPOS as a structured clinical trigger to guide timely ACP discussions in outpatient palliative oncology. Research Sponsor: None.

Early symptom signals preceding end-of-life decline in outpatient palliative oncology.

Flavia Santos Dumont Sorice, Sarah Ananda Gomes, Graziella Eugenio Tocaundo, Lais Luana de Souza Almeida, Renata Rocha da Silva, Juliana Marinho Pinheiro, Camila Nogueira, Karolina da Silva Ferracin, Alexandra Mendes Barreto Arantes, Julia Alvarenga Petrocchi, Hugo Mourao Oliveira, Laura Pessoa Londe de Oliveira, Renata Ferrari, Elaine Cristina de Paula Silva, Barbara Ribeiro Campolina Araujo, Maria Helena Cruz Rangel da Silva, Mariana Lalon, Carlos Gil Moreira Ferreira, Bruno Lemos Ferrari, Cristiane Decat Bergerot; Oncoclinicas & Co - Medica Scientia Innovation Research (MEDSIR), Sao Paulo, Brazil; Oncoclinicas&Co - Medica Scientia Innovation Research (MEDSIR), Sao Paulo, Brazil; Oncoclinicas&Co - Medica Scientia Innovation Research (MEDSIR), Sao Paulo, Brazil; Oncoclinicas & Co - Medica Scientia Innovation Research (MEDSIR), Sao Paulo, SP, Brazil; Oncoclinicas&Co - Medica Scientia Innovation Research (MEDSIR), São Paulo, Brazil; Oncoclinicas & Co - Medica Scientia Innovation Research (MEDSIR), São Paulo, Brazil

Background: Timely recognition of clinical decline is challenging in palliative oncology. Symptom trajectories that precede global deterioration are unclear. We aimed to characterize longitudinal changes in total and domain-specific Integrated Palliative Outcome Scale (IPOS) scores and identify early indicators of decline in outpatient palliative oncology care (OPOC). **Methods:** We conducted a longitudinal study within an OPOC embedded in Brazil. Adults with advanced cancer enrolled for ≥ 6 months were included. IPOS was assessed at baseline, 3 months, 6 months, and the month of death. Paired comparisons evaluated changes in total IPOS scores and individual domains between baseline–3 months and 6 months–month of death. Clinically relevant decline was defined as worsening between 6 months and death. Logistic regression examined associations between IPOS decline, chemotherapy use near death, and place of death. **Results:** Among 126 patients (mean age 64.1 [SD 14.4]; 62.7% women), gastrointestinal (33.3%), breast (19.8%), and lung cancers (11.1%) were most common. At program entry, mean PPS was 65 (SD 13.5). Total IPOS scores improved from baseline to 3 months (mean difference 2.69, $p=0.007$). However, a marked deterioration occurred between 6 months and the month of death (mean difference -3.98 , $p<0.001$). Domain-level analyses demonstrated early improvement in appetite loss (mean 1.56 to 1.28, $p=0.020$) and weakness (1.91 to 1.64, $p=0.034$) from baseline to 3 months, followed by significant worsening as death approached (appetite: 1.42 to 1.75, $p=0.006$; weakness: 1.94 to 2.25, $p=0.003$). Anxiety increased significantly between 6 months and the month of death (1.99 to 2.23, $p=0.008$), whereas pain and depressive symptoms remained relatively stable over time. Neither chemotherapy use in the last 30 days of life (OR 0.78, $p=0.58$) nor place of death (OR 0.56, $p=0.21$) was associated with clinically relevant IPOS decline. **Conclusions:** OPOC is associated with early symptom stabilization, followed by a predictable phase of accelerated deterioration near death. Appetite loss and weakness emerge as early and clinically meaningful indicators of decline within the terminal trajectory, independent of treatment or place of death. Routine longitudinal IPOS monitoring may facilitate earlier recognition of impending decline and support more proactive, patient-centered palliative care. Research Sponsor: None.

Prognostic stratification using baseline objective clinical information in patients with stage IV lung cancer receiving best supportive care alone as initial treatment: A multicenter retrospective study (WJOG20824L).

Shunichi Kataoka, Takehito Shukuya, Kentaro Sakamaki, Taichi Miyawaki, Daichi Fujimoto, Hidetoshi Hayashi, Yukihiro Toi, Toshihide Yokoyama, Terufumi Kato, Teppei Yamaguchi, Kaoru Tanaka, Junko Baba, Motohiro Tamiya, Motoko Tachihara, Kohei Otsubo, Yuki Sato, Satoshi Ikeda, Nobuyuki Yamamoto, Hirotsugu Kenmotsu, Kazuhisa Takahashi; Department of Respiratory Medicine, Juntendo University Graduate School of Medicine, Tokyo, Japan; Faculty of Health Data Science, Juntendo University, Tokyo, Japan; Department of Respiratory Medicine, Juntendo University Hospital, Tokyo, Japan; Hyogo Medical University, Nishinomiya, Japan; Department of Medical Oncology, Kindai University Faculty of Medicine, Osaka-Sayama, Japan; Department of Pulmonary Medicine, Sendai Kousei Hospital, Sendai, Japan; Department of Respiratory Medicine, Kurashiki Central Hospital, Kurashiki, Japan; Department of Thoracic Oncology, Kanagawa Cancer Center, Yokohama, Japan; Aichi Cancer Center, Nagoya, Japan; Kindai University Faculty of Medicine, Osaka, Japan; Department of Internal Medicine, Niigata Cancer Center Hospital, Niigata, Japan; Osaka International Cancer Institute, Osaka, Japan; Department of Oral and Maxillofacial Surgery, Kobe University Hospital, Kobe-Shi, Japan; Kitakyushu Municipal Medical Center, Kitakyushu, Japan; Department of Respiratory Medicine, Kobe City Medical Center General Hospital, Kobe, Japan; Department of Respiratory Medicine, Kanagawa Cardiovascular and Respiratory Center, Yokohama, Japan; Internal Medicine III, Wakayama Medical University, Wakayama, Japan; Shizuoka Cancer Center, Shizuoka, Japan; Department of Respiratory Medicine, Juntendo University Faculty of Medicine and Graduate School of Medicine, Tokyo, Japan

Background: Despite expanded systemic therapy for lung cancer, best supportive care (BSC) alone remains the initial treatment for some patients, often due to advanced age, poor performance status (PS), or comorbidities. However, large-scale data on prognostic heterogeneity and risk stratification in this population are limited. We aimed to stratify overall survival (OS) in stage IV lung cancer patients initially managed with BSC alone using baseline clinical information. **Methods:** We analyzed a multicenter database from WJOG15121L including 6,751 patients with stage IV lung cancer diagnosed between January 2016 and December 2019, identifying those who received BSC alone as initial treatment. Sixty-two baseline variables (demographics, comorbidities, genomic alterations, and laboratory data) were assessed. The primary analysis was conducted in complete cases (BSC complete cohort), with multiple imputation (MI) in the entire cohort as sensitivity analysis. A boosting-based model was used to derive a prognostic risk score for OS and to stratify patients into low-, medium-, and high-risk groups based on the risk score distribution. Survival outcomes were summarized using Kaplan–Meier methods with log-rank tests. Cox regression with Lasso regularization (Cox-Lasso) was also performed as an alternative approach to assess robustness. **Results:** A total of 923 patients received BSC alone as initial treatment; 266 comprised the BSC complete cohort. The BSC population was elderly (mean age: 75.8 years) with a high proportion of poor PS (ECOG PS ≥ 2 : 74.8%). Kaplan–Meier–based risk stratification separated OS (median OS: 277 vs 74 vs 25 days for low-, medium-, and high-risk groups, respectively). The Kaplan–Meier–estimated 90-day OS rates were clearly separated across the three groups (75.4% vs 29.8% vs 0%; log-rank $p < 0.001$). Baseline characteristics differed by risk group, including PS and metastatic burden (e.g., liver metastasis). Risk stratification was largely driven by routinely available laboratory markers (e.g., LDH, neutrophil count, CRP, ALP, platelet count). Findings were consistent in the MI-based sensitivity analysis and were broadly supported by the Cox-Lasso approach. **Conclusions:** Among patients with stage IV lung cancer initially managed with BSC alone, outcomes are heterogeneous and can be stratified into clinically meaningful risk groups using baseline clinical information. Kaplan–Meier summaries (median OS and 90-day OS) demonstrate marked differences across risk strata, and the dominant contribution of routine laboratory variables highlights the potential practicality of this approach in real-world settings. Further validation and comparative analyses with patients receiving systemic therapy who share similar risk profiles are ongoing. Research Sponsor: None.

A first-in-human (FiH) phase I study of GFS202A, a GDF15/IL-6 bispecific antibody, in advanced cancer patients (pts) with pre-cachexia or cachexia.

Hongyun Zhao, Da Li, Yuxiang Ma, Hong Zong, Yusheng Wang, Xiangcai Wang, Haiyu Yang, Zhen Li, Qian Chu, Yue Shan, Lingyu Tai, Jiani Song, Yue Zhang, Huaqiang Zhu, Haige Shen, Yu Wang, Li Zhang; Sun Yat-sen University Cancer Center, Guangzhou, China; Sir Run Run Shaw Hospital, School of Medicine, Zhejiang University, Hangzhou, China; Sun Yat-sen University Cancer Center, Guangzhou, Guangdong, China; The First Affiliated Hospital of Zhengzhou University, Zhengzhou, China; First Hospital of Shanxi Medical University, Taiyuan, China; The First Affiliated Hospital of Gannan Medical University, Ganzhou, China; The First Affiliated Hospital of Gannan Medical College, Ganzhou, China; Linyi Cancer Hospital, Linyi, China; Department of Oncology, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China; GenFleet Therapeutics (Shanghai) Inc., Shanghai, China

Background: Cachexia is a common syndrome in cancer pts, associated with weight loss, impaired quality of life, and poor treatment outcomes. GDF15, a pleiotropic factor of TGF- β super family, has been verified to be correlated with cancer cachexia and anorexia. IL-6 contributes to cancer cachexia progression via both central and peripheral pathways. GFS202A, a first-in-class bispecific antibody dual-targeting GDF15 and IL-6, improves symptoms in preclinical cachexia models with lean body mass and adipose tissue weight increased. Here, we report the preliminary data from the ongoing FiH study of GFS202A. **Methods:** This is the FiH phase I study (NCT06898255) of GFS202A in advanced cancer pts with pre-cachexia or cachexia. Eligible pts are required to have weight loss in the six months prior to the first dose and decreased appetite, with or without anticancer therapy. Enrolled pts will receive GFS202A Q3W at a starting dose of 5 mg for a 12-week treatment period, followed by a 12-week follow-up period. An accelerated titration design, combined with the Bayesian Optimal Interval (BOIN) and backfilling design, is employed. The primary objectives are to assess safety and determine the recommended dose ranges for future clinical studies. The secondary and exploratory objectives include characterization of PK profiles, PD biomarkers, preliminary efficacy and exploratory biomarkers. **Results:** Data cutoff at Dec 26, 2025, 14 pts had received at least one dose of GFS202A ranging from 5 to 400 mg Q3W (5mg: N=1; 25mg: N=4; 100mg: N=4; 200mg: N=4; 400mg: N=1). The overall safety profile was favorable. No DLT was observed. Adverse events (AEs) of any cause were reported in all pts. Six pts experienced at least one treatment-related AEs (TRAEs). Only one pt had G3 hypertension assessed related to GFS202A, which alleviated during the treatment. The pt did not experience any other cardiovascular events and had no clinically meaningful changes in lipid profiles. All other TRAEs were G1. No $\geq$ 2pt experienced an identical TRAE. GFS202A exposure was approximately dose-proportional from 5–200 mg, and the mean half-life was 82–138 hours. GDF15 was not detectable immediately at the end of infusion from the 5mg cohort, and durable inhibition of GDF15 was observed from the 100mg dosing cohorts during 21-day dosing interval. CRP decreased significantly post-infusion, with suppressions sustained through Week 6 in 12 out of 13 pts in 5–200 mg Q3W groups. Weight gain was observed across different dose groups, with least-squares mean increases of 1.8, 1.5 and 2.5 kg at Week 6 in the 25, 100, and 200 mg Q3W groups, respectively. **Conclusions:** GFS202A demonstrated favorable safety and encouraging efficacy with systemic inflammation alleviated and weight gain. The data support that dual-targeting GDF15 and IL-6 is a feasible way to mitigate cancer cachexia clinically. Future studies are warranted. Clinical trial information: NCT06898255. Research Sponsor: GenFleet Therapeutics (Shanghai) Inc.

In-person versus telehealth outpatient palliative care visits in oncology: A multi-center study.

Sarah Ananda Gomes, Flavia Santos Dumont Sorice, Cecilia Emerick Mendes Vaz, Ana Maria do Amaral Ribeiro Alves, Amanda Pifano Soares Ferreira, Júlia Sá, Raquel Gouveia, Jaqueline Santos, Renata Ferrari, Natacha Silva Moz, Christopher Negrete, Rodrigo Dienstmann, Maria Helena Cruz Rangel da Silva, Mariana Laloni, Carlos Gil Moreira Ferreira, Bruno Lemos Ferrari, Rafael Duarte Paes, Cristiane Decat Bergerot; Oncoclinicas & Co - Medica Scientia Innovation Research (MEDSIR), Sao Paulo, Brazil; Oncoclinicas&Co - Medica Scientia Innovation Research (MEDSIR), Sao Paulo, Brazil; Oncoclinicas & Co.-Medica Scientia Innovation Research (MedSir), São Paulo, Brazil; Oncoclinicas & Co - Medica Scientia Innovation Research (MEDSIR), São Paulo, Brazil

Background: As telehealth becomes integral to outpatient palliative care delivery in oncology, evidence comparing consultation duration and time allocation between in-person and remote visits remains limited, especially in low- and middle-income countries. We compared consultation duration and time composition between in-person and telehealth visits after adjustment for visit type and clinical complexity. **Methods:** This observational study evaluated outpatient oncological palliative care consultations conducted between February and May 2025 across seven practices in Brazil. Total consultation time and predefined time components were recorded. Multivariable linear regression models estimated adjusted differences in consultation duration according to care modality, controlling for visit type (first appointment, follow-up, family meeting), performance status (ECOG), quality-of-life (IPOS), and number of participants. **Results:** A total of 269 consultations were analyzed, including 171 in-person and 98 telehealth visits. Care modality was associated with consultation type ($p < 0.001$): telehealth was less frequently used for first consultations (15% vs. 35%) and more frequently used for follow-up visits (76% vs. 63%) and family meetings (9% vs. 3%). Telehealth visits involved patients with worse performance status (ECOG 3-4: 36% vs. 17%; $p=0.007$) and poorer quality of life (higher IPOS distribution; $p=0.037$). In unadjusted analyses, telehealth consultations were shorter than in-person visits, particularly for follow-up visits. After multivariable adjustment, telehealth visits remained independently and significantly shorter by a mean of 10.5 minutes (95% confidence interval [CI] -15.6 to -5.4; $p<0.001$). Follow-up consultations were consistently shorter than first consultations by 19.4 minutes (95% CI -24.9 to -14.0; $p<0.001$), regardless of care modality, while family meetings showed no difference in duration compared with first consultations (95% CI -13.8 to 8.9; $p=0.70$). Each additional healthcare provider was associated with a 2.9 minute increase in consultation time (95% CI 0.1 to 5.6; $p=0.04$). ECOG was not independently associated with total consultation duration. **Conclusions:** After accounting for visit type and clinical context, differences in consultation duration between telehealth and in-person are modest. Telehealth was preferentially used for follow-up care and among patients with poorer functional status and quality of life, while preserving consultation complexity when clinically indicated. These findings support telehealth as a viable modality for outpatient palliative care delivery in resource-limited settings. Research Sponsor: None.

Phase II study of mirogabalin for oxaliplatin-associated chemotherapy-induced peripheral neuropathy in gastrointestinal cancer: The SmiliNg trial.

Reiko Ando Makihara, Hirokazu Shoji, Kengo Nagashima, Miki Chin, Toshiharu Hirose, Hidekazu Hirano, Natsuko Tsuda Okita, Atsuo Takashima, Keisuke Ariyoshi, Eriko Satomi, Ken Kato, Hironobu Hashimoto; Department of Pharmacy, National Cancer Center Hospital, Japan, Tokyo, Japan; Department of Gastrointestinal Medical Oncology, National Cancer Center Hospital, Tokyo, Japan; Biostatistics Unit, Clinical and Translational Research Center, Keio University Hospital, Tokyo, Japan; National Cancer Center Hospital, Chuo-Ku, Tokyo, Japan; Department of Data Management, Japanese Organisation for Research and Treatment of Cancer (JORTC) Data Center, Tokyo, Japan; Department of Palliative Medicine, National Cancer Center Hospital, Tokyo, Japan; Department of Pharmacy, National Cancer Center Hospital, Japan, Chuo-Ku, Tokyo, Japan

Background: Oxaliplatin is a key drug in the treatment of unresectable advanced or recurrent gastrointestinal (GI) cancers, however, chemotherapy-induced peripheral neuropathy (CIPN) often limits its use. Mirogabalin is an oral gabapentinoid that alleviates neuropathic pain by binding to the $\alpha 2\delta$ subunit of voltage-gated calcium channels, but evidence regarding the efficacy of mirogabalin for CIPN induced by oxaliplatin remains insufficient. SmiliNg trial evaluated the efficacy and safety of mirogabalin in patients with unresectable advanced or recurrent GI cancers who have oxaliplatin-associated CIPN. **Methods:** This single-center, single-arm exploratory phase II trial enrolled patients with unresectable or recurrent GI cancer who were receiving ongoing first-line oxaliplatin-based chemotherapy or continuing fluoropyrimidine-based therapy after discontinuation of oxaliplatin, and who had painful CIPN (including numbness/tingling) with a numerical rating scale (NRS) score of ≥ 4 . Mirogabalin was administered orally twice daily and titrated weekly according to Cockcroft–Gault creatinine clearance. The primary endpoint was the change in 24-hour average pain NRS from baseline to week 6. Secondary endpoints included PRO-CTCAE-assessed improvement in numbness/tingling, adverse events (CTCAE v5.0), and attainment of maintenance dose. The planned sample size was 30 patients. Clinical trial information: UMIN000049555. **Results:** Between February 2023 and April 2025, 30 patients were enrolled. The median age was 64 years (range, 36–83), with female patients accounting for 33%. The primary cancer types included colorectal (n=17), small bowel (n=7), gastric (n=6), and esophageal (n=1) cancers. The Mean baseline 24-hour pain NRS was 5.80 (SD 1.97). The mean change from baseline at week 6 was -1.46 (SD 2.66) ($p = 0.010$; 90% CI -2.35 to -0.57), thereby the prespecified primary endpoint was achieved. The proportions of ≥ 1 -point responders were 58%. On the PRO-CTCAE, the proportions of patients achieving a ≥ 1 -category improvement in worst severity were 38% and 38% at weeks 3 and 6, respectively; the corresponding proportions for interference with daily activities were 34% and 27%. Maintenance-dose attainment rates at weeks 3 and 6 were 59% and 68%, respectively. The most common adverse events were somnolence (83%) and dizziness (38%). Grade ≥ 3 adverse events comprised AST/ALT increased, and pulmonary infection, each occurring in one patient; none were related to mirogabalin treatment. **Conclusions:** This study suggests that mirogabalin is effective and well-tolerated for the management of moderate-to-severe painful CIPN during oxaliplatin-based chemotherapy. These findings warrant further evaluation in a confirmatory trial. Clinical trial information: 000049555. Research Sponsor: None.

An automated, EHR-integrated intervention system for patient-reported insomnia symptoms.

Eric S. Zhou, Eva Robinson, Michael Manni, Ann H. Partridge, Alicia K. Morgans, Kelsey Li, Hana Moles, Brittany Black, Edie Weller, Michael J. Hassett, Nadine A. Jackson; Dana-Farber Cancer Institute, Boston, MA; Boston Children's Hospital, Boston, MA; Mass General Brigham, Boston, MA

Background: Insomnia affects >20% of patients on cancer therapy. It is consistently reported to be one of the most burdensome sequelae. Systematic screening for insomnia in cancer patients is uncommon. Without identification, patients cannot access care. Unfortunately, even if insomnia is identified, most cancer centers lack on-site sleep specialists. To address both the screening and treatment gaps, we leveraged our institution's EHR-based patient-reported outcomes (PRO) data collection system to develop a fully automated solution to identify patients with insomnia, and share an evidence-based psychoeducational video intervention with them. **Methods:** Prior to established outpatient appointments at our hospital, all patients are asked to complete eSyM, an electronic PRO-CTCAE symptom assessment. Two insomnia items (symptom severity and interference) are combined to generate an insomnia score (0-3; higher is worse, with present analyses for those reporting a score ≥ 2). Patients with an elevated insomnia score were sent a patient portal message explaining they were identified as having insomnia, and offered an educational video with strategies to improve their sleep. We tracked patient engagement, as well as report of insomnia symptoms via eSyM response at the patient's subsequent appointment closest to 60 days post-Baseline (± 30 days). Data was analyzed from patients who reported completed eSyM insomnia questions at both timepoints between 02/25 to 09/25. **Results:** Patients with insomnia (N=307) were an average of 63 years old, predominantly female (63%), White (84%), married (63%), and possessed a college degree or higher (57%). They were diagnosed with a broad range of cancers (breast = 20%, GI = 15%, thoracic = 10%). The vast majority (92%) opened the patient portal message with the video link, with the video watched in entirety 498 times. Overall, insomnia scores significantly decreased from baseline ($\bar{x} = 2.3$) to follow-up ($\bar{x} = 1.9$; $p < .001$), with 42% reporting symptomatic improvement at follow-up (48% no change and 9% worse). Specifically, 41% reported either Severe or Very Severe insomnia symptoms at baseline, improving to 30% at follow-up; 37% reported insomnia interfered with their life Quite a Bit or Very Much at baseline, improving to 23% at follow-up. Multivariate analyses revealed sociodemographic characteristics (Black, Medicare, and disabled) associated with less insomnia improvement. **Conclusions:** We developed a fully automated system that leverages electronic PRO data and our EHR to identify symptomatic cancer patients with insomnia and intervene. Our findings demonstrate that we can successfully connect with patients reporting insomnia and potentially improve outcomes with a low-intensity intervention. This framework can readily be deployed to identify and address other common side effects of cancer treatment (e.g., fatigue, pain) that impair recovery and quality-of-life. Research Sponsor: American Cancer Society.

Negative effect of malignant pleural effusion on the efficacy of immunotherapy via IL-6-mediated abscopal immunosuppression in advanced non-small cell lung cancer.

Yaping Guan, Yuekai Zhang, Yue Dong, Jiang Chang, Songlin Liu, Fatao Wang, Jun Wang; Department of Oncology, The First Affiliated Hospital of Shandong First Medical University, Jinan, China; Department of Oncology, The First Affiliated Hospital with Shandong First Medical University, Jinan, China

Background: The present study is designed to determine the effect and mechanism of malignant pleural effusion (MPE) on the efficacy of immunotherapy in advanced non-small cell lung cancer (NSCLC). **Methods:** We identified patients with advanced NSCLC who underwent immunotherapy as a first-line or second-line regimen in multiple cohorts. The objective response rate (ORR), disease control rate (DCR), progression-free survival (PFS), and overall survival (OS) were analyzed. Using a mouse model with MPE, we determined whether MPE could affect the efficacy of immunotherapy and investigated the mechanism of MPE-related immunosuppression. **Results:** In a cohort with 269 advanced NSCLC patients who received PD-1 inhibitor alone or combined chemotherapy, MPE occurred in 82 (30.5%) patients. Patients with MPE had a shorter median PFS (4.0 vs. 9.8 months) and OS (21.0 vs. 29.9 months) than those without MPE. MPE was an independent factor affecting PFS (HR:1.87) and OS (HR: 2.73). The ORR for patients with and without MPE was 20% and 34%, respectively. In another cohort with 69 advanced NSCLC patients with MPE who receive PD-1 inhibitor plus chemotherapy plus bevacizumab or PD-1 inhibitor plus chemotherapy, there was no significant difference in median PFS (19.1 vs. 13.2 months) and OS (21.8 vs. 21.6 months), ORR (42.1% vs. 36.8%), and extrapleural ORR (23.9% vs. 26.3%) between the two groups. In addition, IL-6 levels in serum and pleural effusions were significantly higher in NSCLC patients with MPE. Furthermore, in a mouse tumor MPE model by subcutaneous and pleural injection of lung cancer cells, PD-1 inhibitor did not decrease tumor growth and prolong survival in MPE-bearing mice. Immunohistochemistry and flow cytometry demonstrated the proportion of CD3⁺T cells, CD4⁺T cells and CD8⁺T cells were decreased in the subcutaneous tumors with MPE. Dural blockade with PD-1 inhibitor and IL-6 receptor antibody inhibited tumor growth and prolonged survival of MPE-bearing mice. **Conclusions:** The occurrence of MPE is negatively correlated with patient outcomes when receiving PD-1 inhibitor or PD-1 inhibitor plus bevacizumab. Elevated IL-6 levels may be responsible for abscopal inhibitory tumor immune microenvironment and reduced efficacy of immunotherapy. Dural blockade of PD-1 and IL-6 could be a promising therapeutic strategy for advanced NSCLC with MPE. Research Sponsor: None.

Guard-01: A randomized, open-label trial of efbemalenograstim alfa as primary prophylaxis for neutropenia during definitive concurrent chemo-radiotherapy.

Yuanyuan Chen, QiWen Li, Zunbei Wen, Yi Ouyang, Yongling Ji, Rong Huang, Shuzhen Lai, Chen Wang, Min Ying Li, Qingren Lin, Xuefang Zhang, Ming Chen; State Key Laboratory of Oncology in South China, Guangdong Key Laboratory of Nasopharyngeal Carcinoma Diagnosis and Therapy, Guangdong Provincial Clinical Research Center for Cancer, Sun Yat-sen University Cancer Center, Guangzhou, China; Department of Radiation Oncology, Sun Yat-sen University Cancer Center, State Key Laboratory of Oncology in South China, Collaborative Innovation Center of Cancer Medicine, Guangzhou, China; Medical Oncology, Gaozhou People's Hospital, Maoming, Guangdong, China; Sun Yat-sen University Cancer Center, Guangzhou, China; Zhejiang Cancer Hospital, Hangzhou, China; The First People's Hospital of Foshan, Foshan, China; Guangdong Yuebei People's Hospital Affiliated to Shantou University, Shaoguan, China; Ganzhou People's Hospital, Ganzhou, China; Department of Oncology, Zhongshan City People's Hospital, Zhongshan, China; Department of Radiation Oncology, Zhejiang Cancer Hospital, Hangzhou, China; Department of Radiotherapy, Dongguan People's Hospital, Dongguan, China; State Key Laboratory of Oncology in South China, Collaborative Innovation Center for Cancer Medicine, Sun Yat-sen University Cancer Center, Sun Yat-sen University, Guangzhou, Guangdong, China

Background: Concurrent chemoradiotherapy (CCRT), a curative cornerstone for locally advanced malignancies, exerts synergistic antitumor efficacy but is frequently hampered by severe hematologic toxicity (mainly neutropenia), leading to treatment delays, dose reductions and compromised outcomes. GM-CSF, previously evaluated for CCRT-induced hematologic AE prophylaxis, is no longer recommended due to increased immune-related toxicities and limited efficacy. While G-CSF is safe in chemotherapy, high-quality data for long-acting G-CSF as primary CCRT prophylaxis is sparse, creating a critical clinical gap that the Guard-01 study aims to resolve. **Methods:** This multicenter, randomized, open-label, controlled trial plans to enroll 120 patients undergoing definitive CCRT for locally advanced malignancies. Eligible participants are randomized 1:1 to either the study arm or control arm, stratified by chemotherapy regimen. Study arm patients receive efbemalenograstim alfa $\sim 48 (\pm 4)$ h post each chemotherapy cycle; control arm patients receive no primary G-CSF prophylaxis, with secondary efbemalenograstim alfa permitted for febrile neutropenia (FN) or dose-limiting neutropenia. The primary endpoint is the incidence of grade 3/4 neutropenia across the entire CCRT course. **Results:** As of December 2, 2025, 122 patients were enrolled (60 study arm, 62 control arm). The incidence of grade 3/4 neutropenia during the entire treatment course was 16.67% in the study arm versus 53.23% in the control arm, with a significant between-group difference of -36.56% (90% CI: -48.98%, -22.84%; $p < 0.0001$). Rates were significantly lower in the study arm across the first (5.00% vs. 45.16%; $p < 0.0001$) and second (12.28% vs. 27.27%; $p = 0.0393$) chemotherapy cycles. Consistent benefit was observed in subgroup analysis, with a significant difference in paclitaxel- or pemetrexed-based regimens (20.00% vs. 64.52%; $p = 0.0004$). The study arm had shorter grade 3/4 neutropenia duration (0.62 ± 1.57 vs. 3.27 ± 4.84 days; $p < 0.0001$) and higher ANC nadir (2.82 vs. $0.94 \times 10^9/L$; $p < 0.0001$). No neutropenia-related chemotherapy dose reductions or discontinuations occurred in the study arm, compared with 6.45% dose reductions and 1.61% discontinuations in the control arm. The most common TEAEs in the study arm were anemia (71.67%), thrombocytopenia (60.00%), and leukopenia (35.00%). Grade ≥ 3 TEAEs were less frequent in the study arm (41.67% vs. 64.52%), with no grade ≥ 3 TRAEs reported in either group. Exploratory endpoints include 2-year PFS and OS, with immature data pending longer-term follow-up. **Conclusions:** Efbemalenograstim alfa significantly reduces the incidence and duration of grade 3/4 neutropenia in patients undergoing definitive CCRT, with consistent efficacy across different chemotherapy regimens and a favorable safety profile. Clinical trial information: ChiCTR2300077504. Research Sponsor: None.

An anti-EpCAM x anti-CD3 bispecific antibody, M701, for the treatment of malignant pleural effusion due to NSCLC: A prospective randomized controlled phase II trial.

Zhengbo Song, Jun Cai, Dongqing Lv, Tienan Yi, Yanqiu Zhao, Bin Yang, Jun Zhao, Baogang Liu, Huaqiu Shi, Bin Wang, Genhe Wang, Jun Yao, Xiang Wang, Kaijian Lei, Cailing Jin, Zizheng Song, Yanhong Shang, Yu Liu, Zengmei Sheng, Shaoyi Huang; Phase I Clinical Trial Unit, Zhejiang Cancer Hospital, Hangzhou, China; Department of Oncology, The First Affiliated Hospital of Yangtze University, Jingzhou, China; Department of Respiratory Medicine, Taizhou Hospital of Zhejiang Province, Taizhou, China; Oncology Department, Xiangyang Central Hospital, Xiangyang, China; Respiratory Medicine, Department of Gastrointestinal Oncology, The Affiliated Cancer Hospital of Zhengzhou University & Henan Cancer Hospital, Zhengzhou, China; Hubei Cancer Hospital, Wuhan, China; Department of Oncology, Changzhi People's Hospital, The Affiliated Hospital of Changzhi Medical College, Changzhi, China; Harbin Medical University Cancer Hospital, Harbin, China; First Affiliated Hospital of Gannan Medical University, Ganzhou, China; Department of Respiratory Medicine, Huzhou Central Hospital, Huzhou, China; Department of Oncology, Huangshan People's Hospital, Huangshan, China; Department of Oncology, The First Affiliated Hospital of Henan University of Science & Technology, Luoyang, China; Department of Medical Oncology, Xuzhou Central Hospital, Xuzhou, China; Oncology Center, The Second People's Hospital of Yibin, Yibin, China; Department of Oncology, The First Affiliated Hospital of Xinxiang Medical University, Xinxiang, China; Department of Medical Oncology, Affiliated Hospital of Hebei University, Baoding, China; Department of Oncology, The Second People's Hospital of Neijiang, Neijiang, China; Department of Oncology, The Third Hospital of Changsha, Changsha, China; Wuhan YZY Biopharma Co, Ltd., Wuhan, China

Background: Malignant Pleural Effusion (MPE) is a common complication in patients with advanced NSCLC, associated with poor prognosis, severe symptoms, and reduced quality of life. Indwelling pleural catheter (IPC) is the first-line recommended therapy to alleviate MPE-related symptoms; however, no effective pharmacotherapy has been established in current clinical guidelines for MPE management. **Methods:** Patients with advanced NSCLC and symptomatic MPE who had progressed following at least 1 line of systemic treatment were eligible. Patients were randomized 1:1 to experimental arm (Arm E: IPC + M701 IP at 25 µg on day 1, 400 µg on days 4, 7, 10) or control arm (Arm C: IPC + cisplatin IP 40 mg on days 1, 7 or IPC alone), stratified by prior intrapleural chemotherapy (yes/no). Catheters were removed after day 10. Primary endpoint was puncture-free survival (PuFS), defined as time from catheter removal to next puncture or death. Secondary endpoints included time to next puncture (TTNP), overall survival (OS), MPE objective response rate (ORR), investigator-assessed MPE symptoms (Likert scale), and patient-reported symptoms (LC-13 scale). **Results:** As of December 22, 2025, 92 patients were randomized to Arm E (n=45) or Arm C (cisplatin, n=41; thoracentesis, n=6). Baseline characteristics were generally balanced between the two arms. The proportions of patients positive for actionable genomic alterations (AGA) were 77.77% (n=35) in Arm E and 72.34% (n=34) in Arm C, respectively. M701 demonstrated a significant improvement trend in PuFS and TTNP compared with cisplatin (see Table 1). The MPE ORR was 46.7% for Arm E and 34.0% for Arm C (p=0.217). Patients with prior intrapleural (IP) chemotherapy or without AGA had a more favorable treatment response in Arm E relative to Arm C, whereas the remaining patients did not. Dyspnea symptoms also demonstrated a trend toward greater improvement in Arm E, as assessed by both investigators and patients. OS data were immature, and no significant between-group difference was observed (HR=0.94, p=0.855). Grade 3 or higher treatment-related adverse events (AEs) occurred in 2.2% of patients in Arm E and 6.4% in Arm C. Only one serious adverse event (SAE), grade 2 fever, was deemed related to M701. **Conclusions:** M701 IP infusion showed a promising efficacy on re-accumulation of MPE compared with Cisplatin infusion, and was well tolerated, supporting further clinical development, especially in patients with no AGA or patients who received IP chemotherapy priorly. Clinical trial information: NCT05543330. Research Sponsor: Wuhan YZY Biopharma Co. Ltd.

Efficacy of the FAS set and subgroup.

Population	mPuFS (days)	HR	P value	mTTNP (days)	HR	P value
Full analysis (45 vs 47)	170 vs 72	0.72	0.212	NR vs 86	0.05	0.035
Prior IP chemotherapy or no AGA (28 vs 32)	253 vs 55	0.58	0.099	NR vs 65	0.26	0.004
With AGA and no prior IP chemotherapy (17 vs 15)	124 vs 114	1.09	0.832	170 vs NR	1.34	0.582

Performance of the NutriPal nutritional screening algorithm in advanced cancer palliative care: A multicenter study.

Jesse Lopes da Silva, Daiane Almeida Dos Santos, Andreia Cristina de Melo, Karla Rosa, Larissa Pereira Santos, Imanuely Borchardt, Sarah Ananda Gomes, Aline Barcellos Barreto, Gabrielle Da Silva Vargas Silva, Livia Costa de Oliveira; Division of Clinical Research and Technological Development, Brazilian National Cancer Institute (INCA), Rio De Janeiro, Brazil; Oncoclinicas & Co - Medica Scientia Innovation Research (MEDSIR), Sao Paulo, Brazil; Cancer Epidemiology and Palliative Care Research Group (GP-ECPAL), Palliative Care Unit, Brazilian National Cancer Institute (INCA), Rio De Janeiro, Brazil; Oncoclinicas&Co - Medica Scientia Innovation Research (MEDSIR), Sao Paulo, Brazil

Background: Malnutrition is highly prevalent in advanced cancer and is closely associated with functional decline, systemic inflammation, symptom burden, and impaired quality of life (QoL). Although several nutritional screening tools exist, none were specifically developed for patients with advanced cancer receiving palliative care. The NutriPal nutritional screening algorithm, which integrates the Patient-Generated Subjective Global Assessment short form and the Glasgow Prognostic Score, was recently developed for this population; however, evidence of its performance outside the development cohort remains limited. The objective was to evaluate the performance of the NutriPal nutritional screening algorithm in identifying nutritional risk among patients with advanced cancer receiving palliative care in a multicenter clinical setting and its association with functional status, inflammation, muscle strength, and QoL. **Methods:** This multicenter, cross-sectional study included adults with locally advanced or metastatic cancer receiving palliative care in four private oncology centers in Brazil from June 2024 to November 2025. Nutritional risk was classified using NutriPal in degrees 1 (lower) to 4 (greater nutritional risk). Karnofsky Performance Status (KPS), handgrip strength (HGS), neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and QoL (EORTC QLQ-C15-PAL) were evaluated as independent variables. Associations with worsening nutritional risk were examined using ordinal logistic regression. **Results:** A total of 165 patients were included (60% women; 70% ≥ 60 years). NutriPal classified 54% as degree 1, 25% degree 2, 10% degree 3, and 11% degree 4 nutritional risk. Worse nutritional risk was independently associated with KPS < 60% (OR 2.67; 95% CI 1.17 - 6.07), low HGS in women (< 22 kg; OR 2.69; 95% CI 1.19 - 6.12) and men (< 32 kg; OR 2.06; 95% CI 1.02 - 5.44), NLR ≥ 2.78 (OR 2.02; 95% CI 1.18-3.15), and PLR ≥ 171.95 (OR 2.09; 95% CI 1.12 - 3.89). Poorer scores across all QoL domains (except insomnia) were significantly associated with higher nutritional risk (OR range 1.14 - 7.68), including global QoL (OR 4.08; 95% CI 2.14 - 7.61). **Conclusions:** NutriPal effectively discriminated nutritional risk severity and identified clinically relevant profiles characterized by functional impairment, systemic inflammation, and poorer QoL among patients with advanced cancer receiving palliative care in private oncology centers. These findings support its clinical utility as a targeted and pragmatic nutritional screening tool in real-world palliative oncology practice settings. Research Sponsor: None.

Role of palliative care nurse coordination in symptom control and care planning.

Suwanna Rinchai; Bumrungrad International Hospital, Bangkok, Thailand

Background: Effective coordination by palliative care nurses plays a central role in improving communication, symptom assessment, and timely care planning for patients with advanced cancer. However, evidence on the measurable impact of nurse-led palliative coordination—particularly in Asian oncology settings—remains limited. This study evaluates the outcomes of a nurse-coordinated palliative care model on symptom control and care planning among patients with advanced cancer. **Methods:** This retrospective observational study included patients with advanced cancer who received palliative care nurse coordination from January 1, 2025 to December 31, 2025. The intervention consisted of systematic ESAS-based symptom assessment, coordination with oncology teams, family meetings, and facilitation of advance care planning. Outcomes included changes in symptom scores from baseline to follow-up, completion of advance care planning (ACP) and DNR documentation, and health-care utilization indicators. Distress score was derived from the ESAS psychological subscale, calculated as the sum of anxiety and depression scores. Descriptive statistics and paired comparisons were used for analysis. **Results:** A total of 195 patients were included (mean age 60.5 years; range 21–100). Following nurse-led palliative coordination, median pain scores decreased from 8 to 3 ($p < 0.01$). Median dyspnea scores improved from 6 to 1, representing an 83.3% reduction ($p < 0.01$). Median distress scores decreased from 6 to 2, corresponding to a 66.7% improvement ($p < 0.01$). Completion of advance care planning increased from 10% to 97%. DNR documentation improved from 20% to 80%, with the exception of one Arabic patient for whom DNR documentation was not completed. Under the nurse-led palliative care coordination model, 98.5% of patients with advanced cancer did not require unplanned emergency room utilization and avoided unnecessary ICU admissions. These outcomes highlight the effectiveness of proactive symptom management and comprehensive care planning. **Conclusions:** Nurse-led palliative care coordination was associated with significant improvements in symptom control and substantially higher completion rates of care planning among patients with advanced cancer. These results support integrating palliative nurses as key coordinators in oncology settings to enhance patient-centered and goal-concordant care. Research Sponsor: None.

Patterns and timing of palliative care consultation in patients with newly diagnosed metastatic cancer.

Thomas Wayne Butler, Muhammad Dawood Amir Sheikh, Muhammad Areeb Ashfaq, Vishal Shroff; University of South Alabama Mitchell Cancer Institute, Mobile, AL; University of South Alabama, Mobile, AL

Background: Early integration of palliative care (PC) improves symptom burden, quality of life, and healthcare utilization in advanced cancer, yet referrals frequently occur late in the disease course. We evaluated institutional patterns of PC utilization to quantify consultation rates, timing, and demographic predictors of referral among patients with newly documented metastatic disease. **Methods:** We conducted a retrospective cohort study of adults with newly documented metastatic disease identified using ICD-10 secondary lymph node metastasis codes (C77.x) who received oncology care at the Mitchell Cancer Institute between November 2024 and November 2025. The first metastatic code defined time of diagnosis. Outcomes included PC consultation rate, time from diagnosis to consultation, consultation setting, and timing relative to death. Multivariable logistic regression evaluated associations between age, sex, insurance status, and race with receipt of consultation. **Results:** Among 375 patients (median age 66 years, IQR 56–74), 64 (17.1%) received a PC consultation. Consultation rates varied more than fourfold across primary diagnoses (6%–29%). Among patients with post-diagnosis consultations, the median time to consultation was 66 days (IQR 25–130), with more than half occurring >60 days after diagnosis. Most consultations occurred in the outpatient cancer center (78%). Among decedents who received consultation, 64% were first seen within 90 days of death, consistent with late referral. In multivariable analysis, increasing age was associated with a lower likelihood of consultation (OR 0.97 per year, 95% CI 0.95–0.99, p=0.016), while Black patients had higher odds of consultation compared with White patients (OR 1.82, 95% CI 1.02–3.25, p=0.044). Sex and insurance status were not independently associated with referral. **Conclusions:** PC utilization was low, highly variable, and frequently delayed among patients with metastatic cancer. Although most referrals originated in the outpatient setting, many occurred near the end of life. Diagnosis-triggered referral pathways may promote earlier and more equitable integration of supportive oncology services. Research Sponsor: None.

Palliative care utilization and predictors of consultation.	
Characteristic	Value
Total patients	375
Median age, years (IQR)	66 (56–74)
Received PC consultation	64 (17.1%)
Median time diagnosis → consultation, days (IQR)	66 (25–130)
Initial outpatient consultation	78%
Consultation ≤90 days before death (decedents)	64%
Black vs White race, adjusted OR	1.82 (p=0.044)
Age (per year), adjusted OR	0.97 (p=0.016)
Most referrals occurred late in the disease course	>50% after 60 days

PC = palliative care; IQR = interquartile range; OR = odds ratio. Timing calculated among post-diagnosis consultations. Odds ratios from multivariable logistic regression.

Olanzapine for chemotherapy-related anorexia: Impact on body composition.

Sandhya Singuluri; Srivenkateshwara Institute of Cancer Care and Advanced Research, Tirupati, India

Background: Chemotherapy-related anorexia and weight loss are associated with adverse outcomes in patients with advanced gastrointestinal and lung cancers. While olanzapine has demonstrated efficacy in improving appetite and weight gain, the impact of weight gain on body composition remains unclear. We evaluated changes in morphomic parameters among patients receiving olanzapine during chemotherapy. **Methods:** In this phase III, randomized, double-blind, placebo-controlled trial, adults (≥ 18 years) with untreated locally advanced or metastatic gastric, hepatopancreaticobiliary, or lung cancer were randomized to receive olanzapine 2.5 mg once daily or placebo for 12 weeks, along with standard chemotherapy and nutritional counseling. The primary endpoint was the proportion of patients achieving $> 5\%$ weight gain. Secondary endpoints included changes in skeletal muscle index (SMI), subcutaneous fat index (SFI), and visceral fat index (VFI) assessed at the third lumbar vertebra on CT scans. Morphomic analysis was performed in patients with paired baseline and interim CT scans. **Results:** A total of 103 patients (olanzapine, $n = 53$; placebo, $n = 50$) were included in the morphomic analysis. Baseline characteristics were comparable between groups. Weight gain $> 5\%$ was significantly more frequent in the olanzapine group compared with placebo (60% vs 9%, $p < 0.0001$). Both groups experienced a decline in mean SMI; however, among olanzapine-treated patients with $> 5\%$ weight gain, 63% demonstrated improvement or stabilization of SMI. Improvement in SFI was more frequent with olanzapine than placebo (62% vs 40%, $p = 0.047$). Among patients with $> 5\%$ weight gain, a higher proportion in the olanzapine group showed an increase in VFI compared with placebo (72% vs 60%, $p = 0.006$). **Conclusions:** Olanzapine improves weight gain with favorable changes in skeletal muscle and fat indices, indicating true nutritional gain rather than fluid retention in patients with chemotherapy-related anorexia. These findings suggest that olanzapine may favorably modulate cancer-related anorexia and treatment outcomes, warranting further validation in larger focused studies. Clinical trial information: CTRI/2020/08/027133. Research Sponsor: Jawaharlal Institute of Postgraduate Medical Education and Research (JIPMER) – Intramural funding.

Clinical outcomes of gabapentinoids for oncologic pruritus: A retrospective cohort study.

Alim Osman, Ian Nykaza, Stephen W. Dusza, Lavanya Mittal, Allison Gordon, Shamir Geller, Cesar Antonio Virgen, Veronica Rotemberg, Doris Ponce, Jasmeet Chadha Singh, Jodi Victoria Mones, Alina Markova; Department of Medicine, Dermatology Service, Memorial Sloan Kettering Cancer Center, New York, NY; Memorial Sloan Kettering Cancer Center, New York, NY; Dermatology Service, Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, NY; Department of Medicine, Oncology Service, Memorial Sloan Kettering Cancer Center, New York, NY; Department of Medicine, Hematology Service, Memorial Sloan Kettering Cancer Center, New York, NY

Background: Pruritus is a debilitating symptom in oncologic patients, sometimes leading to interruption of cancer therapy. Gabapentinoids such as gabapentin and pregabalin are effective for the treatment of uremic and neuropathic pruritus. We report on the safety and efficacy of gabapentinoids for oncologic pruritus defined as any pruritus originating from malignancy, oncologic therapies, or other cancer-associated toxicities, such as cutaneous graft-versus-host disease (GVHD). **Methods:** In this single-center retrospective cohort study conducted at the Memorial Sloan Kettering Cancer Center between 4/1/2019 and 8/1/2024, 224 patients who were prescribed gabapentinoids for oncologic pruritus were included. Patients taking gabapentinoids for indications other than pruritus were excluded. The primary efficacy endpoint was ≥ 1 -grade improvement for pruritus severity on the Common Terminology Criteria for Adverse Events (CTCAE) v5.0 scale. **Results:** The cohort was predominantly male (54%) and White (67%), with Black (14.3%) and Asian (12.5%) patients also represented; the mean age was 63.2 ± 15 years. Gabapentinoids were most prescribed for drug-induced causes (58.9%) and malignancy-related pruritus (14.3%). Of the drug-induced causes, immune checkpoint inhibitors (40.2%), monoclonal antibodies (12.9%; including mogamulizumab, brentuximab vedotin, and enfortumab vedotin), and tyrosine kinase inhibitors (11.4%) were the most common triggers. Pregabalin was more commonly prescribed compared to gabapentin (80.8% vs. 19.2%). Ninety percent of patients (n=202) experienced a ≥ 1 -CTCAE grade improvement at a median total daily dosage of 50 mg (IQR, 25 mg) for pregabalin and 300 mg (IQR, 50 mg) for gabapentin. Median time for patient-reported improvement was 18.5 days and there was no significant difference in gabapentin response between pruritus etiologies. The most common adverse event was sedation (8.5%), with 3 patients discontinuing gabapentinoids due to fatigue. **Conclusions:** This study is the first to report that gabapentinoids are a safe and effective way to treat oncologic pruritus stemming from malignancy, cancer therapies, or cutaneous GVHD. Prospective trials would further establish gabapentinoids' safety and efficacy profile in the oncologic population. Research Sponsor: None.

Outcomes & adverse events of patients on gabapentinoids.		
Variable	Category/Statistic	N (%)
CTCAE Grade Change	Did Not Improve (0 Grade)	22 (9.8%)
	Improved 1 Grade	132 (58.9%)
	Improved ≥ 2 Grade	70 (31.3%)
Antineoplastic Therapy Interrupted Due to Oncologic Pruritus	Yes	26 (11.7%)
	No	157 (70.4%)
	Not Applicable	40 (17.9%)
Adverse Events*	Sedation	19 (8.5%)
	Leg Swelling	2 (0.9%)
	Other	9 (4.0%)

*The remaining 194 (86.6%) patients did not report any adverse events related to the gabapentinoids.

Cancer cachexia and symptomatic toxicity among 706 older adults with advanced cancer receiving treatment: A URCC NCORP nationwide study.

Lindsey Jean Mattick, Supriya Gupta Mohile, Karen Michelle Mustian, Chin-Shang Li, Marie Anne Flannery, Mostafa Refaat Mohamed, Rachael Tylock, Po-Ju Lin, Yuri Choi, Khalil Katato, Jeffrey L. Berenberg, Nadia N. Ramdin, Richard Francis Dunne; Department of Surgery, Division of Supportive Care in Cancer, University of Rochester Medical Center, Rochester, NY; James P. Wilmot Cancer Center, University of Rochester Medical Center, Rochester, NY; James P. Wilmot Cancer Institute, University of Rochester Medical Center, Rochester, NY; Department of Surgery, Division of Supportive Care in Cancer and URCC NCORP Research Base, University of Rochester Medical Center, Rochester, NY; School of Nursing, University of Rochester Medical Center, Rochester, NY; Division of Epidemiology, Department of Public Health Sciences, University of Rochester Medical Center, Rochester, NY; Department of Hematology/Oncology, School of Medicine and Dentistry, University of Rochester Medical Center, Rochester, NY; Wilmot Cancer Institute, University of Rochester Medical Center, Rochester, NY; Michigan Cancer Research Consortium, Flint, MI; Hawai'i MUNCORP, Honolulu, HI; Geisinger Medical Center, Danville, PA

Background: Cancer cachexia is a severe wasting condition characterized by rapid weight loss.

Its impact on symptomatic toxicity is poorly defined in geriatric oncology populations, who are at high risk for cachexia. Symptomatic toxicity is central to treatment tolerability and is linked to poor quality of life, functional decline, and reduced survival. We evaluated whether cachexia is associated with symptomatic toxicity before and during high-risk cancer treatment in older adults with advanced cancer. **Methods:** In a randomized controlled trial (GAP70+; NCT02054741), adults aged ≥ 70 with stage III or IV solid tumors or lymphoma were recruited prior to starting a new cancer treatment from 40 community oncology practices affiliated with the University of Rochester NCI Community Oncology Research Program (NCORP) Research Base. Cachexia ($\geq 5\%$ weight loss in the past six months) was assessed at baseline via Mini Nutritional Assessment. Symptoms (fatigue, insomnia, pain, anorexia, dyspnea, concentration problems, nausea, sensory neuropathy, constipation, diarrhea) were assessed at baseline and 3 months using the Patient-Reported Outcomes version of the Common Terminology Criteria for Adverse Events (PRO-CTCAE). Symptoms were measured as mild, moderate, severe, or very severe. Log-binomial regression models examined associations of cachexia with baseline and three-month incident symptoms (baseline-adjusted method). **Results:** Among 706 participants (mean age: 77.2 years; 57% male; 59% gastrointestinal or lung cancer; 26% received prior chemotherapy), 42% had cachexia at baseline. Participants with cachexia were more likely than those without to report severe/very severe baseline symptoms (56% vs. 35%, chi-square $p < 0.01$). Analyses show that those with cachexia were 2–3 times more likely to report baseline severe/very severe anorexia (Risk Ratio (RR): 3.64, 95%CI: 2.44 – 5.42), fatigue (RR: 2.28, 95%CI: 1.65 – 3.16), pain (RR: 2.03, 95%CI: 1.36 – 3.04), and constipation (RR: 2.02, 95%CI: 1.27 – 3.22), as well as moderate or worse nausea (RR: 1.72, 95%CI: 1.16 – 2.55) and concentration problems (RR: 1.56, 95%CI: 1.03 – 2.39; all $p < 0.05$). Baseline cachexia was also associated with the development of severe/very severe anorexia (RR: 1.88, 95%CI: 1.20 – 2.94; $p < 0.01$) from baseline to 3-months. **Conclusions:** Nearly half of older adults with advanced cancer initiating a treatment regimen have cachexia. We demonstrate via PRO-CTCAE that cachexia is associated with a significantly worse pre-treatment symptom burden. Cachexia was linked to severe anorexia before and after treatment initiation, highlighting a critical gap in supportive care. As novel agents targeting appetite and cachexia enter phase III trials, further research is needed to establish the temporal course of cachexia-related symptoms to identify ideal timing and candidates for therapeutic strategies. Clinical trial information: NCT02054741. Research Sponsor: National Cancer Institute; UG1CA189961; National Cancer Institute; R01CA177592; National Cancer Institute; T32CA102618; National Cancer Institute; UG1CA189971; National Cancer Institute; UG1CA189847; National Cancer Institute; UG1CA189804.

Enhancing supportive care in malignant bowel obstruction: A QI project using virtual dietitian-led low-fiber diet education.

Bojan Macanovic, Vikas Garg, Nazlin Jivraj, Karmen HT More, Susan Haines, Jennifer M. Croke, Michael F. Milosevic, Kathy Han, Jelena Lukovic, Lauren Philp, Genevieve Bouchard-Fortier, Marcus Bernardini, Liat Frida Hogen, Stephane Laframboise, Rachel Soyoun Kim, Neesha C. Dhani, Ana Veneziani, Robert C. Grant, Amit M. Oza, Stephanie Lheureux; Princess Margaret Cancer Centre, University Health Network, University of Toronto, Toronto, ON, Canada; Princess Margaret Cancer Centre, Toronto, ON, Canada; Princess Margaret Cancer Centre, University Health Network, Toronto, ON, Canada; Princess Margaret - University Health Network, Toronto, ON, Canada; Princess Margaret Cancer Centre - Uhn, Toronto, ON, Canada; Division of Gynecologic Oncology, Princess Margaret Cancer Centre/University Health Network/Sinai Health Systems, Toronto, ON, Canada; University Health Network, Toronto, ON, Canada; Princess Margaret, University Health Network, Toronto, ON, Canada; Division of Medical Oncology and Hematology, Princess Margaret Cancer Centre, University Health Network, University of Toronto, Toronto, ON, Canada; Princess Margaret Cancer Centre, University of Toronto, Toronto, ON, Canada

Background: Malignant bowel obstruction (MBO) is a frequent, debilitating complication in patients with gynecologic malignancies associated with poor prognosis. Low-fibre diet (LFD) is a core component of conservative management; however, adherence is challenging and may be improved with coaching. To address this gap, we implemented a virtual dietitian-led educational intervention and evaluated patient knowledge, attitudes, and practices regarding LFD. **Methods:** This prospective quality improvement project was conducted at Princess Margaret Cancer Centre between October 2024 and April 2025. Adult patients with gynecologic malignancies who had developed or were at risk of MBO participated in interactive virtual LFD classes delivered by a registered dietitian. Electronic surveys assessed patient knowledge, attitudes, and dietary practices at baseline, post-class, and at two-week follow-up. Outcomes were summarized using descriptive statistics. **Results:** Of 71 patients approached, 48 (68%) attended the class. Surveys were completed by 43 patients pre-class (61%), 26 post-class (37%), and 18 at follow-up (25%). Median age was 64 years (range 31–79); 32/43 (74%) had ovarian cancer, and 12/43 (28%) had prior bowel obstruction. At baseline, 40/43 (93%) understood the rationale for LFD, but only 26/43 (60%) reported knowing which foods were permitted and 26/43 (60%) which were restricted. Baseline concerns included inadequate healthy food options (32/43, 74%) and limited cultural food compatibility (12/43, 28%). Following the intervention, understanding of permitted foods increased to 24/26 (92%; +32%) and restricted foods to 22/26 (85%; +24%). Confidence that LFD could reduce the risk of MBO improved from 16/43 (37%) to 16/26 (62%; +25%). The virtual format was well received, with 25/26 (96%) feeling comfortable and 22/26 (85%) identifying the class as an important part of their care. At two-week follow up, 15/18 (83%) felt confident in selecting appropriate foods. Adherence was high with 6/18 (33%) following LFD always and 9/18 (50%) most of the time. Despite improved knowledge and adherence, overall satisfaction with LFD remained low (baseline 7/43, 16%; follow-up 3/18, 17%). Challenges including limited food variety, difficulty identifying appealing options, and managing concurrent dietary restrictions, were reported by 9/18 (50%). Quality of life outcomes were mixed, with equal proportions reporting improved, unchanged or worsened: each 6/18, 33%. **Conclusions:** This quality improvement project demonstrates that a virtual, dietitian-led LFD education is feasible, acceptable, and effective in addressing key knowledge and confidence gaps for patients with or at risk of MBO. Persistent dissatisfaction with LFD highlights the need for future QI efforts focused on developing culturally inclusive resources and integration of multiple dietary needs. Research Sponsor: None.

Fatigue and psychostimulant use in patients with advanced cancer in an oncology palliative care clinic: A retrospective cohort study.

Nicolas Chin-Yee, Breffni Hannon, Timo Carpen, Criselda Isabel Cenizal, Annie Huynh, Camilla Zimmermann; Princess Margaret Cancer Centre, Toronto, ON, Canada; Princess Margaret Hospital, Toronto, ON, Canada; Princess Margaret Cancer Centre, University of Toronto, Toronto, ON, Canada

Background: Cancer-related fatigue (CRF) is the most common symptom experienced by patients with cancer but is underreported and undertreated. Psychostimulants are prescribed for CRF despite limited evidence; data on real-world use of these medications for CRF is scant. We aimed to describe the prevalence and predictors of CRF and psychostimulant use, and the association of psychostimulant use with CRF improvement in an oncology palliative care clinic (OPC). **Methods:** We conducted a retrospective review of new consultations in the Princess Margaret Cancer Centre OPC from Jan 1, 2018 - Jul 30, 2025. Demographic and clinical characteristics, including Palliative Performance Scale (PPS) and Edmonton Symptom Assessment System (revised, with constipation and sleep, ESAS-rCS) scores were recorded. Psychostimulant prescriptions were extracted from Epic, the electronic medical record system as of Jun 4, 2022. We calculated prevalence of fatigue in the total cohort and psychostimulant prescription following initial OPC visit in the subcohort seen on/after Jun 4, 2022. For the latter group, we reviewed charts to assess adherence, CRF severity, patient perception of efficacy and adverse effects. Multivariable logistic regression evaluated baseline factors associated with moderate-severe fatigue ($\geq 4/10$ on ESAS-rCS) and psychostimulant prescription. We compared pre- and post-psychostimulant fatigue scores by Wilcoxon signed rank test. **Results:** 8,439 patients (5,812 with complete ESAS-rCS) were seen in the OPC from Jan 1, 2018 - Jul 30, 2025; 74.4% and 40.6% reported fatigue $\geq 4/10$ and $\geq 7/10$, respectively. Moderate-severe fatigue was independently associated with lower PPS (< 60 vs ≥ 60 , OR 1.66, 95% CI 1.15-2.38, $p < 0.01$) and worse ESAS-rCS scores for pain, drowsiness, appetite, dyspnea, depression, and wellbeing ($p < 0.0001$). Among 3,623 patients seen on/after Jun 4, 2022, 140 (3.9%) were prescribed a psychostimulant by the OPC; no baseline patient factors were associated with psychostimulant prescription. Of these 140 patients, 139 were prescribed methylphenidate at a maximum total daily dose ≤ 10 mg; 77 adhered to treatment and had follow up notes reporting effects. Of evaluable patients, 53 (68.8%) reported improved fatigue, 12 (15.6%) no benefit, and 12 (15.6%) had conflicting notes regarding effectiveness; 3 (3.9%) reported non-serious adverse events related to methylphenidate. Median (interquartile range) fatigue scores pre- and post-psychostimulant treatment were 7 (5-8) and 6 (3-7), respectively ($p < 0.01$). **Conclusions:** Nearly 3/4 of patients with advanced cancer receiving outpatient palliative care experienced fatigue, yet few were treated with psychostimulants. Most patients reported improvement in fatigue with low-dose methylphenidate. Future studies should address knowledge gaps in assessment and management of CRF and the role of psychostimulants. Research Sponsor: None.

Association of iterative cannabis care plans with rates of symptom relief and side effect burden in oncology patients.

Brooke Worster, Kristen Parton, Gregory D. Garber; Sidney Kimmel Comprehensive Cancer Center, Jefferson Health, Philadelphia, PA; EO Care, Boston, MA; Sidney Kimmel Cancer Center at Thomas Jefferson University, Philadelphia, PA

Background: Cannabis is increasingly used to manage cancer-related symptoms including pain, sleep disturbance, anxiety, and appetite or gastrointestinal complaints. However, patient responses are highly variable, clinicians report limited confidence in guiding use, and optimal dosing is difficult to predict from baseline characteristics. We evaluated whether an iterative, guided cannabis care model incorporating ongoing patient feedback and care-plan adjustments is associated with improved symptom relief and lower side-effect burden in a real-world oncology population. **Methods:** We conducted a retrospective observational analysis of cancer patients receiving cannabis-based symptom management through a structured care-planning program. Baseline demographics, cannabis experience, THC dosing, and number of care-plan adjustments were collected. Patients provided longitudinal feedback on symptom outcomes and tolerability at serial check-ins. Significant symptom relief was defined as a ≥ 3 -point reduction in PROMIS T-scores across pain, sleep, anxiety, and appetite/nausea domains. Side-effect burden was assessed as the percentage of follow-up check-ins with reported side effects. Logistic regression examined associations between care-plan adjustments and symptom relief, adjusting for age, cannabis experience, and final THC dose. **Results:** A total of 136 patients receiving active cancer treatment were included (mean age 61 years; range 26–91). Overall, 56% reported significant relief across all symptom domains. Rates of global symptom relief increased with care-plan iteration: 34.6% among patients with no adjustments, 72.4% among those with 1–2 adjustments, and 96.6% among those with ≥ 3 adjustments, demonstrating a strong relationship. Care-plan iteration was also associated with lower longitudinal side-effect burden, with side effects reported at 25.6% of check-ins among patients with no adjustments, 17.5% with 1–2 adjustments, and 11.7% with ≥ 3 adjustments. In adjusted analyses, each additional adjustment was independently associated with higher odds of global symptom relief, while baseline demographic and clinical characteristics were not strong predictors of response. **Conclusions:** Symptom response to cannabis therapy among oncology patients is heterogeneous and not reliably predicted by baseline characteristics. In this real-world cohort, iterative cannabis care plans incorporating ongoing monitoring and adjustment were associated with substantially higher rates of meaningful symptom relief and a lower burden of side effects over time. These findings support adaptive, feedback-driven cannabis care models over fixed dosing strategies in supportive oncology. Research Sponsor: None.

Meaning, distress, and desire for hastened death in homebound adults with advanced cancer: A cluster analysis.

Addison Dean Monroe, Ellen Park, Hayley Pessin, Nicole Onorato, Margaret McDonald, Caraline Dean Demirjian, Elizabeth Schofield, Barry Rosenfeld, William Breitbart, Allison Applebaum, Rebecca Saracino; Memorial Sloan Kettering Cancer Center, New York, NY; Ferkauf Graduate School of Psychology, Bronx, NY; Center for Home Care Policy and Research, New York, NY; Fordham University, Bronx, NY; Icahn School of Medicine at Mount Sinai, New York, NY

Background: Patients with advanced cancer experience significant anxiety and depression exacerbating existential distress, which is often defined as a loss of meaning and dignity, desire for death, hopelessness, and/or demoralization. Such distress is even more pronounced for homebound adults with cancer who are isolated and engage less in enjoyable activities. While meaning in life, affective distress, and existential distress are related, discrepancies exist in the literature which may reflect the presence of distinct psychosocial profiles as opposed to inconsistencies in the literature. **Methods:** Patients with advanced cancer ($N = 64$) who had recently completed an episode of home care and completed baseline assessments in a pilot randomized controlled trial (RCT) of Meaning-Centered Psychotherapy for Hospitals, Hospice, and Home (MCP-H) served as the study sample. Baseline assessments included measures of meaning in life, anxiety, depression, and desire for hastened death. A hierarchical agglomerative cluster analysis was conducted to identify naturally occurring subgroups of participants. Subgroup differences in predictor variables, physical symptom burden, and demographic variables were explored. **Results:** A 2-cluster solution emerged from the data: *Low Meaning, High Distress and DHD* ($n = 29$; 45.3%) and *High Meaning, Low Distress and DHD* ($n = 35$; 54.7%). Subgroups were statistically discrepant on measures of meaning in life ($d = 0.57$), anxiety ($d = 3.07$), depression ($d = 2.57$), and DHD ($d = 2.76$), with medium to large effect sizes. Subgroups were also significantly different in physical quality of life ($d = 16.50$). No significant differences were noted demographically between subgroups. **Conclusions:** To our knowledge, this is the first cluster analysis investigating affective and existential distress in a population of homebound adults with advanced cancer. Results suggest the possibility of 2 distinct subgroups of homebound cancer patients, the first of which is prone to clinically significant anxiety, depression, and moderate DHD, possibly due to a subtle difference in meaning in life. Results also point to physical symptom burden and quality of life being exponentially impacted by affective and existential distress. This study provides valuable information which can aid assessment and treatment for vulnerable homebound adults with advanced cancer. Research Sponsor: National Cancer Institute; National Institute of Nursing Research.

Race/ethnicity-stratified survival differences associated with psychotropic medication use in pancreatic cancer.

Hussein Khalil, Shuang Yang, Yi Guo, Jiang Bian, Lisa Scarton, Diana J. Wilkie, David L. DeRemer, Sherise C. Rogers, John Allen; Purdue University, West Lafayette, IN; University of Florida Health, Gainesville, FL; University of Florida Department of Health Outcomes and Biomedical Informatics, Gainesville, FL; Indiana University, Indianapolis, IN; University of Florida, Gainesville, FL; University of Florida/UF Health Cancer Center, Gainesville, FL; Brown University Health Cancer Institute, Providence, RI

Background: Pancreatic cancer is linked to poor survival and a high burden of neuropsychiatric symptoms. Psychotropic medications are used to manage these symptoms, yet racial/ethnic disparities in use have been reported. The association between psychotropic use and survival in pancreatic cancer across racial and ethnic groups remains unclear. We evaluated race/ethnicity-stratified differences in 2-year survival associated with psychotropic use among older adults with pancreatic cancer. **Methods:** Retrospective cohort study using SEER–Medicare data (2007–2019) including patients aged ≥ 65 years with incident pancreatic cancer and continuous Medicare Parts A, B, and D coverage. Psychotropic use was defined as ≥ 1 Part D claim for antipsychotics, antidepressants, or anxiolytics. Overall survival was assessed using restricted mean survival time (RMST) up to 730 days post-diagnosis. RMST differences between users and non-users were compared within race/ethnicity strata (non-Hispanic White = NHW, non-Hispanic Black = NHB, Hispanic, Other) Sidak-adjusted chi-square tests. **Results:** Among 81,535 patients, 33.8% received at least one psychotropic medication. Overall psychotropic use was associated with a modest increase in RMST (+8.3 days), driven by antidepressants (+10.7 days) and anxiolytics (+26.8 days), while antipsychotic use was associated with shorter RMST (–13.7 days). RMST gains varied by race/ethnicity, with larger increases among NHB (+17.1 days) and Hispanic patients (+16.4 days), smaller gains among NHW (+4.1 days), and no benefit among Other races (–3.6 days). Antipsychotic-associated RMST deficits were greatest among NHB patients (–34.4 days). Antidepressants were associated with longer RMST across all groups whereas anxiolytic benefits were not observed among Other races. **Conclusions:** In this cohort of older adults with pancreatic cancer, psychotropic medication use was associated with modestly longer survival overall, largely attributable to antidepressants and anxiolytics, while antipsychotic use was associated with shorter survival. Survival associations varied by race and ethnicity, with larger gains among NHB and Hispanic patients. These findings underscore the importance of equitable recognition and management of neuropsychiatric symptoms and support further research incorporating symptom severity and medication use. Research Sponsor: None.

RMST difference (days) comparing psychotropic users vs non-users stratified by race/ethnicity.					
	Overall Cohort (N=81,535)	NHW (N=59,059)	NHB (N=8,015)	Hispanic (N=8,993)	Other (N=5,468)
Any psychotropic	8.3 (1.8)	4.1 (2.2)	17.1 (6.0)	16.4 (5.7)	–3.6 (7.4)
Antipsychotics	–13.7 (3.7)	–14.4 (4.4)	–34.4 (11.3)	6.2 (11.9)	–17.0 (14.47)
Antidepressants	10.7 (2.0)	6.6 (2.4)	16.3 (6.8)	16.2 (6.3)	21.1 (8.70)
Anxiolytics	26.8 (2.36)	23.5 (2.7)	44.1 (9.1)	34.2 (7.8)	–2.4 (10.02)

Bolded values are statistically significant.

National trends in palliative care use among hospitalized cancer patients: A seven-year analysis of demographic and socioeconomic disparities.

Aishwarya Ramesh, Kamleshun Ramphul, Chandrikha Chandrasekharan, Ramya Thota, Poornima Ramadas, Michael Maroules; The New York Medical College Graduate Medical Education Program at St. Mary's General Hospital and St. Clare's Health, Denville, NJ; Independent Researcher, Triolet, Mauritius; The University of Texas MD Anderson Cancer Center, Pearland, TX; Intermountain Healthcare, Murray, UT; LSU Health Shreveport, Shreveport, LA; NYMC/St. Mary's General Hospital, Passaic, NJ

Background: The 2016 ASCO guidelines recommend that patients with advanced cancer receive dedicated palliative care (PaC) services early in the disease course, concurrent with active treatment, within 8 weeks of diagnosis. Despite these efforts, disparities persist in the use of PaC across various demographic groups. Our study evaluated the pattern and temporal trends in PaC use among adult cancer patients to identify inequities across various clinical factors.

Methods: We analyzed adult cancer hospitalizations from the 2016–2022 National Inpatient Sample. PaC was identified using ICD-10 code Z51.5. Utilization trends were examined by hospital type, demographics (age, sex, race/ethnicity), income quartile, and insurance type. Trends in mean age and in-hospital mortality among PaC recipients were calculated. Survey-weighted regression models assessed temporal trends, accounting for complex sampling design ($p < 0.05$ significant). **Results:** We analyzed 18,574,934 hospitalizations from 2016 to 2022. PaC utilization increased significantly from 10.61% in 2016 to 14.01% in 2022 ($p < 0.001$), representing a 32% relative increase. The mean age of PaC recipients rose from 68.61 years to 69.63 years ($p < 0.001$), while in-hospital mortality remained stable at approximately 28–29% ($p = 0.144$). Utilization increased across all subgroups (all $p < 0.001$). By hospital type, urban teaching hospitals had the highest overall utilization (12.40%, range 10.72–14.01%), followed by urban nonteaching hospitals (12.07%, range 10.81–14.63%), and rural hospitals had the lowest (10.77%, range 8.81–12.71%). Black patients had the highest overall utilization (13.44%, range 11.75–15.20%), followed by White (12.15%, range 10.52–14.02%) and Hispanic patients (11.57%, range 10.04–12.48%). Females had higher utilization than males (12.72% vs 11.83%). By insurance, Medicaid had 12.79% utilization (range 11.18–14.60%), Medicare 12.72% (range 11.00–14.52%), and private insurance 10.13% (range 8.86–11.56%). The lowest income quartile had 12.47% utilization (range 10.73–14.31%) compared to 12.04% (range 10.45–13.50%) in the highest quartile. All demographic and socioeconomic subgroups demonstrated significant increasing trends over the study period. **Conclusions:** PaC utilization increased significantly across all groups, with stable mortality rates. However, disparities remain, with lower utilization in rural hospitals, among privately insured patients, and among Hispanic populations. Despite progress in overall adoption, these findings highlight ongoing inequities in PaC access that require targeted interventions to achieve equitable guideline implementation. Research Sponsor: None.

Pilot trial of virtual and in-person symptom screening with targeted early palliative care (STEP2).

Camilla Zimmermann, Katayoun Khorramak, Lisa W. Le, Timo Carpen, Eitan Amir, Philippe Bedard, Jennifer J. Knox, Nazanin Fallah-Rad, Monika K. Krzyzanowska, Madeline Li, Gary Rodin, Amit M. Oza, Lawson Eng, Jenny Lau, Jacqueline Alcalde Castro, Stephanie Lheureux, Geoffrey Liu, Natasha B. Leighl, Neesha C. Dhani, Breffni Hannon; Princess Margaret Cancer Centre, University of Toronto, Toronto, ON, Canada; Princess Margaret Cancer Centre, Toronto, ON, Canada; Princess Margaret Cancer Centre, University Health Network, Toronto, ON, Canada; Odette Cancer Centre, Sunnybrook Health Sciences Centre, Toronto, ON, Canada

Background: Routine early palliative care (EPC) for patients with advanced cancer improves quality of life. To increase scalability, models of triggered EPC have been encouraged. We assessed feasibility of hybrid virtual/in person Symptom screening and Targeted Early Palliative care (STEP2) to provide EPC triggered by symptoms. **Methods:** Patients with advanced cancer, ECOG 0-2, prognosis 6-36 months, were recruited from lung, gastrointestinal, genitourinary, breast and gynecology outpatient oncology clinics. Symptoms were screened virtually/in person ≤ 48 hours before oncology visits using Edmonton Symptom Assessment System-revised (ESAS-r+). Moderate to severe symptom scores ("screen positive") triggered an alert to a nurse, who called the patient, offering an EPC visit (in-person/virtual, as per patient preference). Participants completed measures at baseline, 2, 4, and 6 months. The primary endpoint was feasibility, with the following criteria: ≥ 40 patients accrued in 4 months; $\geq 60\%$ complete screening for $\geq 70\%$ of visits; $\geq 50\%$ triggering a call have ≥ 1 EPC visit; $\geq 60\%$ complete all measures. **Results:** From 30/03/2025-26/06/2025 40 patients were enrolled (median age [range], 62 [39-88]; 21/40 [53%] female). Disease site distribution was: 12/40 (30%) lung, 9/40 (23%) gynecology, 8/40 (20%) genitourinary, 6/40 (15%) gastrointestinal, 5/40 (13%) breast. Of the 40 patients enrolled, 36 (90%) completed screening for $\geq 70\%$ of visits and 29 (73%) screened positive: 18 at baseline and 11 later during the trial. The most common triggering symptoms were anxiety (18/29, 62%), sleep (17/29, 59%), depression (10/29, 35%), pain (8/29, 28%), and dyspnea (8/29, 28%); 21/29 (72%) screen-positive and 0 screen-negative patients received EPC before trial end. Measure completion at 2, 4, and 6 months was 90% (36/40), 85% (34/40), and 83% (33/40). Initial EPC visits were in person for 14/21 (67%) and virtual for 7/21 (33%); 20/21 (95%) of patients received ≥ 2 follow-up visits. Results for measures at baseline and at trial end are shown in the Table. **Conclusions:** Virtual/in person STEP2 is feasible and directs EPC to those who most need it, with most screen-positive patients accepting EPC. A phase III trial is underway. Clinical trial information: NCT06326554. Research Sponsor: AMS Healthcare.

Variable	Measure (score range)	Time point	N	Mean	Standard Deviation	Difference, 6 mo. vs. baseline (95% CI)
Quality of life	FACIT_PAL14	Baseline	40	42.2	7.2	0.3
	(0-56; higher is better)	6 mo.	34	42.7	7.7	(-0.9, 1.6)
Symptom Control	ESAS_EDS	Baseline	40	17.5	12.9	0.3
	(0-90; higher is worse)	6 mo.	33	18.9	13.2	(-3.1, 3.7)
Depression	PHQ-9	Baseline	40	5.4	3.4	-1.0
	(0-27; higher is worse)	6 mo.	34	4.6	3.1	(-1.9, 0.0)
Anxiety	GAD-7	Baseline	40	4.9	3.8	-1.4
	(0-21; higher is worse)	6 mo.	34	3.7	3.5	(-2.3, -0.5)
Satisfaction With care	FAMCARE-P16	Baseline	40	72.8	7.2	-5.8
	(16-80; higher is better)	6 mo.	34	67.1	12.0	(-10.1, -1.4)

Integrated assessment of cachexia, body composition, and patient-reported outcomes in unplanned hospitalizations of patients with metastatic cancer (PRO-HAND study).

Enes Yeşilbaş, Galip Can Uyar, Kadriye Başkurt, Mustafa Altınbaş, Berna Oksuzoglu, Osman Sütcüoğlu; Etlik City Hospital, Department of Medical Oncology, Ankara, Turkey; Gazi University Hospital, Department of Medical Oncology, Ankara, Turkey

Background: Patients with metastatic cancer hospitalized for unplanned admissions represent a highly vulnerable population with substantial short-term mortality and readmission risk. Cachexia, altered body composition, and patient-reported outcomes (PROs) frequently coexist in this setting, yet their integrated relevance during hospitalization remains insufficiently characterized. **Methods:** PRO-HAND is a cross-sectional observational study including metastatic cancer patients hospitalized for unplanned admissions between September 2024 and September 2025 who had received systemic anticancer therapy within the preceding 6 months. Cachexia-related indices, bioelectrical impedance analysis (BIA)-derived body composition parameters, and PROs were assessed during hospitalization. Primary outcomes were 30-day mortality, 90-day mortality, and unplanned 30-day hospital readmission. Associations were evaluated using hierarchical multivariable logistic regression models with sequential adjustment for clinical variables, cachexia indices, body composition parameters, and PROs. Results are reported as odds ratios (ORs) with 95% confidence intervals (CIs). **Results:** A total of 233 patients were included (median age 62 years; 71.2% ECOG ≥ 2). Median follow-up was 3.35 months. Thirty-day mortality occurred in 21.9%, 90-day mortality in 23.2%, and unplanned 30-day readmission in 57.9%. Lower handgrip strength-based cachexia index (H-CXI) was associated with higher odds of 30-day mortality (OR per 10-unit decrease 1.43; 95% CI 1.19–1.74; $p < 0.001$). ECOG ≥ 2 and lower phase angle were also associated with early mortality, whereas the composite triglyceride–glucose and inflammation index was not. For 90-day mortality, lower global quality-of-life scores and higher pain burden showed stronger associations than cachexia indices. For unplanned 30-day readmission, a higher total body water/fat-free mass (TBW/FFM) ratio was associated with increased risk. **Conclusions:** Cachexia severity, body composition abnormalities, and PROs show distinct, outcome-specific associations in metastatic cancer patients hospitalized for unplanned admissions. Integrated assessment during hospitalization may provide complementary clinical information across these domains. Clinical trial identification NCT07167082. Research Sponsor: None.

Selected baseline characteristics and outcomes.	
Characteristic	n (%) or median (IQR)
Age ≥ 65 years	98 (42.1)
ECOG performance status ≥ 2	167 (71.7)
Weight loss $\geq 10\%$ (6 months)	126 (54.1)
H-CXI	34.23 (14.95–71.02)
Phase angle, degrees	4.03 (2.95–5.52)
FFMI, kg/m ²	17.14 (15.48–19.31)
FACT-G total score	62 (56–68)
Pain score (VAS 0–10)	4 (2–6)
Unplanned 30-day readmission	135 (57.9)
30-day mortality	51 (21.9)

Dermatologic adverse events (dAEs) and emotional quality of life (QoL) in patients (pts) with breast cancer: A mixed-methods study.

Elyssa Kim, Karen Hurley, Bahar Moftakhar, Bryan T. Carroll, Mara Beveridge; Case Western Reserve University School of Medicine, Cleveland, OH; Case Comprehensive Cancer Center, Cleveland Clinic, Cleveland, OH; University Hospitals Seidman Cancer Center, Cleveland, OH; Department of Dermatology, University Hospitals; Case Comprehensive Cancer Center, Case Western Reserve University, Cleveland, OH; Department of Dermatology, University Hospitals, Cleveland, OH

Background: dAEs are a common and impactful aspect of QoL and have an emotional impact. However, its measurement relating to cancer care is limited. Validated tools focus on dermatology or chemotherapy but can be disconnected. Our pilot study utilized several validated tools to assess overall dAEs and their impact. **Methods:** Mixed methods consisting of a cross-sectional survey with qualitative interviews was conducted on pts with breast cancer who recently completed (<1 year) chemotherapy (acute) or completed chemotherapy ≥ 1 year ago (longitudinal). A panel of dermatologic and oncologic patient-reported outcome measures (PROMs) was: PRO Version of the Common Terminology Criteria for AEs (PRO-CTCAE), Skindex-16 (S-16), Fear of Cancer Recurrence–Short Form (FCR-SF), and Impact of Events–Intrusive Thoughts subscale (IES). Semi-structured interviews were done to elicit responsiveness to this panel. **Results:** 64 pts were screened & 60 enrolled (mean age: 63.0 ± 19.1). Pts were Female and insured (100%), White (78.3%) & Black (20%). Pts were treated with radiation (70%), surgery (66.7%), hormone therapies (23%), targeted or immunotherapies (15%). Common symptoms were xerosis (73.3%), alopecia (66.7%), pruritus (58.3%). Mean total S-16 score was 19.4 (range: 0 (no impact) to 75.5 (most impact)); PRO-CTCAE 22.2 (0, 48.5); FCR-SF 43.2 (0, 97.2); IES 20.8 (0, 65.6). S-16 scores demonstrated moderate correlations with PRO-CTCAE ($r=0.60$, $CI=0.41-0.74$, $p<0.001$), indicating related but nonredundant constructs. The S-16 didn't correlate with the FCR-SF or IES, suggesting distinct emotional burdens on pts with cancer. There was no significant difference in survey scores between acute and longitudinal groups. Qualitative analyses revealed this combination of surveys encapsulated QoL and emotional experiences related to dAEs. Several pts were unaware of the dAEs they could experience as well as how to treat them. **Conclusions:** This is a novel assessment of dAEs in QoL, implementing and comparing cancer-specific PROMs to common dermatologic PROMs. Results indicate that dAEs significantly impact QoL and oncological psychometric outcomes are not fully captured with current dermatologic PROMs. Research Sponsor: None.

Correlations between PROM scores.

Instrument Pair	Correlation (r)	95% CI	P-value
PRO-CTCAE total			
S-16 total	0.60	0.41 to 0.74	<.001
S-16 symptoms	0.65	0.48 to 0.78	<.001
S-16 emotional	0.48	0.26 to 0.66	<.001
S-16 functioning	0.40	0.17 to 0.60	0.001
FCR-SF total			
S-16 total	-0.15	-0.39 to 0.11	0.252
S-16 symptoms	-0.08	-0.32 to 0.18	0.562
S-16 emotional	-0.17	-0.40 to 0.09	0.207
S-16 functioning	-0.14	-0.38 to 0.12	0.295
PRO-CTCAE total	-0.06	-0.31 to 0.20	0.646
IES total	0.06	-0.20 to 0.31	0.657
IES total			
S-16 total	0.14	-0.12 to 0.38	0.287
S-16 symptoms	-0.03	-0.28 to 0.23	0.845
S-16 emotional	0.19	-0.07 to 0.42	0.148
S-16 functioning	0.19	-0.07 to 0.42	0.142
PRO-CTCAE total	0.24	-0.01 to 0.47	0.062

Sociodemographic determinants of end-of-life care settings and place of death among patients with lung cancer in the United States.

Ali Mushtaq, Mohanad Baroudi, Darshan Shivanne Gowda, Tarek Arabi, Omer Sayed Ashruf, Ahmed El-Shaer, Abdullah Shaik, Moaath Ali Mustafa; Cleveland Clinic Foundation, Cleveland, OH; Hassan Institute of Medical Sciences, Hassan, Karnataka, India; Alfaisal University College of Medicine, Riyadh, Saudi Arabia; Indiana University School of Medicine, Indianapolis, IN; Creighton University School of Medicine, Omaha, NE; Henry Ford St. John Hospital, Detroit, MI; Department of Hematology and Medical Oncology, Cleveland Clinic Taussig Cancer Institute, Cleveland, OH

Background: Optimizing the place of death is a key component of quality end-of-life (EOL) cancer care, with home and hospice settings generally preferred over acute care hospitals. While lung cancer mortality has declined, disparities in EOL care utilization remain a concern. This study utilized the CDC WONDER database to analyze longitudinal trends and sociodemographic predictors of place of death for lung cancer decedents over a 25-year period. **Methods:** We performed a retrospective analysis of death certificate data for all lung cancer-related deaths in the U.S. from 1999 to 2023. Place of death was categorized as Decedent's Home, Hospice/Nursing Facility, Medical Facility-Inpatient (referent), or Outpatient/ER. Multinomial logistic regression estimated adjusted odds ratios (aOR) with 95% confidence intervals (CI) for predictors, adjusting for age, sex, race, ethnicity, urbanization, and year. **Results:** A total of 3,563,902 lung cancer deaths were identified. The most common place of death was the decedent's home (44.9%), followed by inpatient medical facilities (30.7%) and hospice/nursing facilities (22.1%). There was a significant longitudinal shift away from inpatient death. For every advancing calendar year, the odds of dying at home increased by 3% (OR 1.03; 95% CI 1.03-1.03) and the odds of dying in a hospice/nursing facility increased by 4% (OR 1.04; 95% CI 1.04-1.04). Compared to White patients, Black patients had significantly lower odds of dying at home (OR 0.57; 95% CI 0.57-0.58) or in a hospice facility (OR 0.68; 95% CI 0.68-0.68). Notably, Black patients had 53% higher odds of dying in an Outpatient/ER setting (OR 1.53; 95% CI 1.53-1.53) compared to White patients. Patients in rural areas had higher odds of dying at home (OR 1.17; 95% CI 1.16-1.17) but lower odds of dying in a hospice/nursing facility (OR 0.93; 95% CI 0.92-0.93) compared to those in large metropolitan areas. **Conclusions:** From 1999 to 2023, lung cancer mortality shifted significantly from inpatient settings to home and hospice care. Yet, Black patients remain significantly less likely to utilize home/hospice care and more likely to die in acute ER settings. Additionally, rural patients show high home death rates but lower facility-based hospice use, suggesting infrastructure gaps. Targeted interventions are required to ensure equitable EOL care access. Research Sponsor: None.

More than pain relief: Associations between provider compassion, anxiety, and burnout in ED oncology care.

Christopher John Coyne, Mariam Mansour, Jesse Brennan; University of California, San Diego, San Diego, CA; University of California San Diego, School of Medicine, San Diego, CA

Background: Compassionate care is a cornerstone of high-quality oncology practice, especially in high-stress environments like the emergency department (ED). However, the relationship between perceived provider compassion and patient outcomes such as pain, psychological distress, and provider wellbeing is not well understood. **Methods:** We conducted a cross-sectional survey of oncology patients presenting to the ED. Participants completed validated assessments including the Brief Pain Inventory, the Schwartz Center Compassionate Care Scale (SCCCS), the Pain Catastrophizing Scale, the Pain Anxiety Symptom Scale, and the Self-Compassion Scale. Separately, ED providers were surveyed to assess their own burnout, rated on a 0–8 scale. Patients were grouped into High Compassion (SCCCS >100) and Low Compassion (≤ 100) categories based on their ratings of provider compassion. Group comparisons were performed using t-tests, and linear regressions explored associations between compassion scores and patient-reported and provider-reported outcomes. **Results:** Of 57 patients, 22 (39%) reported high provider compassion. Median final pain was lower in the High Compassion group (2.0 vs 4.0), though not statistically significant ($p=0.18$). Patients in the High Compassion group had significantly lower pain anxiety scores (29.2 vs 52.5, $p=0.014$) and were seen by providers with significantly lower burnout scores (3.1 vs 5.6, $p=0.022$). A trend toward lower pain catastrophizing was also observed (15.6 vs 25.7, $p=0.069$). No significant differences were found in pain reduction or self-compassion. **Conclusions:** In a cohort of ED oncology patients, higher perceived provider compassion was significantly associated with lower pain anxiety and with lower provider-reported burnout, but not with pain scores. These findings suggest that compassion may be more strongly linked to patients' emotional experiences and the wellbeing of the providers delivering care. Integrating compassionate care practices into acute oncology settings may support both patient psychological health and provider sustainability. Research Sponsor: None.

Key outcomes by compassion group (>100 vs. ≤ 100).

Outcome	High Compassion (Mean)	Low Compassion (Mean)	p-value
Final Pain (0–10)	2.33	3.67	0.183
Pain Anxiety Total	29.2	52.5	0.014
Catastrophizing Total	15.6	25.7	0.069
Self-Compassion Total	23.7	23.7	0.996
Provider Burnout (0–8)	3.1	5.6	0.022

Denosumab versus zoledronic acid in patients with breast cancer: A propensity-matched real-world time-to-event analysis.

Mohammad Salameh, Jamil Nazzal, Bugra Zengin, Jasneet Randhawa, Ahmad Alkhatib, Abdulla Massad, Lisa A. Duhaime; Hamilton Medical Center, Dalton, GA; Medstar-Baltimore, Baltimore, MD; University of Texas Medical Branch, Galveston, TX; Peeples Cancer Institute at Hamilton Medical Center, Dalton, GA

Background: Bone-modifying agents are routinely used in patients with breast cancer to reduce skeletal-related complications and metabolic disturbances. Denosumab and zoledronic acid are commonly prescribed; however, comparative real-world data evaluating their relative safety and effectiveness remain limited. We compared time-to-event outcomes associated with denosumab versus zoledronic acid in a large real-world cohort of patients with breast cancer.

Methods: We conducted a retrospective cohort study using the TriNetX US Collaborative Network, comprising electronic health records from 70 healthcare organizations. Adult patients with breast cancer who received either denosumab or zoledronic acid were identified, excluding those with underlying osteoporosis. Patients were propensity score-matched 1:1 based on demographics, comorbidities, concomitant oncologic therapies, and baseline laboratory parameters, yielding 15,147 patients per cohort. Outcomes assessed over a 5-year follow-up period included time to hypercalcemia, severe hypercalcemia (serum calcium ≥ 14.0 mg/dL), hypocalcemia, pathological fracture in neoplastic disease, and bone pain. Time-to-event analyses were performed using Kaplan-Meier methods and compared with log-rank testing; hazard ratios (HRs) with 95% confidence intervals (CIs) were estimated. **Results:** After propensity score matching, 15,147 patients were included in each cohort with well-balanced baseline characteristics. Over 5 years of follow-up, hypercalcemia did not differ between patients treated with zoledronic acid and denosumab (hazard ratio [HR] 0.99, 95% CI 0.88–1.10; log-rank $p = 0.831$). Severe hypercalcemia (serum calcium ≥ 14.0 mg/dL) was uncommon, with no significant difference between groups (HR 1.25, 95% CI 0.94–1.68; log-rank $p = 0.129$). Pathological fracture in neoplastic disease occurred less frequently in the zoledronic acid cohort, although this difference did not reach statistical significance (HR 0.88, 95% CI 0.76–1.01; log-rank $p = 0.060$). Hypocalcemia was significantly less frequent among patients receiving zoledronic acid compared with denosumab (HR 0.44, 95% CI 0.40–0.49; log-rank $p < 0.001$). Bone pain did not differ significantly between treatment groups (HR 0.95, 95% CI 0.89–1.02; log-rank $p = 0.186$). **Conclusions:** In this real-world analysis of patients with breast cancer, denosumab and zoledronic acid demonstrated similar time-to-event outcomes for hypercalcemia, severe hypercalcemia, pathological fracture, and bone pain, while zoledronic acid was associated with a significantly lower risk of hypocalcemia. These findings highlight important distinctions in toxicity profiles between agents and may inform individualized selection of bone-modifying therapy. Prospective studies are warranted to further define optimal agent selection in specific clinical subgroups. Research Sponsor: None.

BXQ-350 in combination with FOLFOX7 and bevacizumab: Evaluation of effect on oxaliplatin-induced CIPN and neutropenia—A phase 1b/2a trial to assess the efficacy and safety of BXQ-350, a first-in-class sphingolipid metabolism modulator, in newly diagnosed metastatic colorectal carcinoma.

Tariq Arshad, Michael Gazda, Gilles Tapolsky, Jim Beach, Reema Anil Patel, Daniel Blake Flora, Davendra Sohal, Saima Sharif, Fa-Chyi Lee, Ki Young Chung, Vivek R. Sharma, Julie Anne L. Gemmill, Agustin Pimentel, Nashat Y. Gabrail, Darryl Alan Outlaw, Brian C. Boulmay, Deirdre J. Cohen; Bexion Pharmaceuticals, Covington, KY; University of Kentucky, Lexington, KY; St Elizabeth Medical Center, Edgewood, KY; Division of Hematology/Oncology, University of Cincinnati Cancer Center, Cincinnati, OH; University of Iowa, Coralville, IA; University of California, Irvine Medical Center, Orange, CA; PRISMA Health Cancer Institute, Institute for Translational Oncology Research, Boiling Springs, SC; James Graham Brown Cancer Center, Louisville, KY; Stony Brook University Hospital, Stony Brook, NY; University of Miami, Miami, FL; Gabrail Cancer and Research Center, Canton, OH; Division of Hematology/Oncology/O'Neal Comprehensive Cancer Center, University of Alabama at Birmingham, Birmingham, AL; Louisiana State University Health New Orleans, New Orleans, LA; Division of Hematology and Medical Oncology, Icahn School of Medicine at Mount Sinai, New York, NY

Background: Chemotherapy-induced peripheral neuropathy (CIPN) and Neutropenia are significant side effects associated with many cancer drugs and are highly prevalent in mCRC patients receiving oxaliplatin-based regimens. CIPN can severely impact quality of life (QoL) and may require dose vacation, reduction or interruption. CIPN pathology is complex and not completely understood; preclinical and clinical data have shown inflammatory (IL-6, IL-8, IL-10) and immune involvement as well as elevated levels of sphingolipids, a class of bioactive signaling molecules. Neutropenia can also be a potentially severe side effect and may occur in up to 40% of mCRC patients receiving FOLFOX. BXQ-350 is a nanovesicle formulation of Saposin C, an allosteric activator of sphingolipid metabolism that normalizes dysregulated sphingolipid metabolism by lowering S1P, GM3 and GluCer levels while it increases ceramide level, promoting a return to homeostasis. **Methods:** BXQ-350 is being investigated in a Phase 1b/2 study in combination with mFOLFOX7 and Bevacizumab (SoC) in newly diagnosed mCRC patients (NCT05322590). Primary objectives are to assess safety and preliminary efficacy of this combination, and to determine cumulative oxaliplatin dose. Secondary objectives include intensity, frequency and time to onset of CIPN. **Results:** The Phase 1b trial enrolled 33 oxaliplatin dosing evaluable patients; all patients completed the primary treatment period (6 months of SoC treatment plus BXQ-350). Amongst the 33 patients, 19 completed the full 12 Cycles of oxaliplatin dosing, 28 completed at least 8 Cycles with only 2 patients having dosing halted before Cycle 8 due to CIPN. There were no reported Grade 4 and only 3 reported Grade 3 CIPN AEs, all occurred after Cycle 12. Analysis of Neurofibrillary Light Chain (NfL) biomarkers suggests concordance with physician and patient reported outcomes. Grade 3 or higher Neutropenia was meaningfully reduced to 5% in mCRC patients receiving FOLFOX plus Bevacizumab. **Conclusions:** Results show that BXQ-350 was safe and well tolerated in the combination. Data suggest that BXQ-350 may provide additional clinical benefits and may reduce intensity or delay onset of CIPN while meaningfully reducing Grade 3 or higher Neutropenia, allowing for increased cumulative dosing of oxaliplatin and relative dose intensity in 1L mCRC. Clinical trial information: NCT05322590. Research Sponsor: Bexion Pharmaceuticals.

Results from a pilot feasibility study of a novel community health worker–led intervention delivering stepped palliative care and care navigation for patients with pancreatic ductal adenocarcinoma.

Nikhil Ravi Thiruvengadam, Maud Joachim-Celestin, Nishita Matangi, Lizbeth Rivas, Gina Mohr, Emanuel Eguia, Joel M. Brothers, Raja R. Narayan, Betty R. Ferrell, Susanne Montgomery; Loma Linda University, Loma Linda, CA; Loma Linda University School of Behavioral Health, Loma Linda, CA; Loma Linda University School of Medicine, Loma Linda, CA; Department of Oncology/Hematology, Loma Linda University Medical Center, Loma Linda, CA; Loma Linda University, Division of Surgical Oncology, Department of Surgery, Loma Linda, CA; City of Hope Medical Center, Duarte, CA

Background: Pancreatic Ductal Adenocarcinoma (PDAC) is associated with substantial morbidity, poor quality of life, and poor overall survival. Early palliative care (PC) has been shown to improve quality of life and reduce symptom burden in PDAC, but specialty PC services are often unavailable for this fast-progressing illness, and even then are only utilized by a minority of PDAC patients. To address this challenge, we developed a digitally enhanced CHW-led intervention to deliver stepped PC to patients with PDAC and to report its feasibility and preliminary efficacy. **Methods:** Adults (aged ≥ 18 years) with newly diagnosed PDAC (within 2 weeks of diagnosis) were enrolled in a single-arm pilot feasibility study from January to August 2025 (N = 48). The intervention involved early palliative care engagement with targeted escalation (stepping) for patients with untreated symptoms, leading to expedited PC visits, patient education, care navigation, and providing targeted financial resources for patients. The digital component involves using short educational videos and the Twilio SMS to administer the Edmonton Symptom Assessment Scale weekly, with patients with high symptom scores being stepped up to PC visits. The CHW-led intervention was delivered over 12 weeks. Feasibility outcomes were patient engagement with the CHW and completion of the intervention. The acceptability outcome was defined using the AIM-IAM-FIM instrument. Secondary outcomes include symptom burden (NCCN/FACT Hepatobiliary Cancer Symptom Index-18), Advanced Care Planning (ACP) compliance rates, and financial toxicity (measured by the COST instrument). **Results:** The median age of pts (N = 48) was 69 (IQR 62–76), and 29 (60%) were Hispanic. 25 (52%) had metastatic PDAC, 14 (29.1%) had borderline resectable PDAC, and 9 (18.8%) had resectable PDAC at diagnosis. Four patients died before the intervention was completed, while the remaining patients completed it. Regarding acceptability, 94% strongly agreed that the intervention was acceptable. Themes identified from exit-interviews included the critically important role of the CHW in the process, including appointment scheduling, especially as symptoms worsened. Patient's symptom burden (median 68 vs. 55, $P = 0.02$) and rates of financial toxicity (39% vs. 25%, $p = 0.01$) decreased from baseline to 12 weeks, while 83% of patients completed ACP by 12 weeks. **Conclusions:** Our digitally-enhanced CHW-led intervention delivering stepped PC was feasible and acceptable to patients with PDAC. The intervention was associated with improvement in symptom burden, reduction in financial toxicity, and higher ACP planning rates. Future prospective comparative studies are needed to understand the intervention's ability to help manage the morbidity associated with PDAC. Research Sponsor: DOD/CDMRP PCARP; PA230343.

Expressive writing for body image distress and anxiety in adolescent and young adult cancer survivors: A pilot, randomized controlled trial.

Victoria A. Wytiaz, John Rice, Amy Hecht-Zizes, Robert Knoerl, Yasmin Karimi, Tarek Haykal, Leslie Anne Fecher, Rashmi Chugh; Department of Internal Medicine, University of Michigan Rogel Cancer Center, Ann Arbor, MI; University of Michigan, Ann Arbor, MI; University of Michigan Comprehensive Cancer Center, Ann Arbor, MI; University of Michigan Rogel Cancer Center, Ann Arbor, MI; Rogel Cancer Center, University of Michigan, Ann Arbor, MI; Michigan Medicine, Ann Arbor, MI

Background: Up to 60% of adolescent and young adult cancer survivors (ages 15–39) experience body image distress but this is not well-managed due to multiple factors, including lack of provider expertise and patient hesitancy. Expressive writing invites participants to write openly about their thoughts and feelings related to a traumatic event, such as the cancer experience, to facilitate cognitive and emotional processing of the event. Expressive writing has not been explored in the AYA survivorship population with body image distress. The purpose of this pilot study is to determine the feasibility of implementing a four-week, in-home body image-focused expressive writing intervention for AYA cancer survivors with clinically significant body image distress. **Methods:** AYA cancer survivors with body image distress were recruited from oncology clinics at the University of Michigan and through institutional social media campaigns. Participants were randomized (1:1) to either a 4-week body image-focused expressive writing intervention or a control writing condition. Feasibility was based on recruitment and adherence, defined as completing 75% of writing sessions. Pre- and post-intervention, participants self-reported body image distress and anxiety utilizing the ten-item Body Image Scale (BIS) and the Generalized Anxiety Disorder 7 Scale (GAD-7). Changes in patient-reported outcomes were analyzed using linear mixed-effects models. **Results:** 27 participants were randomized (n=14 expressive writing, n=13 control) and were mainly female (96%) with locally advanced or metastatic cancer (60%). 26/27 (96.3%) completed all writing prompts outcome measures. Both groups demonstrated improvement in body image distress over the 4-week period. Expressive writing participants showed a numerically greater reduction (estimated change -5.57 , 95% CI $[-8.34, -2.8]$). The difference-in-change between groups was -2.77 (time $\times$ treatment interaction, not significant). Results in Table 1. **Conclusions:** A four-week, in-home body image-focused expressive writing intervention demonstrated feasibility among AYA cancer survivors with body image distress. AYA cancer survivors face persistent body image distress that can affect quality of life. This intervention can offer a feasible, accessible, and low-cost approach to help mitigate these concerns. Further research is needed to determine the efficacy of the intervention to reduce body image distress among AYA cancer survivors. Clinical trial information: NCT06046014. Research Sponsor: Conquer Cancer Anna Braglia Endowed Young Investigator Award in Cancer Supportive Care.

Estimated change in BIS and GAD-7 from baseline to week 4 by group.

Outcome	Group	Estimated Change	95% CI	p-value
BIS score	Expressive Writing	-5.57	[-8.34, 2.8]	<0.001
BIS score	Control Writing	-2.77	[-5.75, 0.22]	0.0676
GAD-7 score	Expressive Writing	-0.93	[-3.34, 1.48]	0.435
GAD-7 score	Control Writing	-4.67	[-7.26, 2.08]	0.001

The psychosocial status of children who have a parent with cancer.

Erdinc Nayir, Nilda Ata, Fevziye Toros, Aynur Çelik, Mehmet Ali Sungur, Rahime Gokboga, Aydan Akdeniz; Toros University, Mersin, Turkey; Dover Bay Secondary High School, Nanaimo, BC, Canada; Mersin University, Mersin, Turkey; Duzce University, Duzce, Turkey; Istanbul Gedik University, Istanbul, Turkey; Mersin University Hospital, Haematology Department, Mersin, Turkey

Background: While numerous studies have investigated the psychosocial status of children affected by childhood cancer, the number of studies investigating this situation in children whose parents have cancer is extremely limited. The purpose of this study is to determine the prevalence and causes of emotional and behavioral problems in children whose parents have cancer. **Methods:** We conducted the study in the medical oncology outpatient clinics between February and April in 2025. We included 73 children who have a parent diagnosed with cancer (case group) and an age- and gender-matched control group from healthy 59 children between the ages of 8–16. We subjected all the participants to the Revised Child Anxiety and Depression Scale (RCADS), recording their age, gender, parent gender and age, educational status, duration and severity of disease, number of siblings. **Results:** No statistically significant difference was found between the groups in terms of age, gender, education level, parent's age, gender, education level, and number of siblings ($p > 0.001$). The case group exhibited significantly elevated anxiety ($p < 0.001$) and depression scores ($p = 0.002$), along with higher total scale scores ($p < 0.001$), in comparison to the control group. Correlation analyses revealed weak but statistically significant positive correlations between age and total anxiety, depression, and total score in the case group ($p = 0.010$). Further examination of anxiety subdimensions showed similarly weak yet significant correlations with PaD, SAD, and OCD ($p < 0.001$). The females within the case group exhibited significantly higher anxiety ($p = 0.030$) and depression ($p = 0.035$) scores, and higher total scale score ($p = 0.025$) compared to males. Significant differences were observed in anxiety scores ($p = 0.018$) and total scale scores ($p = 0.047$) according to parental education level, with the highest scores consistently found among children whose parents held a master's degree. No significant differences were observed in anxiety, depression, or total scale scores according to the child's educational level, parent age, whether the patient was the father or the mother, disease duration and severity, and sibling status. **Conclusions:** Children of cancer patients are affected by their parents' health problems. These children should be considered in light of the "comprehensive approach to cancer". It should be noted that these children may need psychological rehabilitation at least as much as their parents with cancer. Research Sponsor: None.

Hearing/vestibular dysfunction and longitudinal changes in psychosocial well-being among breast cancer survivors.

Jincong Q. Freeman, Armaan Jamal, Yijia Sun, Fangyuan Zhao, Wenji Guo, Megan Huisingh-Scheetz, Jayant M. Pinto, Olufunmilayo I. Olopade, Dezheng Huo; Cancer Prevention and Control Research Program, UChicago Medicine Comprehensive Cancer Center, Chicago, IL; Department of Public Health Sciences, The University of Chicago, Chicago, IL; Key Laboratory of Carcinogenesis and Translational Research, Peking University Cancer Hospital & Institute, Beijing, China; Section of Hematology & Oncology, Department of Medicine, University of Chicago, Chicago, IL; Section of Geriatrics & Palliative Medicine, Department of Medicine, University of Chicago, Chicago, IL; Department of Surgery, University of Chicago Medicine, Chicago, IL; University of Chicago Medical Center, Chicago, IL

Background: Breast cancer treatment, in some cases, can cause hearing/vestibular dysfunction and negatively affect patients’ quality of life. The breast cancer survivor population is both growing and aging. Despite evidence that other cancer survivors have higher rates of hearing/vestibular problems than the general population, little is unknown about the impact of hearing/vestibular dysfunction on long-term changes in psychosocial well-being (PSWB) among breast cancer survivors. **Methods:** We surveyed the Chicago Multiethnic Epidemiologic Breast Cancer Cohort regarding whether patients had ever been told by a doctor that they had tinnitus, hearing loss, and/or vertigo between July and September 2023. PSWB was assessed repeatedly using the 10-item PROMIS on psychological distress/social isolation in 2020, 2021, 2022, and 2025. Total scores range from 0 to 40, with higher scores reflecting better PSWB. We fit separate linear mixed-effects models for hearing/vestibular dysfunction, controlling for age, race/ethnicity, marital status, income, insurance, comorbidity, AJCC stage, and treatment modality. Adjusted coefficients (β) and 95% CIs were calculated. **Results:** 1,466 breast cancer survivors were included: the mean age at survey was 63.5 years (SD 11.7); 69.6% identified as White, 22.6% as Black, 3.7% as Asian or Pacific Islander, and 3.6% as Hispanic. Overall, 16.5%, 17.4%, and 8.6% had tinnitus, hearing loss, and vertigo, respectively. The distribution of PSWB scores and trend over time are presented in the table. Survivors with hearing/vestibular dysfunction had lower mean scores than those without. After covariate adjustment, tinnitus (β -1.12; 95% CI -1.93, -0.30), hearing loss (β -1.12; 95% CI -1.93, -0.30), and vertigo (β -1.34; 95% CI -2.44, -0.24) were associated with significantly lower PSWB scores. In all subgroups, the PSWB score increased significantly over the years. Furthermore, Hispanic ethnicity, Medicaid, and being single were correlated with lower scores; whereas higher income levels were associated with higher scores. **Conclusions:** In this diverse cohort, breast cancer survivors with hearing/vestibular dysfunction experienced suboptimal PSWB over the study period. PSWB also varied by socioeconomic status. Oncology programs should consider screening for hearing/vestibular dysfunction and unmet sensory healthcare needs to improve PSWB and quality of life among breast cancer survivors. Research Sponsor: National Institute on Aging; T32AG000243; National Cancer Institute; P20CA233307; Breast Cancer Research Foundation; BCRF-23-071; Susan G. Komen; TREND21675016.

Survey year	PSWB score, mean (SD)					
	Tinnitus		Hearing loss		Vertigo	
	No	Yes	No	Yes	No	Yes
2020	28.7 (6.0)	28.4 (6.0)	28.8 (6.0)	28.2 (5.9)	28.7 (6.0)	28.3 (6.1)
2021	29.4 (5.6)	28.9 (5.9)	29.4 (5.6)	29.0 (5.5)	29.5 (5.6)	27.8 (6.0)
2022	30.1 (5.6)	29.2 (6.1)	30.0 (5.7)	29.7 (6.0)	30.1 (5.6)	28.5 (6.5)
2025	33.3 (5.6)	32.1 (6.4)	33.3 (5.6)	32.4 (6.2)	33.2 (5.6)	31.8 (6.3)
Trend per year	0.89	0.75	0.87	0.86	0.89	0.66
(p-value)	(<0.001)	(<0.001)	(<0.001)	(<0.001)	(<0.001)	(<0.001)

Cognitive impairment during anti-EGFR targeted therapy in metastatic colorectal cancer patients.

Liubov Yu Vladimirova, Elvina Gevorkyan, Alexey Bobrov, Natalia Semenova, Svetlana Shport, Oleg Ivanovich Kit; National Medical Research Centre for Oncology, Rostov-on-Don, Russian Federation; V. Serbsky National Medical Research Centre for Psychiatry and Narcology, Moscow, Russian Federation

Background: Cognitive function is a critical determinant of psychosocial adaptation and quality of life in patients with cancer. Even mild cognitive impairment may negatively affect daily functioning, communication, compliance, and social participation. The psychosocial consequences of cognitive changes during medical treatment are insufficiently studied in metastatic colorectal cancer (mCRC) patients. Anti-EGFR-targeted therapy affects downstream MAPK signaling, a pathway involved in synaptic plasticity and cognitive processes. This provides a biological rationale for investigating cognitive outcomes and their psychosocial relevance.

Methods: This study included patients with mCRC who received FOLFOX6-based first-line treatment. The main group (n = 50) received FOLFOX6 combined with an anti-EGFR monoclonal antibody (cetuximab or panitumumab), while the control group (n = 50) received FOLFOX6 +/-bevacizumab. Cognitive function was assessed at baseline and after eight cycles of therapy using the Addenbrooke's Cognitive Examination-Revised (ACE-R) and the Frontal Assessment Battery (FAB). Changes in cognitive performance were analyzed in relation to patients' functional vulnerability during ongoing treatment. Cognitive side effects were also evaluated according to CTCAE V.5.0. **Results:** Baseline cognitive performance was comparable between groups. After eight cycles of therapy, patients receiving anti-EGFR-targeted treatment demonstrated a significant decline in cognitive performance, including ACE-R total scores (from 93 [90; 94.5] to 87 [85; 90.5], $p < 0.001$), memory domain scores (from 22 [22; 23.5] to 20 [19; 20], $p < 0.001$), and attention/orientation scores (from 18 [16; 18] to 17 [15; 18], $p = 0.005$). In contrast, cognitive measures in the control group showed only minimal changes or remained stable over the same observation period. Evaluation according to CTCAE V.5.0. showed cognitive disturbance, memory and concentration impairments of mild and moderate grades, which were significantly more frequent in the anti-EGFR targeted group than in the control group ($p < 0.005$). **Conclusions:** Anti-EGFR-targeted therapy in metastatic colorectal cancer patients may cause significant cognitive impairment, which undoubtedly contributes to psychosocial maladaptation and reduced quality of life. This pattern of selective cognitive decline may compromise functional independence, communication, and psychosocial adaptation during active anticancer treatment. Routine cognitive assessment during treatment may facilitate early identification of patients at risk and support multidisciplinary management strategies. In addition, the role of the MAPK signaling pathway in memory formation should be studied. Research Sponsor: None.

Burnout among caregivers of hospitalized medical oncology patients: A cross-sectional survey study.

Suleyman Sami Guzel, Kubilay Tay, Serkan Nebi Demirci, Ozkan Alan; Istanbul University-Cerrahpasa, Cerrahpasa Medical Faculty, Department of Internal Medicine, Division of Medical Oncology, Istanbul, Turkey

Background: Caregivers of patients hospitalized in medical oncology wards play a crucial role in daily care and clinical decision-making, yet they are rarely screened for burnout. While caregiver burden has been widely studied in outpatient and palliative care settings, data focusing on inpatient oncology caregivers remain limited. This study aimed to evaluate burnout levels among caregivers of hospitalized medical oncology patients and to identify associated demographic and caregiving-related factors. **Methods:** This cross-sectional study included 91 caregivers of patients hospitalized in a medical oncology ward. Burnout and psychosocial distress were assessed using a structured 10-item survey developed based on established conceptual domains of burnout and caregiver burden. Items were rated on a 5-point Likert scale, with higher scores indicating greater burnout. Burnout levels were categorized as low (≤ 2), moderate (2–4), or high (≥ 4). Internal consistency was assessed using Cronbach's alpha. Group comparisons were performed using Mann–Whitney U and Kruskal–Wallis tests. Correlations were analyzed using Spearman's rho. Multiple linear regression analysis was conducted to identify independent predictors of burnout. **Results:** The median caregiver age was 49 years and 73.6% were female. The median burnout score was 3.0. Overall, 23.1% of caregivers reported low burnout, 57.1% moderate burnout, and 19.8% high burnout. Female caregivers had significantly higher burnout scores compared with males ($p = 0.008$). Caregivers with additional caregiving responsibilities also reported higher burnout levels ($p = 0.026$). Burnout scores correlated positively with duration of in-hospital caregiving ($\rho = 0.228$; $p = 0.030$). In multivariable regression analysis, female gender remained an independent predictor of higher burnout ($\beta = -0.298$; $p = 0.003$). Table 1 shows demographic and clinical characteristics of caregivers and patients. **Conclusions:** Caregivers of hospitalized medical oncology patients experience substantial levels of burnout, with nearly one in five reporting high burnout. Female caregivers appear to be at particularly high risk. These findings highlight the need for routine psychosocial screening and targeted supportive interventions for caregivers in inpatient oncology settings. Research Sponsor: None.

Variable	N=91 (%)
Caregiver gender (F/M)	67 (73.6)/24 (26.4)
CG age (years) (median)	49 (23-75)
CG Education level (L/Medium/H)	39 (42.9)/27 (29.7)/25 (27.5)
Relationship to patient (Spouse/Child/ First degree relatives/Other)	32 (35.2)/29 (31.1)/19 (20.9)/11 (12.9)
Additional caregiving responsibility (Y/N)	29 (31.9)/62 (68.2)
Burnout level [L/Moderate/H]	21 (23.1)/52 (57.1)/18 (19.1)
Patient gender (F/M/Other)	41 (45.1)/46 (50.5)/4 (4.4)
Patient age (years) (median)	61 (20-81)
Cancer diagnosis groups	
Lung and H&N	27 (29.7)
GI	23 (23.3)
GU+breast	22 (24.2)
Other	8 (8.8)

Longitudinal associations between patient and caregiver quality of life following hematopoietic stem cell transplantation.

Daniel Yang, Jesse D. Troy, Brenda Branchaud, Kris W. Herring, Areej El-Jawahri, Thomas William LeBlanc; Duke University School of Medicine, Durham, NC; Department of Biostatistics and Bioinformatics, Duke University School of Medicine, Durham, NC; Duke Cancer Institute, Durham, NC; Massachusetts General Hospital, Harvard Medical School, Boston, MA; Division of Hematologic Malignancies and Cellular Therapy, Department of Medicine, Duke University Medical Center, Durham, NC

Background: Caregivers of patients undergoing hematopoietic stem cell transplantation (HSCT) experience high rates of psychological distress, yet patient-level factors most strongly associated with caregiver outcomes over time remain poorly understood. We evaluated longitudinal associations between patient and caregiver quality of life (QoL) following HSCT. **Methods:** We conducted a secondary analysis of the PROTECT randomized trial of integrated palliative care during HSCT. Among enrolled patient-caregiver dyads, we measured patient (FACT-BMT) and caregiver (CarGOQoL) QoL at baseline, week 2, and months 3, 6, and 12. Only patient-caregiver dyads that completed both measures were included in analyses at each timepoint. Linear mixed-effects models were used to assess the relationship between changes in patient QoL and changes in caregiver QoL, adjusting for time and treatment arm. **Results:** Among 186 enrolled patient-caregiver dyads, patients had a mean age of 55.2 ± 12.4 years and 65% were male. Mean CarGOQoL remained stable from baseline through month 12 (range: 74.1–75.9). FACT-BMT declined at week 2 (91.9 ± 20.4) compared to baseline (105.0 ± 18.8), then recovered and improved by month 3 through month 12 (Table 1). In multivariable mixed-effects modeling, within dyads, visits where the patient’s QoL exceeded their usual level were associated with higher caregiver QoL ($\beta = 0.11$ per 1-point above the patient’s mean; $p < 0.001$), adjusted for time and arm. **Conclusions:** While average caregiver QoL remained stable throughout the follow-up period despite changes in average patient QoL, individual caregiver QoL closely tracked their patient’s QoL over the post-HSCT follow-up period. Patient-reported QoL represents a clinically meaningful marker to identify at-risk caregivers. Interventions targeting patient QoL may yield dual benefits for patient-caregiver dyads. Clinical trial information: NCT03641378. Research Sponsor: None.

Patient and caregiver quality of life by timepoint.					
Outcome	Baseline (n = 183)	Week 2 (n = 157)	Month 3 (n = 126)	Month 6 (n = 112)	Month 12 (n = 109)
Patient FACT-BMT (mean +/- SD)	105.0 +/- 18.8	91.9 +/- 20.4	107.0 +/- 18.4	111.0 +/- 19.6	112.0 +/- 19.9
Caregiver CarGOQoL (mean +/- SD)	74.1 +/- 12.0	74.1 +/- 12.7	75.9 +/- 12.8	75.8 +/- 13.8	75.7 +/- 14.8
Spearman	0.37 (p < 0.001)	0.27 (p < 0.001)	0.25 (p = 0.004)	0.40 (p < 0.001)	0.38 (p < 0.001)

Closing the depression gap in community oncology: Real-world outcomes from collaborative care.

Tyler Jones, Elizabeth Cleary, Cameron Schilling, Casey Patterson, Ramy Sedhom, Jesse R. Fann; Colla Health, Portland, OR; Colla Health, Dallas, TX; Colla Health, Seattle, WA; Colla Health, San Francisco, CA; University of Pennsylvania, Philadelphia, PA; University of Washington, Seattle, WA

Background: Depression is prevalent among patients with cancer, yet access to evidence-based care remains uneven. Community oncology clinics, where the majority of cancer care occurs, are less likely to offer integrated mental health services compared to comprehensive cancer centers, resulting in higher underdiagnosis, undertreatment, and persistent depressive symptoms. The Collaborative Care Model (CoCM) offers a potential strategy to address this disparity in community oncology. **Methods:** Community oncology patients with clinically significant symptoms of depression, as measured by a baseline PHQ-9 score ≥ 5 , and receiving collaborative care, delivered primarily remotely, for at least 80 days were analyzed as part of this observational study. Patients had their PHQ-9 assessed after 90 (≥ 80 & ≤ 100) days, including evidence of remission (PHQ-9 < 5) and signs of response (decrease of PHQ-9 score by $\geq 50\%$ or ≥ 5 points). Mean within-patient changes among all patients, stratified by baseline depression severity, were measured using paired t-tests. **Results:** Among 307 patients, mean PHQ-9 scores were observed to decline from 12.9 (SD 4.7) at baseline to 8.2 (SD 5.1) after 90 days of collaborative care (mean change -4.72, 95% CI -5.30 to -4.14, $P < 0.001$); 26.7% were observed to have depressive symptoms in remission and 51.5% had a clinical response. Patients with severe depression (PHQ-9 ≥ 20) at baseline had the largest improvement (mean change -9.60, 95% CI -11.78 to -7.42, $P < 0.001$). **Conclusions:** Community oncology patients with depressive symptoms receiving collaborative care experienced reductions in PHQ-9 scores after 90 days of care, with a substantial proportion experiencing clinical response and/or remission in this brief timeframe. Symptom changes were observed across the full spectrum of symptom severity. These real-world outcomes highlight meaningful decreases in depressive symptoms, underscoring the promise of CoCM as a scalable care model for community oncology clinics. Research Sponsor: None.

Observed depression outcomes among community oncology patients engaged in Collaborative Care Model (CoCM) psychosocial care for 90 days, stratified by baseline PHQ-9 severity.

PHQ-9 Score Category at Baseline	N	Mean PHQ-9 Score at Baseline (SD)	Mean PHQ-9 Score at 90 Days (SD)	N Observed in Remission at 90 Days (%)	N Experiencing Response at 90 Days (%)	Mean Total PHQ-9 Score Change (95% CI)
All (5-27)	307	12.9 (4.7)	8.2 (5.1)	82 (26.7)	158 (51.5)	-4.72*** (-5.30, -4.14)
Mild (5-9)	81	7.2 (1.4)	5.4 (3.6)	36 (44.4)	26 (32.1)	-1.86*** (-2.64, -1.08)
Moderate (10-14)	113	11.9 (1.4)	7.8 (4.2)	28 (24.8)	55 (48.7)	-4.08*** (-4.85, -3.31)
Moderately Severe (15-19)	83	16.5 (1.4)	9.9 (5.5)	15 (18.1)	55 (66.3)	-6.61*** (-7.85, -5.38)
Severe (20-27)	30	21.9 (1.6)	12.3 (6.0)	<11	22 (73.3)	-9.60*** (-11.78, -7.42)

*** $P < 0.001$.

Impact of structured oncologist-led home visits on psychological distress and resilience in patients with solid tumors undergoing chemotherapy: A comparative study.

Sonya Kircheva Draganova, Radostina Gencheva, Mariyana Eneva, Petya Kraveva, Mohamed Alhalabi, Daniela Ilieva, Rosalina Pechlivanova, Mila Petrova, Ivan Donev, Georgi Stamenov; Nadezhda Hospital, Sofia, Bulgaria; MHAT "Nadezhda", Sofia, Bulgaria; Hospital Pharmacy MHAT "Nadezhda", Sofia, Bulgaria; Medical Oncology Department, MHAT Nadezhda Hospital, Sofia, Bulgaria; MHAT Nadezhda Hospital, София, Bulgaria; MHAT Nadezhda Hospital, Sofia, Bulgaria; MHAT "Nadezhda", Sofia, Bulgaria; Department of Medical Oncology, Nadezhda Hospital, Sofia, Bulgaria; MHAT Nadezhda Women Health Hospital, Sofia, Bulgaria

Background: Psychological distress is prevalent among patients receiving chemotherapy. Home-based supportive interventions have the potential to address early psychosocial needs; however, data regarding their impact on both distress and resilience remain limited. **Methods:** Between March 1 and December 1, 2025, chemotherapy-naïve patients with solid tumors were invited to participate in a home-based supportive care study. Patients who opted for the intervention received a structured home visit by a medical oncologist following each of the first two chemotherapy cycles. These visits included patient-led discussions where the oncologist addressed questions regarding disease staging, prognosis, treatment protocols, and anticipated side effects. Before each chemotherapy cycle, patients completed self-reported assessments of psychological distress and resilience. Distress was measured using the Distress Thermometer (scale 0–10), with scores ≥ 4 categorized as high distress. Resilience was evaluated using the 10-item Connor-Davidson Resilience Scale, a unidimensional instrument where items are rated on a 5-point Likert scale. Higher scores indicate greater resilience. The control group consisted of patients who did not receive home visits; they completed the same assessments during routine clinic visits. In both cohorts, breast, lung, and colorectal cancers were the most frequent diagnoses. Distress and resilience outcomes were analyzed within each group across three time points using Cochran's Q and Friedman test. **Results:** The intervention group included 66 patients (12 male, 54 female) with a mean age of 58 years ($SD \pm 13.58$). The proportion of patients reporting high distress decreased progressively: 72.7% at baseline, 53.0% after the first visit, and 45.5% after the second visit ($p < 0.001$). Mean distress scores also declined significantly from 4.91 ± 2.79 at baseline to 3.55 ± 2.71 and 3.53 ± 2.59 following the first and second visits, respectively ($p < 0.001$). In contrast, mean resilience scores remained stable (30.26 ± 7.06 , 29.95 ± 8.82 , and 28.24 ± 12.12 ; $p = 0.72$). The control group included 145 patients (39 male, 106 female) with a mean age of 58 years ($SD \pm 12.58$). In this group, the prevalence of distress remained relatively stable across the three assessments: 66.2% at baseline, 57.9% at the second assessment, and 56.6% at the third ($p = 0.074$). Mean distress scores showed minimal variation: $4.45 \pm$, $4.08 \pm$, and $4.09 \pm$, respectively ($p = 0.163$). Mean resilience scores exhibited a downward trend from 30.19 ± 7.74 to 27.03 ± 12.20 and 25.52 ± 13.21 , though this did not reach statistical significance ($p = 0.076$). **Conclusions:** This study demonstrates that oncologist-led home visits during the early stages of chemotherapy can significantly reduce psychological distress in cancer patients while preserving resilience. Research Sponsor: None.

Impact of volunteer-integrated palliative home visits on psychological well-being among metastatic breast cancer patients in northern Malaysia.

Siti Khairizan Binti Rahim, Hairunnisa binti Mohamad Ibrahim, Siti Nooraini Mohamad Yusof, Mohamad Zulfadhli Abdullah, Norjalilah binti Umar; Universiti Sains Malaysia (USM) Medical Center Bertam, Kepala Batas, Malaysia; Taylor's College, Subang Jaya, Malaysia; Universiti Sains Malaysia (USM) Medical Center Bertam, Kepala Batas, Penang, Malaysia

Background: Metastatic breast cancer patients face overlooked psychosocial challenges, mitigated through home visits. Universiti Sains Malaysia’s volunteer-integrated palliative home visits bridge access gaps, support mental health (SDG 3), and foster partnerships (SDG 17). As Malaysia’s most common female cancer (2017–2021: 16,430 cases, 22.2% stage IV), breast cancer highlights early palliative integration, yet local home-based outcomes remain unstudied. **Methods:** This prospective cross-sectional study (October 2024 to January 2026) in Northern Malaysia (Penang, Kedah) evaluated the impact of volunteer-integrated palliative home visits on Psychological Well-Being (Ryff 42-item scale, baseline and after 12 weeks). Healthcare professionals provided symptom and psychosocial care, while trained volunteers focused on emotional and practical support. Mixed teams (professionals and volunteers) conducted visits 1 and 6, with flexible staffing for intervening visits. Of 94 recruited patients, 81 completed the study and domain changes analyzed via descriptives, paired t-tests, and Cohen’s d. **Results:** Participants were predominantly female (99%), aged 40 to 49 years (34.6%), low-income B40 group (64%) and multi-racial (78% Malay, 15% Chinese, 7% Indian). All had ECOG 0–3 at baseline, but 38% in ECOG 4 post-intervention. High-score groups (>30 on Ryff’s subscale sums) increased for positive relations (70% to 95%), environmental mastery (47% to 69%), self-acceptance (45.5% to 68%), and personal growth (70% to 85%), but declined for autonomy (55.6% to 54.3%) and purpose in life (74% to 35%). Paired t-tests (Table 1) revealed significant small-to-moderate improvements in environmental mastery ($p<0.001$, $d=0.46$), positive relations ($p<0.001$, $d=0.41$), self-acceptance ($p=0.042$, $d=0.23$), and purpose in life ($p=0.016$, $d=0.27$). Changes in autonomy and personal growth were not statistically significant. Purpose-in-life declines reflect disease progression. **Conclusions:** The volunteer-integrated palliative care significantly improved environmental mastery, positive relations, self-acceptance, and purpose in life among breast cancer patients, despite ECOG deterioration. Findings support that the home visit enhanced psychological well-being amid disease progression, though refinement is needed for domains with non-significant changes. Research Sponsor: Pfizer Inc; 90835877.

Paired t-test results for Ryff Psychological Well-Being (PWB) domains (pre- vs. post-intervention).					
PWB domains	Mean Difference (SD)	t(80)	p value	Cohen’s d	Effect Size
Autonomy	1.10 (6.51)	1.52	0.133	0.17	Small
Self-Acceptance	1.99 (8.66)	2.07	*0.042	0.23	Small
Positive Relations with Others	3.00 (7.31)	3.7	*0.000	0.41	Small to Medium
Personal Growth	1.07 (8.75)	1.11	0.272	0.12	Small
Environmental Mastery	3.27 (7.10)	4.15	*0.000	0.46	Medium
Purpose in Life	1.59 (5.84)	2.46	*0.016	0.27	Small

Influence of socioeconomic factors on patient-reported provider communication among patients with cancer.

Nishwant Swami, Edward Christopher Dee, James Fan Wu, Erin Feliciano, Fumiko Chino; Hospital of the University of Pennsylvania, Philadelphia, PA; Department of Radiation Oncology, Memorial Sloan Kettering Cancer Center, New York, NY; Division of Hematology and Oncology, Department of Medicine, Medical College of Wisconsin, Milwaukee, WI; NYC Health + Hospitals/Elmhurst, New York, NY; The University of Texas MD Anderson Cancer Center, Houston, TX

Background: Patient-provider communication is central to patient's understanding and overall experience, particularly in multi-disciplinary cancer care. Socioeconomic disadvantages may amplify downstream consequences of poor communication by eroding trust and exacerbating structural and access-related barriers. Using nationally representative survey data, we examined the association between socioeconomic factors and patient-reported communication experiences among adult cancer survivors. **Methods:** We analyzed pooled 2011-2023 data from the US Medical Expenditure Panel Survey (MEPS) to identify adults (≥ 18 years) with a history of cancer. Patient-provider communication was assessed by how often providers (1) treated patients with respect, (2) listened carefully, (3) explained things in a way they understood, and (4) spent enough time. Survey-weighted estimates compared communication scores across income and insurance groups. Multivariable ordinal logistic regression (MVA) models including survey year, race/ethnicity, education, region, sex, marital status and age estimated adjusted odds ratios (aORs) for the association of income level and insurance with patient-provider communication. **Results:** Among 9,535 cancer survivors, those in the lowest income quintile (family income $<$ federal poverty line (FPL)) reported the lowest rates of effective provider communication across all domains (57% listened, 53% time, 61% respect, and 57% explained). Survivors who reported being uninsured similarly reported the lowest rates of provider communication (50% listened, 43% time, 49% respect, and 51% explained). In adjusted analyses, lowest-income survivors were less likely than the highest income quintile survivors ($> 4 \times \text{FPL}$) to report being listened to (aOR 0.76, 95% CI 0.63–0.91), respected (aOR 0.76, 95% CI 0.63–0.93), or receiving clear explanations (aOR 0.75, 95% CI 0.63–0.91). Compared with privately insured patients, uninsured survivors were less likely to report clear explanations (aOR 0.57, 95% CI 0.39–0.85), or feeling listened to (aOR 0.56, 95% CI 0.38–0.82). Both uninsured and Medicaid-insured survivors were less likely to report adequate time (uninsured: aOR 0.54, 95% CI 0.36–0.82; Medicaid: aOR 0.89, 95% CI 0.79–0.99), or feeling respected (uninsured: aOR 0.51, 95% CI 0.35–0.73; Medicaid: aOR 0.86, 95% CI 0.76–0.98). **Conclusions:** Lower income and lack of insurance were associated with worse communication among US cancer survivors. Given substantial financial, logistical, and personal burdens of cancer care, these communication gaps may weaken trust and undermine patients' ability to understand and engage with recommended treatments. Targeted provider interventions aimed at improving clinician communication and care coordination will be essential to advancing equitable cancer care and rebuilding trust in an increasingly fractured healthcare system. Research Sponsor: None.

Pilot RCT of a patient-centered communication intervention to promote values-based treatment decision-making in older adults with AML.

Rachel Rodenbach, Atena Rahman, Yingzhu Chen, Emily Oh, Soroush Mortaz, Jason Harold Mendler, Jane Liesveld, Eric Huselton, Bassil Botros, Craig Maguire, Ronald M. Epstein, Sally Norton, Joanne Terhune, Jim Terhune, Supriya Gupta Mohile, Heidi D. Klepin, Daniel R. Richardson, Kah Poh Loh; James P. Wilmot Cancer Center, University of Rochester Medical Center, Rochester, NY; University of Rochester, Rochester, NY; James P. Wilmot Cancer Institute, University of Rochester Medical Center, Rochester, NY; University of Rochester, Wilmot Cancer Institute, Rochester, NY; University of Rochester Medical Center, Rochester, NY; Myeloid Cancer Advisory Board, James P. Wilmot Cancer Institute, Rochester, NY; Wake Forest University School of Medicine, Winston-Salem, NC; The University of North Carolina at Chapel Hill, Chapel Hill, NC

Background: Older adults with acute myeloid leukemia (AML) often have limited involvement in high-stakes treatment decisions that involve tradeoffs between survival and quality of life. We developed a patient-centered communication intervention (UR-GOAL) to support values-based decision-making. We assessed how patients and oncologists discuss values during treatment decision-making and explored whether UR-GOAL improves these discussions. **Methods:** This pilot RCT randomized patients ≥ 60 years old with newly diagnosed AML to UR-GOAL vs. usual care. UR-GOAL uses best-worst scaling to help patients prior to deciding on treatment to prioritize their values, which are shared with the oncologist. Two team members blinded to arm independently coded transcribed treatment conversations for values talk, defined as discussion of what matters to patients in treatment decisions. Values included patient, disease/treatment, and sociocultural priorities; examples include quality of life, treatment effectiveness, and physician recommendation, respectively. Coders assessed the depth of values discussion (the extent to which the oncologist explored patient values beyond acknowledgment), patient engagement (e.g. patient elaborating on values and asking questions), and values alignment (whether the oncologist incorporated patients' most important values into the treatment plan). Differences in coding were resolved by consensus. Continuous outcomes were compared using t-tests or ANOVA and categorical outcomes using chi-square or Fisher's exact tests. **Results:** We included 92 patients (mean age 74 and SD 7; 63% male; 93% white). A mean of 6.0 values was discussed per encounter (SD 3.0), with fewer explored in depth (mean 1.5; SD 1.5). The number of values discussed in total and in depth did not differ between arms (total values: UR-GOAL 6.4 vs. usual care 5.7, $p = 0.28$; and in depth: UR-GOAL 1.4 vs. usual care 1.6, $p = 0.14$). However, patients showed a trend toward greater engagement in values discussions in the UR-GOAL arm compared with usual care (78% vs. 59%, $p = 0.07$). The values most commonly expressed by patients as most important in driving treatment decisions were treatment effectiveness (44%) and care logistics (e.g. treatment in hospital vs. clinic, 19%), followed by physician recommendation (7%), treatment toxicity (4%), and quality of life (3%). Values aligned with the treatment plan in 70% of cases (UR-GOAL 76% vs. usual care 63%, $p = 0.26$). Patients whose values aligned discussed more values compared with those whose values were not aligned, not discussed, or indeterminate (6.9 vs. 4.0, $p < 0.01$). **Conclusions:** Older adults with AML discuss several values with their oncologists during treatment decision-making, though fewer in depth. The UR-GOAL communication intervention may promote patient engagement in shared decision-making and value alignment. Clinical trial information: NCT05335369. Research Sponsor: Conquer Cancer Career Development Award; American Cancer Society.

Using the NCCN distress thermometer to evaluate clinically elevated levels of distress among caregivers of HSCT patients.

Christine Vinci, Steve Sutton, Marilyn Horta, Ranjita Poudel, Min-Jeong Yang, Maija Reblin, Joseph A. Pidala, Heather S.L. Jim, Sierra Washington, Halle Smith; Department of Health Outcomes and Behavior, H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL; H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL; Rutgers University, New Brunswick, NJ; University of Vermont College of Medicine, Burlington, VT

Background: Caregivers of patients receiving an allogeneic hematopoietic stem cell transplant (HSCT) play a vital role in the care and recovery of patients. They must be present with the patient 24/7 for up to 100 days post-transplant, and they often report levels of distress higher than patients. Importantly, caregiver and patient distress are interdependent. Thus, knowing when to deploy appropriate resources and support to a distressed caregiver is essential. To date, the NCCN Distress Thermometer (DT) is a validated, single-item clinical measure consistently used in the oncology setting to assess and intervene upon patient distress. If such a tool was available for HSCT caregivers, oncology providers could assess and provide support for those in heightened distress. To date, limited research has been conducted in this area. This study examines the relationship of DT with self-reported depression and anxiety in a large sample of HSCT caregivers with the goal of proposing a potential clinical cut-point of elevated distress on the DT. **Methods:** Caregivers completed the DT, Center for Depression Studies Depression Scale (CESD), and Generalized Anxiety Disorder 7 (GAD7) 1-2 weeks pre-transplant as part of a larger study. Spearman correlation coefficients evaluated the association of the DT with CESD and GAD7. Logistic regression evaluated DT as a predictor of clinically elevated levels of depression (CESD >16) and anxiety (GAD7 >10). DT cut points (e.g., ≥ 4) as predictors of clinically elevated depression and anxiety were evaluated using sensitivity, specificity, and area under the curve (AUC). **Results:** Caregivers (N = 287) were 73% female, 75% spouse/partner of the patient, and ranged in age from 22-87 years (M = 58.2, SD = 13.4). The DT ranged from 0-10 with M = 4.5 (SD = 2.6). The CESD ranged from 0-51 with M = 13.3 (SD = 10.3) and 36% scored >16. The GAD7 ranged from 0-21 with M = 6.4 (SD = 5.5) and 24% scored >10. The DT was very strongly correlated (p 's < .0001) with the CESD ($r_s = .69$) and GAD7 ($r_s = .76$). DT score significantly predicted elevated depression (OR = 1.92, 95% CI[1.64-2.24]) and elevated anxiety (OR = 2.30, 95% CI[1.84-2.86]). Table 1 presents sensitivity, specificity, and AUC for DT cut points of 4-7. **Conclusions:** Findings suggest that although a cut-point of 4 on the DT has high specificity and a cut-point of 7 has high sensitivity, a cut-point of 6 indicates more balanced specificity and sensitivity when considering both depression and anxiety. In the clinical setting, providing the single-item DT as a measure of caregiver distress should allow for a brief and useful assessment indicating a greater need to provide support resources. Research Sponsor: National Cancer Institute.

DT cut point: N (%)	CESD			GAD7		
	Sensitivity	Specificity	AUC	Sensitivity	Specificity	AUC
4: 173 (60%)	.60	.95	.77	.52	.99	.75
5: 148 (52%)	.69	.88	.78	.61	.93	.77
6: 114 (40%)	.80	.75	.78	.74	.85	.80
7: 80 (28%)	.89	.58	.73	.86	.73	.80

A digital educational and decision-support intervention for patients with advanced lung cancer receiving immunotherapy: Results of a multi-phase, mixed-methods study.

Matthias Villalobos, Phoebe Ullrich, Henrike Voss, Marie Therese Leimbach, Laura Unsoeld, Michael Thomas; Department of Thoracic Oncology, Thoraxklinik, Heidelberg University Hospital and National Center for Tumor Diseases (NCT), NCT Heidelberg, Translational Lung Research Center Heidelberg (TLRC-H), Member of the German Center for Lung Research (DZL), Heidelberg, Germany

Background: Immunotherapy has transformed the treatment of advanced lung cancer, but it has also increased the complexity of information that patients must navigate. Knowledge deficits may compromise disease-management, shared decision-making, and goal-concordant care including timely integration of palliative care. This study aimed to develop and evaluate a digital application to support patients throughout this process. **Methods:** We employed a multiphase, mixed-methods design comprising: (1) a questionnaire-based online-survey with descriptive analysis ($n = 186$; SPSS); (2) semi-structured interviews with patients with advanced lung cancer analyzed using qualitative content analysis ($n = 20$; MAXQDA); (3) user-centered app development involving patients and health-care professionals; and (4) a pre-post pilot study ($n = 69$) analyzed using Wilcoxon signed-rank test. Primary outcomes for the pilot study were decisional conflict and knowledge; secondary outcomes included preparedness for decision-making, self-efficacy, usability, and acceptability. **Results:** Pre-development data integration revealed limited and frequently inaccurate patient knowledge regarding immunotherapy and treatment goals, as well as a discrepancy between patients' desired and actual involvement in treatment decisions, with minimal participation in physician-patient decision-making. The developed app demonstrated high usability and acceptability. In the pilot study, use of the app was associated with a statistically significant reduction in decisional conflict (median [IQR]: 20.3 [6.6–34.0] pre vs. 10.9 [3.1–29.7] post; $p = 0.001$), significant improvements in knowledge ($p < 0.001$), and increased preparedness for decision-making. **Conclusions:** Insufficient patient participation in decision-making, combined with knowledge deficits about immunotherapy, underscores the need for enhanced communication strategies. The digital application developed in this study appears to be a feasible, acceptable, and effective tool to support informed decision-making among patients with advanced lung cancer. Future research should evaluate integration into routine clinical workflows, long-term impact, and adaptations to address diverse patient needs and evolving treatment options. Clinical trial information: 00032683. Research Sponsor: AstraZeneca.

Protective factors supporting caregiver well-being in glioblastoma.

Desiree Reinken, Sean Reed; CEUFast, Villa Ridge, MO; University of Colorado, Anschutz Medical Campus, Aurora, CO

Background: Caregiving in glioblastoma (GBM) means dealing with cancer symptoms, plus the neurological decline that comes with this disease. Becoming a caregiver is rarely straightforward. Caregivers often become essential to the patient's daily life and well-being, though this may result in neglecting their own health. Most caregivers develop coping strategies (protective factors such as caregiver mastery or spiritual beliefs) to manage the responsibility of caring for a terminally ill loved one. This study looked at how caregiver protective factors shifted across the disease trajectory and whether these factors were connected. **Methods:** This was a secondary analysis of data from a three-group randomized clinical trial testing a needs-based intervention for neuro-oncology caregivers (NINR # R01NR013170). Caregivers were included if they were 21 or older, identified by the patient as their unpaid primary caregiver, spoke English, had phone access, were not caring for anyone else (except children under 21), and scored above 6 on the CES-D. Recruitment occurred from March 2014 to July 2016 at the University of Pittsburgh Medical Center, the University of Pittsburgh Cancer Institute, and the MD Anderson Cancer Center. Patients and caregivers gave informed consent prior to participation in the primary study. We conducted an a priori power analysis to determine the sample size required for detecting minimal differences in quality of life (QOL). The final sample included 60 caregivers. We measured outcomes at baseline, two, four, six, and ten months. Analysis used paired samples t-test, bivariate correlations, and linear mixed models. **Results:** Caregiver QOL changed significantly over time, particularly from baseline to four months ($p = 0.02$) and four to six months ($p = 0.01$). Protective factors correlated with one another at varying strengths (weak, moderate, and strong). At each time point, religion and spirituality were related to other protective factors. Spirituality had significant positive correlations with caregiver mastery ($r = 0.32-0.65$, $p = < .001-0.01$) and QOL ($r = 0.44-0.70$, $p = < .001-0.01$) throughout the study. After factoring in optimism, we found significant associations for caregiver mastery, positive aspects of caregiving, social support, and religion. **Conclusions:** Spirituality emerged as a key protective factor, yet most caregiver interventions ignore it. Providers should recognize and support spiritual coping mechanisms throughout GBM care, offering resources that match caregiver values and beliefs. Monitoring caregiver QOL is equally critical as tracking patient outcomes. When QOL declines, early interventions can prevent caregiver burnout and improve care quality for both members of the dyad. Research Sponsor: None.

“When I’m translating, I’m a daughter as well”: Perspectives of caregivers supporting patients with limited language proficiency.

Rinat Nissim, Paige Chu, Marianna Calamia, Shabbir M.H. Alibhai, Madeline Li, Martine Puts, Sarah Hales, Camilla Zimmermann, Breffni Hannon; Princess Margaret Cancer Centre, Toronto, ON, Canada; University Health Network, Toronto, ON, Canada; Princess Margaret Cancer Centre, University Health Network, Toronto, ON, Canada; University of Toronto, Toronto, ON, Canada; Princess Margaret Cancer Centre, University of Toronto, Toronto, ON, Canada

Background: Family caregivers of people with advanced cancer provide essential support but often experience significant emotional distress. Caring for patients with limited language proficiency (LLP) introduces additional, distinct challenges. Patients with advanced cancer and LLP experience barriers to access and quality of care and advance care planning, resulting in increased reliance on family caregivers even when professional language services are available. This study explored the experiences and challenges of caregivers supporting advanced cancer patients with LLP to inform future interventions aimed at improving patient and caregiver outcomes. **Methods:** Caregivers supporting patients with advanced cancer and limited English proficiency treated at the Princess Margaret Cancer Centre (Toronto, Canada) were recruited via clinician referral and study flyers. Participants completed semi-structured interviews or focus groups exploring healthcare navigation, interpreter use, support needs, and recommendations for service improvement for patients with LLP. Transcripts were analyzed iteratively using practical thematic analysis. **Results:** Ten caregivers (ages 34–63; 6 female, 4 male; 2 spouses, 8 adult children; 5 supporting Chinese-speaking patients) participated. Participants acted as informal interpreters and mediators between patients and providers, a form of ‘language brokering’ that added substantial emotional and cognitive burden. Their experiences are subsumed under 4 interrelated themes: 1) Protective buffering and information gatekeeping: caregivers often filtered or withheld prognosis and end-of-life information to protect patients’ emotional well-being or align with cultural values; 2) Interpreter use representing both relief and loss of control: professional interpretation reduced linguistic burden but created new concerns regarding privacy, cultural sensitivity, and control over sensitive discussions; 3) Constant vigilance: caregivers felt constant pressure to monitor and understand patients’ symptoms and preferences, communicate them to providers, and support patient understanding and reassurance; and 4) Invisibility of caregiver needs: caregivers rarely recognized or prioritized their own needs, framing language brokering and caregiving as an expected familial or cultural duty. **Conclusions:** Family caregivers supporting patients with advanced cancer and LLP perform substantial emotional and cognitive labor that remains largely unrecognized in clinical practice. Interventions such as consistent and proactive access to professional interpreters and multilingual educational resources delivered across multiple modalities may support both patients and caregivers. These findings highlight an under-recognized but critical dimension of equitable, patient-centered oncology care. Research Sponsor: Princess Margaret Cancer Centre.

Assessing loneliness in glioblastoma patients and caregivers using a nationwide survey.

Jacob Ellen, Quinn T. Ostrom, Fabio M. Iwamoto, Lakshmi Nayak, Kelli Duprey, Ed Pilkington, David Robles; Harvard Medical School, Boston, MA; Duke University, Durham, NC; Columbia University Irving Medical Center, New York, NY; Dana-Farber Cancer Institute, Boston, MA; OurBrainBank, Telluride, CO; OurBrainBank, Brooklyn, NY

Background: Loneliness is associated with poorer health outcomes and quality of life in cancer patients, yet its prevalence in the glioblastoma (GBM) population remains understudied. GBM's rapid progression and intensive treatment demands affect both patients and caregivers, but the burden of loneliness in these groups is unknown. We conducted a nationwide survey that assessed loneliness prevalence within the GBM community. **Methods:** OurBrainBank, a patient-led GBM nonprofit, distributed a HIPAA-compliant survey from February to September 2024 to GBM patients, current caregivers, and caregivers bereaved within 12 months. Loneliness was measured using the validated 3-item UCLA Loneliness Scale (range 3–9), with scores ≥ 6 indicating loneliness. Multivariable linear and logistic regression examined associations between caregiver status, race (white vs non-white), and financial difficulties in the past year and loneliness, adjusting for age, gender, and urban vs rural residence. **Results:** Among 525 respondents (404 caregivers, 121 patients), median age at diagnosis was 59 years. Overall, 52.0% (273/525) met criteria for loneliness, and the median UCLA score of the sample was 6.0. Caregivers reported higher loneliness than patients: 57.4% (232/404) vs 33.9% (41/121) were lonely, with mean UCLA scores of 5.88 (SD 1.90) versus 4.78 (SD 1.81). In adjusted models, caregivers had nearly threefold higher odds of loneliness (OR 2.97, 95% CI 1.91–4.67) and UCLA scores 1.22 points higher on average compared to GBM patients (95% CI 0.83–1.61; both $p < 0.001$). Financial difficulty in the last year (29% of sample) was similarly associated with greater loneliness (OR = 1.85 for loneliness, $p = 0.002$; 0.68-point higher average UCLA scores, 95% CI 0.32–1.05, $p < 0.001$). Finally, non-white respondents (12% of the sample) had higher odds of high loneliness compared to white respondents (OR = 4.00, $p = 0.01$) and had a 0.59 point higher UCLA score on average ($p = 0.03$). **Conclusions:** In this nationwide survey, GBM caregivers experienced substantially greater loneliness than patients themselves, and loneliness was also concentrated among those facing financial hardship and among non-white respondents. These findings highlight an underrecognized psychosocial burden and support integrating caregiver-focused and equity-oriented interventions into GBM care. Research Sponsor: None.

Parent willingness to enroll children with acute lymphoblastic leukemia in escalation and de-escalation clinical trials.

Kellee Nicole Parker, Sarah Weeks Alexander, Lisa M. Jacola, Kimberly Buff, Kyobin Hwang, Elham Hashemi, Lindsay Jibb; The University of Utah, Salt Lake City, UT; BC Children's Hospital, Vancouver, BC, Canada; St. Jude Children's Research Hospital, Memphis, TN; Momcology, Saint Johns, FL; University of Toronto, Toronto, ON, Canada; The Hospital for Sick Children, Toronto, ON, Canada

Background: Patient and parent willingness to participate in clinical trials has and will continue to be essential to improve care for children with acute lymphoblastic leukemia (ALL). Clinical trials for ALL can involve escalation of therapy (i.e., addition or intensification of chemotherapy or immunotherapy) or in subgroups with excellent prognosis, de-escalation of therapy (i.e., removal of agents or blocks of therapy with aim of minimizing toxicity). Understanding parents' decision making for trial participation is particularly important in de-escalation trials. We aimed to characterize parent willingness to enroll children with ALL in escalation and de-escalation clinical trials, identify sociodemographic and clinical determinants of willingness, and delineate decision making information needs. **Methods:** Parents of children currently or previously treated for ALL who are members of the Momcology support and advocacy organization completed an investigator-developed, parent-piloted online survey. Parents were presented with theoretical escalation and de-escalation trial scenarios and completed items about willingness to enroll their child and associated informational needs. Quantitative data were summarized descriptively and Spearman correlations examined associations with sociodemographic and clinical determinants. Qualitative data were analyzed using content analysis. **Results:** A total of 456 parents responded. Mean child age at diagnosis was 5.5 years [SD = 0.2, range 0-19]; 79% (369) had B-ALL and 17% (78) had T-ALL; and 65% (297) had completed therapy and were alive at the time of survey. Results showed that 22% (99) of parents would consider enrolling their child in a de-escalation clinical trial, 47% (216) would not, and 31% (141) were unsure. Responses for escalation trials (N = 423) were similar, with 21% (90) yes, 42% (179) no, and 36% (154) unsure. There was a significant negative correlation between both parent education level ($\rho = -0.12$, $p = 0.013$) and annual household income ($\rho = -0.10$, $p = 0.047$) with willingness to consider de-escalation, but not escalation, trial enrollment. Child age at diagnosis, current treatment status and distance from treatment center were not correlated with willingness. Parent decision making information needs clustered into three overarching domains: 1) impact on likelihood of relapse, survival outcome, and late effects, 2) evidence credibility, and 3) applicability to their child's individual risk profile. **Conclusions:** Across a large parent sample, substantial hesitation to enroll children with ALL in both escalation and de-escalation trials exists. Sociodemographic factors were associated with de-escalation decision making. Further research is needed to incorporate evidence-based parent decision making support in future ALL trials and to evaluate decision making and correlates in real world scenarios. Research Sponsor: University of Utah, Department of Pediatrics; Children's Oncology Group.

New paradigms of cancer and new language: A qualitative study exploring language around goals of cancer surgery.

Bonnie Odelia Wong, Orly Farber, Amanda Jane Reich, Zara J. Cooper, Jennifer W. Mack, Thomas E. Clancy, Chandrajit P. Raut, Elizabeth Lilley; Brigham and Women's Hospital, Boston, MA; Brigham and Women's Hospital, Center for Public Health, Boston, MA; Dana-Farber Cancer Institute, Boston, MA; Brigham Women's Hospital, Boston, MA

Background: Cancer interventions are often discussed amongst providers and presented to patients within the dichotomy of “curative” vs. “palliative” interventions. However, as understanding of cancer biology has shifted and as cancer treatments have evolved, some cancers have become chronic diseases for which surgery may have a non-curative but disease-targeted role. Despite new paradigms of cancer care, language has not evolved to reflect new goals of cancer surgery. **Methods:** Semi-structured interviews were conducted with cancer surgeons from throughout the U.S. via purposive and snowball sampling. Interviews included discussions of two hypothetical scenarios describing non-curative surgical operations and discussion of the term “disease-controlling” surgery as a category of neither palliative nor curative surgical intent. Transcribed and de-identified interviews were analyzed inductively using grounded theory. **Results:** 18 surgeons from 16 institutions were interviewed. Surgeons collectively outlined how changes in the paradigm of cancer treatment have resulted in challenges describing intent of cancer surgery. Specifically, responses to the term “disease controlling” surgery elicited examples of cancer pathologies and treatment courses which fail to fit existing treatment-intent language and which captured new roles for surgery in cancer treatment paradigms. These roles of surgery include "surgery as curative treatment" (including both curative intent with probability of cure and curative intent with possibility of cure), "surgery as adjuvant treatment" (targeted surgery to assist systemic therapies with possible change in disease course), and "surgery as palliative treatment" (symptom relief surgery without possible change in disease course). Within the 'targeted surgery' category, participants described expanded surgical roles for numerous metastatic diseases including debulking for improved systemic therapy efficacy, resection of treatment-resistant disease sites, and "resetting the clock" for indolent tumors. These operations require multidisciplinary coordination and understanding of available systemic treatments, as surgical goals are increasingly defined by each patient's broader treatment trajectory. **Conclusions:** Traditional “curative” vs. “palliative” surgical intent categories inadequately describe contemporary cancer surgery. The emergence of life-extending but non-curative treatments necessitates new language frameworks that better align with current understandings of cancer biology and new treatment modalities. New language is necessary to facilitate clearer communication between providers and patients about surgical goals and expected outcomes and to allow for better research evaluating whether surgical treatments achieve those goals and outcomes. Research Sponsor: National Institute of Health National Cancer Institute; T32CA092203.

Assessing the efficacy of cognitive behavioral therapy on anxiety, depression, and distress in people with cancer.

Daniela Tregnago, Alice Avancini, Lorenzo Belluomini, Jessica Insolda, Alessandra Auriemma, Camilla Zecchetto, Elena Fiorio, Elena Giontella, Ilaria Trestini, Matteo Lovo, Marco Sposito, Ilaria Mariangela Scaglione, Christian Ciurnelli, Gloria Adamoli, Adele Bonato, Serena Eccher, Michela Rimondini, Emilio Bria, Michele Milella, Sara Pilotto; Section of Innovation Biomedicine - Oncology Area, Department of Engineering for Innovation Medicine (DIMI), University of Verona, Verona, Italy; University of Verona, Verona, Italy; Section of Innovation Biomedicine - Oncology Area, Department of Engineering for Innovation Medicine (DIMI), University of Verona, Verona, Italy, Italy; Section of Oncology, Department of Engineering for Innovation Medicine (DIMI), University of Verona School of Medicine and Verona University Hospital Trust, Verona, Italy; Medical Oncology Section, Department of Medicine, University of Verona, Verona, Italy; Medical Oncology Unit, Azienda Ospedaliera Universitaria Integrata, Verona, Italy; Azienda Ospedaliera Universitaria Integrata Verona, Verona, Italy; Medical Oncology, Azienda Ospedaliera Universitaria Integrata Verona, Verona, Italy; Medical oncology, Azienda Ospedaliera Universitaria Integrata di Verona, Verona, Italy; Department of Neurosciences, Biomedicine and Movement, University of Verona, Italy, Verona, Italy; Comprehensive Cancer Center, Medical Oncology Department, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Italy; Medical Oncology, University of Verona, School of Medicine and Verona University Hospital Trust, Verona, Italy

Background: Patients with cancer frequently experience psychological impairments, including anxiety, depression, and emotional distress, which may significantly affect quality of life and overall well-being. Third-generation cognitive-behavioral interventions such as Mindfulness-Based Cognitive Therapy-Cancer (MBCT-Ca), Acceptance and Commitment Therapy (ACT) and Compassion Focused Therapy (CFT) have shown potential benefits in reducing psychological burden, although evidence of their efficacy remains limited. This study aimed to evaluate the efficacy of a structured third-generation cognitive behavioral therapy (CBT) intervention in reducing psychological symptoms in patients (pts) with cancer undergoing active cancer treatment. **Methods:** A third-generation CBT intervention was delivered twice a month. The eight individual 45-minute sessions included psychoeducation, behavioral activation, relaxation and breathing techniques, present-moment awareness, self-compassion, problem-solving, and assertiveness training. Psychological outcomes were assessed using the Hospital Anxiety and Depression Scale (HADS) and Distress Thermometer (DT) at baseline (To) and post- psychological intervention (T1). Descriptive statistics, Student t-test and Chi-square test were performed. **Results:** Overall 341 pts were recruited. The mean age was 65.8 years ($SD = 11.80$); 60% ($n = 204$) were women. Most patients were married or partnered 82% ($n = 279$). Regarding education level, 65% ($n = 221$) had higher education, 29% ($n = 100$) secondary education, and 6% ($n = 20$) primary education.. At baseline psychological assessment, 4.4% of patients ($n = 15$) had early-stage disease (stage I-II), 50.7% ($n = 173$) had locally advanced disease (stage III), and 44.9% ($n = 153$) had advanced-stage disease (stage IV). The most represented cancer sites were gastrointestinal cancer 55.7% ($n = 190$), followed by lung 11.7% ($n = 41$) and breast cancer 10.6% ($n = 36$). Chemotherapy was the most frequently administrated treatment 74% ($n = 254$), followed by targeted therapy 10% ($n = 35$) and immunotherapy 10% ($n = 34$). At To, clinically significant levels of anxiety, depression, and distress were reported in 33.2%, 31.3%, and 86.9% of patients, respectively. A total of 313 patients completed the intervention (dropout rate 8.2%, mainly due to disease progression), resulting in an adherence rate of 91.8%. At three-months follow up (T1), significant reductions in clinically relevant symptoms were observed for anxiety (-24.6% , $p < 0.001$), depression (-24.0% , $p < 0.001$), and distress (-30.0% , $p < 0.001$). **Conclusions:** These findings support the routine use of validated psychological screening tools in oncology and highlight the clinical value of structured CBT-based psycho-oncological interventions delivered by trained professionals to improve psychological well-being in patients with cancer. Research Sponsor: None.

Baseline predictors of treatment response in the bounce back mind-body resiliency trial for AYA cancer survivors.

Lucy Finkelstein-Fox, Tara Pattilachan Menon, Zeba Ahmad, Elyse Richelle Park, Giselle K. Perez; Health Promotion and Resilience Intervention Research Center, Massachusetts General Hospital/Harvard Medical School, Boston, MA; Virginia Tech Carilion School of Medicine, Roanoke, VA

Background: Mind-body interventions hold promise for improving coping and reducing psychological distress among adolescent and young adult (AYA) cancer survivors, yet benefits vary across participants. Little research has identified which survivors stand to benefit most from these programs. This secondary analysis of a randomized controlled trial of a mind-body group intervention tested whether baseline emotion regulation-related factors (worry and intolerance of uncertainty) moderated intervention effects on coping and distress (anxiety and depression). **Methods:** AYA cancer survivors (N = 72; ages 18–39) were randomized 1:1 to an 8-week virtual mind-body resiliency program (Bounce Back) or waitlist control. Primary outcomes were PROMIS anxiety and depression scores and total Measure of Current Status (MOCS) coping score at post-intervention (approximately 3-month follow-up), along with coping self-efficacy. Linear regression models, adjusted for baseline levels of each outcome, tested Randomization Group $\times$ Moderator interaction terms for two baseline moderators examined separately: Penn State Worry Questionnaire (PSWQ) and Intolerance of Uncertainty Scale (IUS). Interactions with $p < 0.05$ were considered evidence of moderation. **Results:** Compared to waitlist, participants assigned to Bounce Back showed greater improvements in anxiety and coping outcomes but similar depression outcomes overall. Randomization group differences in post-intervention anxiety were significantly moderated by both worry and intolerance of uncertainty. The intervention–control difference in anxiety (adjusted for baseline) was larger among participants reporting higher baseline worry (interaction $\beta = -0.39$, $p = 0.033$) and higher baseline intolerance of uncertainty ($\beta = -0.48$, $p = 0.033$). Neither moderator significantly altered randomization group differences in depression. For coping-related outcomes, higher baseline intolerance of uncertainty strengthened the intervention effect on coping self-efficacy (interaction $\beta = 1.92$, $p = 0.047$), and there was a trend for greater total MOCS improvement among participants with higher baseline worry (interaction $\beta = 0.33$, $p = 0.086$). **Conclusions:** In this secondary analysis of a randomized trial, the Bounce Back mind-body resiliency program produced the largest anxiety and coping benefits for AYA cancer survivors with relatively higher baseline worry and intolerance of uncertainty, whereas depression outcomes did not vary by these baseline characteristics. These findings suggest that emotion regulation vulnerabilities such as worry and uncertainty intolerance may help identify higher-risk AYAs who are most likely to benefit from group-based mind-body stress-management interventions. Future trials should confirm these moderators and test whether triaging higher-risk AYAs to mind-body programs improves psychological outcomes. Research Sponsor: None.

COMFORT Survey: A comparison of the comfort level of hematologic and solid tumor oncology specialists with serious illness conversations.

Michael J. Tang, Kayley Ancy, Allison De La Rosa, Jessica H. Brown, Linh Nguyen, Clark Andersen, Eduardo Bruera, Nico Nortje, Christopher Flowers, Jeffrey Edwin Lee, David Hui; Department of Palliative, Rehabilitation and Integrative Medicine, The University of Texas MD Anderson Cancer Center, Houston, TX; Center for Goal Concordant Care Research, The University of Texas MD Anderson Cancer Center, Houston, TX; Division of Geriatric and Palliative Medicine, McGovern Medical School at UT Health, Houston, TX; Department of Biostatistics, The University of Texas MD Anderson Cancer Center, Houston, TX; Department of Critical Care Medicine, The University of Texas MD Anderson Cancer Center, Houston, TX; Department of Lymphoma/Myeloma, Division of Cancer Medicine, The University of Texas MD Anderson Cancer Center, Houston, TX; Department of Surgical Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX

Background: Serious illness conversations (SICs) are essential in aligning medical care with the values and goals of patients with advanced cancer. It is unclear if hematologic and solid tumors specialists (i.e., physicians [MDs] and advanced practice providers [APPs]) differ in their comfort level with SICs, which may drive end-of-life care outcomes. We compared the comfort level with SICs between hematologic and solid tumor specialists and examined contributing factors. **Methods:** We surveyed 186 hematology and 186 solid tumor specialists at MD Anderson Cancer Center. The 64-question survey examined their comfort with SICs under 5 domains (Transitions of Care [TOC, primary outcome], Dying Process [EOL], Prognosis, Goals, Advance Care Planning [ACP]). Responses were rated from 0 (extremely uncomfortable) to 10 (extremely comfortable). The TOC domain included 4 questions (i.e., stopping cancer therapy / transfusions / artificial nutrition and recommending hospice). We compared groups using simple linear and multivariable models accounting for specialist demographics. **Results:** 245 specialists completed this survey, with a response rate of 66%. Hematologic and solid tumor specialists both reported high comfort with TOC (7.0 [2.4] vs 7.1 [2.2]), with no significant difference between groups (mean difference [95% CI]: 0.1 [-0.5, 0.7]; $P=0.78$). In univariate analysis, APPs were significantly less comfortable with TOC than MDs among both hematologic (2 [1.2, 2.8]; $P<0.0001$) and solid tumor specialists (1.4 [0.7, 2.2]; $P=0.001$). In multivariate analysis, APPs remained the only significant variable associated with less comfort with TOC in hematologic (1.5 [0.4, 2.7]) and solid tumor groups (1.2 [0.2, 2.1]). Similarly, we found no significant difference between hematologic and solid tumor specialists in comfort level with the other 4 SIC domains and observed significant differences between APPs and MDs (Table). **Conclusions:** Both hematologic and solid tumor specialists reported high levels of comfort with SIC; however, APPs were significantly less comfortable. Given that APPs are increasingly involved in SIC, our study underscores the need to provide more training and support for APPs. Research Sponsor: None.

Self-reported comfort levels for 5 SIC domains.

Domains	Mean [SD]				MD vs. APP Mean differences [95% CI]; p-value	
	Solid MD	Solid APP	Heme MD	Heme APP	Heme	Solid
TOC	7.8 [1.7]	6.4 [2.5]	8.1 [1.9]	6.1 [2.4]	2 [1.2,2.8]; <.0001	1.4 [0.7,2.2]; 0.001
Prognosis	8.5 [1.4]	7.1 [2.1]	8.6 [1.8]	6.8 [1.8]	1.9 [1.2,2.5]; <.0001	1.4 [0.8,2]; <.0001
Goals	8.5 [1.2]	7.8 [1.7]	8.9 [1.4]	7.5 [1.9]	1.4 [0.8,2]; <.0001	0.7 [0.1,1.2]; 0.09
EOL	7.9 [1.9]	6.3 [2.6]	8 [2.3]	6.2 [2.8]	1.8 [0.9,2.7]; 0.0005	1.6 [0.8,2.4]; 0.0009
ACP	8.6 [1.2]	7.2 [2.5]	9.1 [1.1]	7.3 [2.4]	1.7 [1.2,5]; <.0001	1.4 [0.7,2.1]; 0.0006

Defining when and how to support palliative care communication: International consensus on timing and clinician training priorities for adolescents and young adults with cancer.

Ursula Sansom-Daly, Holly Evans, Madeleine Juhmann, Lori Wiener, Abby R. Rosenberg, Meaghann Weaver, Anne-Sophie Darlington, Jennifer W. Mack, Fiona Schulte, Susan Trethewie, Ruwanthie Amanda Fernando, Toni Lindsay, Anthony Herbert, Maria Cable, Nancy Briggs, Richard J. Cohn, Antoinette Anazodo, Claire E. Wakefield, Global Adolescent and Young Adult Cancer Accord End-of-Life Study Group; University of New South Wales and Kids Cancer Centre, Sydney Children's Hospital, Sydney, NSW, Australia; UNSW Sydney, Sydney, Australia; National Cancer Institute, National Institutes of Health, Bethesda, MD; Dana-Farber Cancer Institute, Boston, MA; St Jude Children's Research Hospital, Memphis, TN; Southampton University, Southampton, United Kingdom; University of Calgary, Calgary, AB, Canada; Sydney Children's Hospital, Sydney, Australia; Liverpool Hospital, Sydney, Australia; Chris O'Brien Lifehouse, Camperdown, Australia; Queensland Children's Hospital, Brisbane, Australia; Institute of Clinical Sciences within the College of Medical and Dental Sciences, University of Birmingham, Birmingham, United Kingdom; The University of New South Wales and the Kids Cancer Centre, Sydney Children's Hospital, Sydney, NSW, Australia; Kids Cancer Centre, Randwick, Australia; Division of Quality of Life and Pediatric Palliative Care, Department of Pediatrics, Stanford University and Stanford Medicine Children's Health, Palo Alto, CA

Background: Early, developmentally appropriate palliative care communication is an international standard for adolescents and young adults (AYAs) with cancer, yet remains inconsistently implemented. Clinicians report uncertainty regarding the optimal timing of palliative care discussions and around what training they need. This study aimed to establish international consensus on when key palliative care topics should be introduced with AYAs across the cancer trajectory and to identify clinician training priorities. **Methods:** A three-round international Delphi study was conducted with multidisciplinary health professionals who had worked with at least five AYAs who had died from cancer or its complications. Participants rated the appropriateness of introducing four palliative care communication topics (prognosis/goals of care, emotional/existential issues, quality of life, and end-of-life-related medical care) across prognosis levels and treatment phases. Participants also rated the importance of clinician training topics and likelihood of attending different training modalities. Consensus was defined a priori as $\geq 80\%$ agreement. **Results:** Seventy-seven experts from 14 countries completed the final round. Consensus indicated that emotional and existential issues were appropriate to discuss early, including during active cancer treatment. In contrast, end-of-life-related medical decisions were considered appropriate later, most commonly following relapse, disease progression or poor prognosis. Discussions about prognosis, goals of care and quality of life were generally considered appropriate once cure was uncertain. Conversation timing was the only training topic to reach consensus as a priority (85.8%). Although no training modality reached formal consensus, learning from bereaved family members was the most highly endorsed approach (72.8%), followed by experiential and interdisciplinary learning formats. The presence of complex family or culturally and linguistically diverse dynamics did not fundamentally alter clinicians' views on timing, but was associated with a need for greater team support and time. **Conclusions:** This international consensus provides clear guidance on when different palliative care topics should be discussed with AYAs with cancer and identifies timing as the primary area in which clinicians require additional support. Strong clinician endorsement of experiential and family-informed training approaches highlights opportunities to strengthen workforce capacity for earlier, developmentally appropriate palliative care communication. Research Sponsor: Adolescent and Young Adult Cancer Global Accord; Cancer Institute New South Wales; 2020/ECF1163; National Health and Medical Research Council; APP1111800; APP2008300; Intramural Research Program of the National Institutes of Health (NIH); American Cancer Society; Seattle Children's Research Institute; Cambia Health Solutions; Arthur Vining Davis Foundations; National Palliative Care Research Center; CureSearch for Children's Cancer; Conquer Cancer, the ASCO Foundation.

Reproductive and pregnancy-related outcomes among adolescent and young adult female cancer survivors (15–39 years): A nationwide population-based study in South Korea.

Ja Yoon Heo, Jisun Yoon, Ju Hyun Jin, Tae Mi Youk; Odette Cancer Centre, Sunnybrook Health Sciences Centre, Toronto, ON, Canada; National Health Insurance Service Ilsan Hospital, Goyang, South Korea

Background: As survival rates among adolescent and young adult (AYA) female cancer patients improve, increasing numbers of survivors pursue pregnancy and childbirth. However, population-level data on reproductive outcomes and pregnancy-related complications among female cancer survivors remain limited. **Methods:** This study collected de-identified data from the South Korean National Health Insurance Service Database. Among 95,264 women aged 15–39 years newly diagnosed with cancer between 2007 and 2010, we identified 58,107 eligible survivors. This cohort was age-matched 1:10 with 719,213 women without cancer. Reproductive outcomes were assessed in the full cohort, and pregnancy-related complications were evaluated among women with documented pregnancies. Odds ratios (ORs) and 95% confidence intervals (CIs) were estimated using logistic regression. **Results:** Compared with matched controls, female cancer survivors had a higher risk of infertility (OR 1.25; 95% CI 1.21–1.28) and lower odds of pregnancy (OR 0.94; 95% CI 0.93–0.96) and childbirth (OR 0.81; 95% CI 0.78–0.84). Among women who became pregnant, cancer survivors experienced higher risks of ectopic pregnancy (OR 1.20; 95% CI 1.11–1.29), miscarriage or abortion (OR 1.23; 95% CI 1.14–1.32), intrauterine infection (OR 1.26; 95% CI 1.01–1.57), and preterm labor (OR 1.21; 95% CI 1.14–1.29). **Conclusions:** AYA female cancer survivors face increased risks of infertility and adverse pregnancy-related outcomes. These findings highlight the need for specialized reproductive counselling and high-risk obstetric care for female cancer survivors. Research Sponsor: National Health Insurance Ilsan Hospital grant (NHIMC 2020-20-009).

Reproductive outcomes in the full matched cohort and pregnancy-related outcomes among the pregnancy cohort.

Outcomes, No. (%)	Survivor (N=58,107)	Control (N=719,213)	OR	95% CI
Reproductive Outcomes				
Infertility	5,439 (9.4)	55,111 (7.7)	1.245	1.209 1.282
Pregnancy	16,974 (29.2)	218,901 (30.4)	0.944	0.926 -0.961
Childbirth	10,912 (18.8)	98,229 (20.8)	0.810	0.780 -0.842
Pregnancy-related Outcomes				
Ectopic pregnancy	783 (4.6%)	8,495 (3.9%)	1.198	1.111 -1.291
Miscarriage / abortion	866 (5.1%)	9,182 (4.2%)	1.228	1.143 -1.319
Preeclampsia / eclampsia	507 (3.0%)	6,488 (3.0%)	1.008	0.920 -1.105
Gestational diabetes	3,139 (18.5%)	40,317 (18.4%)	1.055	0.965 -1.046
Intrauterine infection	85 (0.5%)	872 (0.4%)	1.259	1.007 -1.574
Premature Rupture of Membranes / amniotic fluid disorders	2,131 (12.6%)	28,002 (12.8%)	0.978	0.933 -1.025
Placental disorders	238 (1.4%)	2,776 (1.3%)	1.107	0.969 -1.265
Preterm labor	1,168 (6.9%)	12,601 (5.8%)	1.210	1.137 -1.287

CI, confidence interval; No., number; OR, odds ratio.

Standardized birth rates and access to assisted reproductive technology among female cancer patients in the United States.

Isabel Beshar, Chi-Fang Wu, Caitlin C. Murphy, Roni Nitecki Wilke, Nuria Agusti, Alexander Melamed, Maria Iniesta-Donate, Karla Liliana Barajas, David Viveros Carreno, Alexandra Bercow, Hazel Nichols, Jose Alejandro Rauh-Hain; The University of Texas MD Anderson Cancer Center, Houston, TX; University of Chicago, Chicago, IL; Massachusetts General Hospital, Boston, MA; Clínica Universitaria Colombia, Bogota, Colombia; The University of North Carolina at Chapel Hill, Chapel Hill, NC

Background: Fertility after cancer is critically under-defined on a national scale, reflecting a substantial gap in survivorship care. We constructed a novel longitudinal dataset to describe 1) live births and 2) use of assisted reproductive technology (ART) among female cancer patients from 2004–2022. **Methods:** We linked population-based cancer registry data (2004–2018 in 12 states; 2004–2011 in California) with live birth certificates and the Society for Assisted Reproductive Technology database (2004–2022), which captures ~90% of ART cycles nationally, to create a dataset integrating oncologic characteristics, obstetric outcomes, and ART utilization. Female patients aged 15–45 at diagnosis of cancer were included. The primary outcome was the standardized birth ratio (SBR) >9 months after cancer diagnosis stratified by age, race/ethnicity, cancer site, stage, and receipt of systemic therapy calculated using Centers for Disease Control (CDC) general population birth rates from the 13 states. Secondary outcome was ART use after cancer diagnosis (≥ 1 autologous oocyte/embryo cryopreservation or embryo transfer cycles). Patients were categorized by expected fertility detriment, defined as pelvic malignancy and/or receipt of chemotherapy, hormone therapy, or abdominal/pelvic radiation. Associations with ART were evaluated with Cox proportional hazards models adjusted for age, cancer stage, insurance, and race/ethnicity. Person-years accrued from diagnosis date to first post-diagnosis birth/use of ART, death, age 51 (oldest age a post-cancer birth was observed), or December 31, 2022. The study was approved by the institutional review board. **Results:** 286,198 female cancer patients were included, with 25,586 babies born to 19,713 women over a mean follow up of 8.3 years. The overall SBR compared to the general population was 0.38 [0.36, 0.40], with lowest rates in gynecologic and breast cancers (0.22[0.18, 0.27], 0.26[0.23, 0.30]). 46.2% (n=9,110) of patients with births had thyroid cancer or lymphoma. Median time from diagnosis to birth was 3.27 years (2.00–5.27). Only 1.56% (n=5343) of the cohort used ART, with highest use among patients with breast cancer (n=2506, 46.9%). Expected fertility detriment was associated with higher hazard of ART use (aHR 2.37, 95% CI 2.20, 2.54), specifically cryopreservation (5.53[4.89, 6.26]). The 2022 live birth rate from our cohort (44.0%, 70/159) paralleled national trends (42.5%) reported from 457 fertility clinics by the CDC (p=0.69). **Conclusions:** The burden of infertility among reproductive-aged cancer patients is profound, with observed birth rates less than half that of the general population. Among patients who access ART, however, birth rates mirror those published by fertility clinics nationally. Despite this, ART services among cancer patients are underused, highlighting unmet needs in survivorship care delivery. Research Sponsor: U.S. National Institutes of Health; MD017999.

National trends and disparities in early-onset non-colorectal cancer mortality in the United States, 1999–2023: A population-based analysis of 240,190 deaths.

Kumail Mustafa Ali, Shree Rath, Muhammad Ali, Farwa Naveed, Umama Alam, Amar Lal; Jinnah Sindh Medical University, Karachi, Pakistan; All India Institute of Medical Sciences, Bhubaneswar, Bhubaneswar, India; Dow International Medical College, Karachi, Pakistan; Dow Medical College, Karachi, Pakistan; Khyber Medical College, Peshawar, Pakistan; Penn State Health Milton, St. Hershey Medical Center, The Pennsylvania State University, Hershey, PA

Background: Early-onset non-colorectal malignancies account for a substantial share of premature cancer mortality in the United States, yet comprehensive national evaluations of long-term trends and disparities remain limited. **Methods:** We analyzed CDC WONDER Multiple Cause-of-Death data from 1999–2023, identifying deaths among individuals aged 15–54 years with non-colorectal malignancies. Age-adjusted mortality rates (AAMRs) per 1 million population were standardized to the 2000 U.S. standard population. Temporal trends were assessed using Joinpoint regression to estimate annual percent change (APC) and average annual percent change (AAPC). **Results:** A total of 240,190 deaths from early-onset non-colorectal malignancies occurred during the study period. Overall AAMRs declined from 61.45 (95% CI 60.22–62.68) in 1999 to 52.76 (95% CI 51.67–53.87) in 2023. Largest proportion of deaths occurred at home (43.4%), followed by inpatient or medical facilities (39.6%). Among women, AAMRs increased steadily from 36.01 (95% CI 35.02–37.04) in 1999 to 39.03 (95% CI 38.03–40.05) in 2023 (AAPC +0.33%, 95% CI 0.20–0.47). In contrast, men exhibited substantially higher but declining mortality, with an accelerated decline after 2012 (APC –2.25%, 95% CI –2.67 to –2.02). Racial and ethnic disparities persisted. Non-Hispanic Black populations showed significant reductions (AAPC –2.25%), Non-Hispanic Asian/Pacific Islander populations experienced the steepest declines (AAPC –2.22%), while Non-Hispanic American Indian/Alaska Native populations exhibited an early surge (APC +9.57%) followed by prolonged plateauing with persistently high rates. Metropolitan areas experienced faster declines (AAPC –0.72%) than non-metropolitan areas. **Conclusions:** The post-2012 acceleration in mortality reduction suggests progress in cancer management; however, these gains were uneven and masked substantial disparities. Men experienced marked declines but continued to have significantly higher mortality than women, while the steady increase in female mortality raises concern for unaddressed sex-specific risk and disease dynamics. Stagnant trends among individuals aged 15–34 years indicate limited benefit of advances in oncology for the youngest patients. Racial, ethnic, and geographic inequities remained pronounced, with persistently elevated mortality among Non-Hispanic Black and American Indian/Alaska Native populations, slower improvements in non-metropolitan areas, and consistently high rates in several Southern and Appalachian states. Together, these findings indicate that national progress has not translated into equitable outcomes and highlight the urgent need for targeted prevention, earlier diagnosis, and region- and population-specific cancer control strategies to reduce avoidable early-life cancer mortality. Research Sponsor: None.

Bone mineral density changes in patients treated with anti-PD-1 immune checkpoint inhibitors.

Roma A. Kankaria, Rachelle W. Johnson, Douglas Buckner Johnson, Laura Carpin Kennedy, Jessica Mezzanotte Sharpe; Vanderbilt University School of Medicine, Nashville, TN; Vanderbilt University Medical Center, Nashville, TN

Background: Immune checkpoint inhibitors (ICIs) have revolutionized cancer treatment (tx), with almost half of all cancer patients (pts) today eligible for ICI tx. However, these agents frequently cause immune-related adverse events (irAEs). While many irAEs are well-documented, emerging reports suggest that skeletal toxicity may represent an underrecognized complication of ICI tx, particularly with agents that target PD-1. Preclinical models show that global deletion of the PD-1 gene (*Pdcd1*) or anti-PD-1 tx increases bone resorption, decreases bone formation, and weakens bones. However, skeletal effects remain poorly characterized in humans. We performed a retrospective analysis to assess bone mineral density (BMD) changes via dual-energy X-ray absorptiometry (DXA) results in pts treated with anti-PD-1 ICIs. **Methods:** We retrospectively analyzed adult pts from a single institution who received at least one dose of an anti-PD-1 agent with or without chemotherapy from 2014 to 2025 and who had pre- and post-tx DXA scans available. We collected demographics, cancer and treatment history, DXA data (including BMD, T-scores, and Z-scores), and scan timing relative to ICI tx. Descriptive statistics and paired t-tests ($p < 0.05$) were used for data analysis. **Results:** Of 382 pts who received anti-PD-1 tx, 103 had only post-tx DXA scans, and 28 had both pre- and post-tx DXA scans. Of these 28 pts, 93% were female with a median age of 70 at the time of tx (range 58–88). Pts had statistically significant decreases in femur BMD and T-scores pre- vs. post-tx: mean BMD 0.85 vs. 0.81 g/cm² ($p = 0.04$) and mean T-score -0.95 vs. -1.66 ($p = 0.02$). Mean Z-scores decreased but were not statistically significant: 0.05 vs. -0.24 ($p = 0.09$). In contrast, there was a trend toward increases in lumbar spine BMD, T-scores, and Z-scores, but none of these changes were statistically significant: mean BMD 1.16 vs. 1.15 g/cm² ($p = 0.93$), mean T-score -0.19 vs. -0.06 ($p = 0.73$), and mean Z-score 0.96 vs. 0.99 ($p = 0.72$). **Conclusions:** This is the largest reported study to date examining BMD changes after anti-PD-1 ICI tx. Although this sample size is small and consists of mostly female pts, these results show significant decreases in femur BMD and femur T-scores after anti-PD-1 ICI tx, resulting in potentially increased fracture risk. T-scores in particular are more accurate in this older pt population than Z-scores. The site-specific changes seen in this dataset align with preclinical studies showing that in female PD-1 knockout mice of all ages, spinal bone mass does not change, but femoral bone mass is reduced. This could reflect differences in cortical vs. trabecular bone or mechanical loading. These findings underscore the importance of skeletal monitoring and indicate that prospective studies are needed to validate the observed bone changes and better characterize fracture risk in patients receiving anti-PD-1 therapy. Research Sponsor: Scholarship.

Conditional survival in advanced melanoma treated with immune checkpoint inhibitors.

Chloe Lim, Thi Phuong Le Nghiem, Arkhjamil Angeles, Eric Michael Sonke, Ben Garbuz, Navindi De Silva, Thea Leavitt, William Lee, Vincent Isaac Poon, Thao Phuong Nguyen, Vanessa Bernstein, Kerry J. Savage, Alison Weppeler; BC Cancer - Vancouver, Vancouver, BC, Canada; BC Cancer, Vancouver, BC, Canada; BC Cancer, Victoria, Victoria, BC, Canada; Faculty of Medicine, University of British Columbia, Vancouver, BC, Canada; BC Cancer, Abbotsford, BC, Canada; BC Cancer Agency Vancouver Island Centre, Victoria, BC, Canada

Background: Immune checkpoint inhibitors (ICI) have improved survival in advanced melanoma, with some patients achieving durable remissions. Traditional survival estimates at diagnosis do not reflect how prognosis changes over time. Conditional survival (CS) provides a framework for time-dependent prognostication in long-term responders. **Methods:** We conducted a population-based retrospective cohort study of patients with unresectable/metastatic cutaneous melanoma treated with ≥ 1 dose of PD1-inhibitor based therapy in British Columbia (2012 -2022). Progression-free survival (PFS), overall survival (OS), and melanoma-specific survival (MSS) were estimated using Kaplan-Meier methods. Median follow-up was estimated using reverse Kaplan-Meier methods. Conditional PFS was calculated from ICI initiation and stratified by baseline characteristics and treatment response. **Results:** Among 897 patients, median age was 65 years (range 19-99); 48% (n=436) were M1c-d and 32% (n=290) received dual ICI. Median follow-up was 6.0 years (95% CI 5.7-6.3) and median OS was 3.2 years (95% CI 2.8-3.8); 5- and 10-year OS rates were 41% and 27%, respectively, while MSS rates were 49% and 38%, respectively. 5- and 10-year PFS rates were 31% and 22%, respectively. Conditional PFS analyses showed a decreasing risk of progression over time, most pronounced in patients achieving a complete response (Table 1). At 3-years post ICI initiation, patients in a complete response had a 5-year conditional PFS rate of 91% (95% CI 85-95%). Further analysis will assess whether their mortality normalizes relative to age- and sex-matched population controls to contextualize long-term survivorship. **Conclusions:** CS demonstrates dynamic improvement in prognosis among advanced melanoma patients who remain progression-free after ICI and provides clinically meaningful, time-updated prognostic information to guide patient counseling and follow-up strategies. Research Sponsor: None.

Five-year conditional PFS rate at ICI initiation (year 0) and subsequent PFS timepoints.

Strata (%; 95% CI)	Year 0	Year 1	Year 2	Year 3	Year 4
All patients	31% (28-34%)	53% (48-57%)	67% (62-72%)	80% (75-84%)	90% (85-93%)
ECOG 0 or 1	34% (31-38%)	55% (50-59%)	68% (63-73%)	81% (76-85%)	90% (85-94%)
ECOG ≥ 2	17% (11-24%)	42% (28-55%)	60% (40-75%)	72% (48-86%)	86% (55-96%)
M0/M1a/M1b	33% (29-38%)	52% (46-58%)	67% (60-73%)	81% (73-86%)	90% (83-94%)
M1c/M1d	29% (25-33%)	54% (47-60%)	67% (59-74%)	79% (71-85%)	90% (82-94%)
Complete response	77% (71-82%)	82% (76-87%)	88% (82-92%)	91% (85-95%)	95% (90-98%)
Partial response	27% (21-33%)	36% (28-43%)	50% (41-59%)	68% (57-78%)	88% (76-94%)
PD1-inhibitor only	28% (24-32%)	47% (42-52%)	62% (56-68%)	77% (70-82%)	89% (83-93%)
PD1 with CTLA4	38% (32-44%)	66% (57-73%)	78% (69-85%)	87% (77-93%)	92% (82-96%)

Impact of prior malignancy on cardiac complications and mortality in patients with COVID-19.

Samuel Condon, Haley Wilkes, Joshua Davis; UT San Antonio, South Texas Veterans Health Care Center, San Antonio, TX

Background: Cancer accounts for approximately 600,000 deaths annually in the United States, and patients with cancer are estimated to have nearly twice the risk of death following COVID-19 infection. While active malignancy and cancer-directed therapies are known to increase the risk of cardiac complications, it remains unclear whether patients with a prior history of cancer remain at elevated risk for cardiac events or mortality after COVID-19. This study aimed to evaluate whether a prior history of malignancy is associated with increased cardiac complications or all-cause mortality among Veterans diagnosed with COVID-19. We hypothesized that Veterans with a history of malignancy would have higher rates of cardiac complications and mortality following COVID-19 infection. **Methods:** We conducted a prospective observational cohort study of Veterans diagnosed with COVID-19 at the South Texas Veterans Health Care Center in San Antonio, Texas, using REDCap electronic data capture. Index dates ranged from March 13, 2020, through December 31, 2021, with a 10-month follow-up period. Both inpatient and outpatient Veterans were included. Patients with active malignancy or missing post-COVID cardiac outcome data were excluded. Patients were stratified into two groups: those with a prior history of malignancy and those without. The primary outcome was a composite of acute cardiac complications (arrhythmia, myocarditis, viral pericarditis, or viral cardiomyopathy) and all-cause mortality at 30 and 365 days. **Results:** Among 2,042 patients identified, 90 with active malignancy were excluded, leaving 1,952 patients for analysis. Of these, 5.3% (n=103) had a prior history of malignancy and 94.7% (n=1,849) had no malignancy history. Significant differences were observed in age, race, and BMI between groups. The composite primary outcome occurred more frequently in patients with prior malignancy at both 30 days (50% vs. 26%; OR 2.87, 95% CI 1.92–4.28, $p<0.0001$) and 365 days (53% vs. 29%; OR 3.06, 95% CI 2.05–4.58, $p<0.0001$). All-cause mortality was higher among patients with prior malignancy at 30 days (16% vs. 7%; OR 2.51, 95% CI 1.43–4.42, $p=0.0013$) and 365 days (16% vs. 14%; OR 3.03, 95% CI 1.97–4.66, $p<0.0001$). Cardiac complications alone were also more common in patients with prior malignancy (41% vs. 23%; OR 2.41, 95% CI 1.60–3.62, $p<0.0001$). **Conclusions:** In this large Veteran cohort, patients with a prior history of malignancy were approximately three times more likely to experience cardiac complications or death following COVID-19 infection compared with patients without a cancer history. These findings suggest that increased risk extends beyond active malignancy and highlight the need for targeted strategies to reduce adverse cardiac outcomes in patients with any history of cancer who develop COVID-19. Research Sponsor: None.

Microbiome associations with chemotherapy-induced nausea and vomiting: A metagenomic shotgun sequencing study.

Aasha I. Hoogland, Martine Extermann, Jin Xu, Youngchul Kim, Taylor Welniak, Oanh Nguyen, Yvelise Rodriguez, Sylvia Crowder, Xiaoyin Li, Brent Small, Stacy Fischer, Kristen Carpenter, Daneng Li, Anita Kinney, Donna L. Berry, Heather S.L. Jim; H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL; The University of North Carolina at Chapel Hill, Chapel Hill, NC; University of Colorado Anschutz, Aurora, CO; The Ohio State University, Columbus, OH; City of Hope National Comprehensive Cancer Center, Duarte, CA; Rutgers Cancer Institute, New Brunswick, NJ; University of Washington School of Nursing, Seattle, WA; Department of Health Outcomes and Behavior, H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL

Background: Chemotherapy-induced nausea and vomiting (CINV) is common, with four out of every ten patients reporting moderate to severe nausea even after treatment with antiemetics. Existing risk prediction models have focused on demographic, clinical, and patient-reported factors, but predictive accuracy remains low. A missing predictor may be the gut microbiome, or gut microorganisms that engage in reciprocal signaling with the brain via many of the same pathways known to cause nausea. **Methods:** In this original research study, we conducted whole-metagenomic shotgun sequencing of the gut microbiome to evaluate its association with patient-reported CINV and improve existing risk prediction algorithms by employing a random forest approach. Nausea and vomiting were reported 24 hours after infusion (acute) and 5 days after infusion (delayed) in patients treated with moderately- or highly-emetogenic chemotherapy using the MASCC Antiemesis Tool. Participants were recruited from five ORIEN centers: City of Hope, Moffitt Cancer Center, Ohio State University, Rutgers University, and University of Colorado-Denver. Fecal samples were collected prior to chemotherapy using at-home fecal occult blood test (FOBT) cards. **Results:** Participants (n=233) were 57 years of age on average (SD=12), and most were female (80%), White (89%), with breast cancer (55%). More than half of participants (65%) had early stage cancer. Any acute and delayed self-reported nausea was reported by 40% and 67% of participants, respectively. Any acute and delayed vomiting was reported by 3% and 12% of participants, respectively; the low rate of acute vomiting precluded additional analyses. No significant difference was observed in microbial diversity and the abundance of dominant bacteria at the phylum level between patients who reported nausea or vomiting and those who did not. Bacillota and Pseudomonadota were two phyla identified as the most significantly enriched in patients who reported nausea or vomiting, at either timepoint (FDR-adjusted $p < 0.05$). The predictive performance of risk models based on established factors were improved by incorporating the top 15 differentially abundant bacterial species for acute nausea (AUC=69% vs. 58%), delayed nausea (AUC=68% vs. 53%), and delayed vomiting (AUC=77% vs. 54%). **Conclusions:** Gut microbial diversity did not differ between patients who self-reported acute or delayed nausea and those who did not, but risk prediction models for acute nausea, delayed nausea, and delayed vomiting were all improved by incorporating differentially abundant bacterial species. Results suggest that the gut microbiome is an important factor associated with the development of CINV. Research Sponsor: National Cancer Institute; R01CA219389.

Longitudinal physical activity patterns and patient-reported cognitive function among patients with lymphoma receiving chemotherapy in a nationwide prospective cohort.

Tianming Zhao, Leanna Birsner, Elizabeth A. Salerno, Hongying Sun, Yuri Choi, Po-Ju Lin, Lindsey Jean Mattick, Benjamin T. Esparaz, Carla Jorgensen, Jamal Misleh, Karen Michelle Mustian, Michelle Christine Janelins, AnnaLynn Williams; Department of Public Health Sciences, University of Rochester Medical Center, Rochester, NY; Department of Surgery, Division of Supportive Care in Cancer, University of Rochester Medical Center, Rochester, NY; Program of Applied Exercise Science, School of Kinesiology, University of Michigan, Ann Arbor, MI; Heartland Cancer Research National Cancer Institute Community Oncology Research Program (NCORP), Decatur, IL; Carolinas - Prisma Health NCORP, Greenville, SC; Delaware/Christiana Care NCORP, Newark, DE

Background: Up to 70% of patients with cancer experience cancer-related cognitive impairment and physical activity (PA) may prevent or mitigate this concerning symptom. However, longitudinal data on PA before and during therapy for lymphoma and their associations with cognitive function across the treatment continuum are limited. This study examined PA patterns before, during, and after chemotherapy in patients with lymphoma compared with controls, and associations between pre-chemotherapy PA and cognitive changes over time in patients only. **Methods:** Cognitive function was assessed via the patient-reported Functional Assessment of Cancer Therapy-Cognitive Function perceived cognitive impairment subscale, and PA via the Aerobics Center Longitudinal Study questionnaire at pre-chemotherapy (T1), 1 month post-chemotherapy (T2), and 6 months following T2 (T3) in patients with lymphoma and age- and sex-matched non-cancer controls recruited from 19 NCORP sites across the US. MET-hours per week (MET-hrs/wk) were calculated, and meeting PA guidelines was defined as ≥ 150 minutes/week of moderate intensity or ≥ 75 minutes/week of vigorous intensity PA, or an equivalent combination. Linear mixed-effects models (LMMs) examined longitudinal PA changes between patients and controls and pre-chemotherapy PA's association with cognitive changes in patients only, adjusting for age, sex, race, education, cognitive reserve, BMI, anxiety, and depression at T1. **Results:** Participants included 242 patients with lymphoma (74.4% non-Hodgkin) and 209 controls (mean age [SD], 55.3 [14.8] vs 53.7 [14.9] years; male, 62.8% vs 58.9%). In patients, 36.8% met PA guidelines at T1, decreasing to 23.3% at T2 and rising to 40.8% at T3, whereas about half of controls met guidelines across T1-T3 ($p < 0.05$ at T1 and T2). Compared to controls, patients had lower PA (MET-hrs/wk) at T1 (β [95% CI] -4.81 [-9.64, 0.02]; $p = 0.051$), which declined to T2, resulting in significantly lower PA at T2 (β [95% CI] -7.48 [-11.93, -3.03]; $p = 0.001$); from T2 to T3, PA increased more in patients vs controls (β [95% CI] 6.38 [2.31, 10.45]; $p = 0.002$), reaching comparable levels at T3. Cognition declined from T1 to T2 in patients meeting (β [95% CI] -11.42 [-15.19, -7.66]; $p < 0.001$) and not meeting (β [95% CI] -9.29 [-12.09, -6.49]; $p < 0.001$) PA guidelines at T1; however, only those meeting guidelines showed cognitive recovery from T2 to T3 (β [95% CI] 3.64 [0.28, 7.00]; $p = 0.034$). **Conclusions:** In patients with lymphoma, PA significantly declined during chemotherapy; despite recovery to pre-treatment levels by 6 months post-chemotherapy, most remained insufficiently active. Further, active patients before treatment showed cognitive recovery after chemotherapy, suggesting that pre-chemotherapy PA may support post-treatment cognitive resilience, warranting further investigation. Research Sponsor: National Cancer Institute; R01CA231014; National Cancer Institute; UG1CA189961; National Cancer Institute; 3UG1CA189830-11S1; National Cancer Institute; 3UG1CA189972-11S1; National Cancer Institute; 3UG1CA189819-11S1.

Organ-specific proteomic aging clocks (PACs) and mortality in cancer survivors.

Shuo Wang, Aditya Surapaneni, Weihua Guan, Elizabeth Platz, Anne Hudson Blaes, Anna Prizment; University of Minnesota, Minneapolis, MN; NYU Grossman School of Medicine, New York, NY; Johns Hopkins University, Baltimore, MD

Background: Our study suggested that plasma conventional PACs can reflect, on average, accelerated aging in cancer survivors (Wang et al., JNCI 2026), but may overlook organ-specific variations. Organ-specific PACs may better predict CVD and cancer mortality in this group. **Methods:** We compared the associations of one conventional and 11 organ-specific PACs (Oh et al., Nature 2023) with mortality in 806 cancer survivors (aged 66–90) in the Atherosclerosis Risk in Communities (ARIC) study, 2+ yrs post-diagnosis (up to 12-yr follow-up). ARIC measured 4,712 plasma proteins by SomaScan. We computed PACs (conventional, adipose, artery, brain, heart, immune, intestine, kidney, liver, lung, muscle, pancreas) and their deviations from chronological age (age gap) after regressing PAC on age via LOWESS model. Multivariable Cox proportional hazards regression estimated hazard ratios (HRs) for mortality associated with age gap in survivors of any cancer (455 deaths: 127 CVD, 137 cancer deaths) and the most common cancers (165 breast (BrCa), 255 prostate (PrCa), and 78 colorectal cancer (CRC)). **Results:** In BrCa survivors, all age gaps (except intestine) were higher for those diagnosed 2–10 vs. >10 yrs before the start of follow-up. The pattern was opposite for all age gaps in CRC survivors (except heart and lung gaps). There was no specific pattern across age gaps in PrCa survivors. Further, in all cancer survivors, all age gaps, but artery and kidney, were associated with all-cause mortality (all $p<0.05$), with highest HRs for conventional, heart, and liver gaps (Table 1). Only heart age gap was associated with CVD mortality (HR per 1 SD=1.29, $p<0.05$), with no associations of any age gaps with cancer mortality. In BrCa survivors, conventional (HR=1.81) and 4 organ age gaps (brain, heart, immune, intestine; HRs = 1.45–1.68) were associated with all-cause mortality (all $p<0.05$). In PrCa survivors, conventional, heart, and liver age gaps were associated with all-cause mortality [all HRs=1.35, $p<0.05$]. In CRC survivors, conventional, heart, and immune age gaps were positively, but non-significantly, associated with all-cause mortality [HRs = 1.48–1.56], likely limited by sample size. **Conclusions:** Conventional and heart PACs demonstrated consistent associations with all-cause mortality beyond chronological age and lifestyle factors in total and individual cancer survivors. Heart PAC was most strongly associated with CVD mortality. Further work is needed to replicate this analysis and to test these age gaps as a predictor for mortality. Funding: NHLBI, NCI, NPCR. Research Sponsor: National Cancer Institute; National Center for Advancing Translational Sciences (NCATS); National Heart, Lung, and Blood Institute (NHLBI); National Program of Cancer Registries (NPCR).

Age gaps and all-cause mortality in cancer survivors; ARIC (2011-23).			
Age gap	HR (95% CI) per 1 SD	Age gap	HR (95% CI) per 1 SD
Conventional	1.48 (1.32, 1.66)	Intestine	1.13 (1.01, 1.26)
Adipose	1.13 (1.00, 1.27)	Liver	1.42 (1.26, 1.60)
Brain	1.19 (1.05, 1.34)	Lung	1.14 (1.02, 1.26)
Heart	1.41 (1.26, 1.59)	Muscle	1.19 (1.06, 1.33)
Immune	1.24 (1.10, 1.40)	Pancreas	1.33 (1.18, 1.49)

Common symptoms, quality of life, and lifestyle factors reported by cancer survivors attending the Sydney Cancer Survivorship Multidisciplinary Clinic.

Janette L. Vardy, Kim Kerin-Ayers, Eric Chen, Cole Deguchi, Marlena Hua, Fiona Lieu, Rebecca Norwood, Jane Turner, Carolyn Wildbore, Haryana M. Dhillon, Ashanya Malalasekera, Sim Yee Tan; Faculty of Medicine and Health, University of Sydney & Sydney Cancer Survivorship Centre, New South Wales, Australia; Sydney Cancer Survivorship Centre, Concord Cancer Centre, Concord Hospital, Concord West, NSW, Australia; Faculty of Science, School of Psychology, Centre for Medical Psychology & Evidence-Based Decision-Making, Psycho-Oncology Cooperative Research Group, The University of Sydney, Sydney, NSW, Australia; Faculty of Medicine and Health, University of Sydney and Sydney Cancer Survivorship Centre, Concord Cancer Centre, Concord Hospital, Concord West, NSW, Australia

Background: Sydney Cancer Survivorship Clinic (SCSC) provides multidisciplinary care for cancer survivors. During an initial visit, survivors consult with a medical oncologist or hematologist, cancer nurse specialist, dietitian, clinical psychologist, and exercise physiologist. Over 12 years, we assessed the health status of cancer survivors after curative-intent treatment. **Methods:** Survivors completed patient-reported outcomes assessing symptoms (PT-DATA), quality of life (QOL) (FACT-G), distress (Distress thermometer), fear of cancer recurrence (FCR-7, and psychologist assessment), diet, and physical activity (LTEQ) before initial clinic visit. Clinical data were obtained from the medical record. Simple descriptive statistical methods were used. FACT-G scores were standardized and compared to Australian general population and population with cancer (T-score 50, SD 10). **Results:** Between September 2013 and December 2025, 1181 survivors attended initial SCSC; 1081 (95%) consented to the use of their data. Of these, 68% were female; median age 58 years (range 18–91). Median time from diagnosis 10.7 months (IQR 8.4–16.6). Tumor types: 38% breast, 33% colorectal, 16% hematological, 14% other. Primary treatment: surgery 84%, chemotherapy 90%, radiotherapy 40%. Overall, 47% had 5+ symptoms of at least moderate severity (4+/10). Most frequently reported moderate-severe symptoms were: fatigue (50%), insomnia (40%), anxiety (36%), pain (35%), numbness (33%), sore hands/feet (32%), trouble concentrating (32%). Moderate-severe distress was reported in 44%. On the FCR-7, 32% had moderate-severe FCR. The psychologist rated 46% as having moderate-severe FCR. Mean QOL (FACT-G): total 79.9: domains physical 22.1; social 21.2, emotional 18, functional 18.6. Comparison to Australian populations: Total T-score 46.0: physical and emotional domains both 0.8 SD below. 59% were overweight or obese (mean BMI 27.2kg/m² (range 16.2–59.1)). Only 7% met national exercise guidelines for both resistance and aerobic exercise (18% resistance exercise alone, 24% aerobic exercise alone). **Conclusions:** Symptom burden remains high almost a year after diagnosis, with 47% reporting at least five moderate-severe symptoms; most commonly distress, fatigue, insomnia, anxiety and FCR. Overweight/obesity (59%) and physical inactivity remain lifestyle risk factors. Research Sponsor: National Health and Medical Research Council Australia.

Prevalence and financial burden of WHO-defined disability among childhood cancer survivors: A report from the St. Jude Lifetime Cohort study (SJLIFE).

Joshua Burns, Gregory T. Armstrong, I-Chan Huang, Yan Chen, Sedigheh Mirzaei, Daniel M. Green, Kevin R. Krull, Lisa M. Jacola, Tara M. Brinkman, Thomas Edward Merchant, Johnnie Kramer Bass, Jeanette Lavecchia, Jessica Sparrow, Kristin Szymanek, Robert J. Ferguson, Angela Delaney, Matthew J. Ehrhardt, Melissa M. Hudson, Kirsten K. Ness; St. Jude Children's Research Hospital, Memphis, TN

Background: Survivors of childhood cancer are at high risk for chronic health conditions that may result in disability. However, the prevalence and financial burden of disability, defined using the World Health Organization International Classification of Functioning, Disability and Health (WHO ICF), have not been described in this population. **Methods:** Disability-related items ascertained using clinical and patient-report data from SJLIFE were classified using standardized WHO ICF childhood cancer components, including impairments in body function or structure (strength, neurocognition, vision, hearing, speech, balance, neuropathy, ataxia, hemiparesis, tone, bowel and bladder, flexibility, gait, posture, pain, fatigue), activity limitations (motor function, communication, personal care), and participation restrictions (physical activity, education, independent living, employment, quality of life). Aggregate disability severity scores (ADSS) were calculated by summing item-level indicators (0 = none/mild; 1 = moderate, severe, or life-threatening disability) across 55 items spanning 3 components (38 body impairments, 5 activity limitations, and 12 participation restrictions). Disability was classified using either age- and sex-specific z-scores derived from 815 community controls ($0 \geq -1.5$; $1 < -1.5$) or NCI Common Terminology Criteria for Adverse Events (CTCAE) grades ($0 < 2$; $1 \geq 2$). Logistic regression evaluated associations between disability and financial burden (cancer-related financial impact), adjusting for sex, race, age at evaluation, and cancer treatment exposures (chemotherapy, cranial radiation, amputation). **Results:** Among 3,549 survivors (mean age at evaluation 33.6 years; range 18.0–68.9; 52.1% male; 80.7% White non-Hispanic), the most common diagnoses were acute lymphoblastic leukemia (31.9%), central nervous system tumors (14.5%), and Hodgkin lymphoma (10.5%). The point (most recent visit) prevalence (95% CI) of ≥ 1 item rated as moderate or greater disability was 87.4% (86.3–88.5). Component-specific prevalence was 74.6% (73.2–76.0) for body impairments, 32.9% (31.3–34.4) for activity limitations, and 63.3% (61.7–64.9) for participation restrictions; all were higher than controls ($p < 0.001$). Higher overall ADSS was associated with greater financial hardship (OR = 2.97; 95% CI 2.05–4.30) with similar associations across all components, including body impairments (OR = 2.67; 95% CI 2.09–3.41), activity limitations (OR = 2.28; 95% CI 1.91–2.72), and participation restrictions (OR = 2.61; 95% CI 2.13–3.21). **Conclusions:** WHO-defined disability is highly prevalent among adult survivors of childhood cancer and is strongly associated with financial burden. These findings highlight the need for integrated survivorship care that addresses both medical and socioeconomic risk factors. Research Sponsor: NIH, NCI; U01 CA195547.

The neurotoxicity rating scale: A novel patient-reported outcome (PRO) measure for neuro-psycho-behavioral late effects in head and neck cancer (HNC) survivors.

Matthew Stewart, Derek Smith, Zachary Kohutek, Elizabeth Wulff, Phyllis Kilpatrick, Barbara Murphy; Vanderbilt University Medical Center, Nashville, TN; University of Iowa College of Dentistry, Iowa City, IA; University of Kansas Medical Center, Kansas City, KS

Background: Chronic fatigue, mood disorders and cognitive dysfunction are well recognized but understudied late toxicities experienced by HNC survivors. In addition to these well recognized central symptoms, patients also experience an array of less well recognized psycho-behavioral complaints (see table below). These symptoms may profoundly affect a patient's ability to function within society. The neurotoxicity rating scale (NRS) was developed to assess the breadth of neuro-psycho-behavioral symptoms in cancer patients treated with interferon. We conducted a prospective cohort study in HNC survivors to assess the psychometric properties of this tool. **Methods:** Eligible patients included HNC survivors without evidence of disease ≥ 6 months after completion of therapy. The NRS was administered as part of a battery of patient reported outcome measures to assess pain and central symptoms. The NRS is a patient reported outcome measure which includes 36 items ranked from 0–4 (0 = no symptoms, 4 = severe). Hierarchical clustering was applied. **Results:** 243 patients were included with an average age of 72 years. Patients experienced clinically significant levels of neuro-psycho-behavioral symptoms; prevalence for selected items are shown in the table below. Preliminary analysis results in a group of six of clusters. The six-cluster solution was chosen as the most appropriate fit based on expert opinion. Clusters included: pain ($\alpha=0.89$), sleep ($\alpha=0.83$), general systemic symptoms ($\alpha=0.67$), neuromotor-autonomic ($\alpha=0.73$), cognitive ($\alpha=0.82$), and psycho-behavioral ($\alpha=0.94$). **Conclusions:** The NRS is a unique tool that comprehensively captures neuro-psycho-behavioral symptoms not assessed by existing instruments. The preliminary analysis amongst HNC survivors confirms the high prevalence of neuro-psycho-behavioral symptoms in this population. We identified six distinct symptom clusters: all demonstrated good internal constancy. This instrument allows for systematic study of neurotoxicity patterns, identification of high-risk patients, and evaluation of targeted interventions. Future directions include longitudinal validation and correlation with objective neuropsychiatric testing. Research Sponsor: None.

Selected items from the NRS with prevalence.

Item	Prevalence (%)
Tiredness/Fatigue	68%
Difficulty staying asleep	58%
Loss of interest in sex	41%
Restlessness	44%
Distractibility	41%
Word-finding difficulty	41%
No interest in activities	35%
Memory problems	50%
Decreased motivation	43%

Effect of "watch and wait" on fear of recurrence in rectal cancer: A multicenter cross-sectional study.

Ahmet Oruc, Galip Can Uyar, Latif Karahan, Tuba U    ur Tuzcu, Ece Ulukal Karancı, Gamze Emin, Fatih Kemik, Atila Yıldırım, Deniz Can Guven, Fatih Selcukbiricik, Nuriye   zdemir, Banu Ozturk, Berna Oksuzoglu, Murat Araz, Melek Karakurt Eryılmaz, Mehmet Artac; Necmettin Erbakan University Meram Medical Faculty Medical Oncology Department, Konya, Turkey; Etlik City Hospital, Department of Medical Oncology, Ankara, Turkey; Hacettepe University Faculty of Medicine Department of Medical Oncology, Ankara, Turkey; Gazi University Faculty of Medicine, Department of Medical Oncology, Ankara, Turkey; Antalya Egitim ve Arastirma Hastanesi, Antalya, Turkey; Medical Oncology Department, Karadeniz Technical University, Trabzon, Turkey; Department of Medical Oncology, Ko  University School of Medicine, Istanbul, Turkey; Karadeniz Technical University, Trabzon, Turkey; Hacettepe University Cancer Institute, Ankara, Turkey; Gazi University School of Medicine, Department of Medical Oncology, Ankara, Turkey; Antalya Education and Research Hospital, Antalya, Turkey; Necmettin Erbakan University, Meram Faculty of Medicine, Department of Medical Oncology, Konya, Turkey; Necmettin Erbakan University, Meram Medical Faculty, Department of Medical Oncology, Konya, Turkey

Background: Total neoadjuvant therapy (TNT) is now the standard of care for locally advanced rectal cancer. Watch-and-wait (WW) is the most commonly used approach for patients with a complete clinical response. This study aimed to investigate fear of recurrence, presence of depression, clinical symptoms, and functional capacities in WW patients and to identify differences between them and patients who underwent surgery after TNT. **Methods:** In this multicenter, cross-sectional study, patients were interviewed individually and completed the Fear of Cancer Recurrence Inventory-Short Form (FCRI-SF), Patient Health Questionnaire-9 (PHQ-9), and EORTC QLQ-ANL27. The EORTC QLQ-ANL27 results in two parameters: the symptom scale (SS) and the functional scale (FS). **Results:** The study included 121 patients who received TNT. The median age was 60 (54-65), and male patients were in the majority at 71 (58.7%). The most common disease location was the distal rectum at 56 (46.3%). In clinical staging, the most common findings were T3 disease at 86 (71.1%) and N1 lymph node status at 63 (52.1%). The number of patients followed up with WW after TNT was 17 (14%). 27 (22.3%) patients achieved a pathological complete response (pCR) after surgery. The median disease-free survival was 21 (11-37.5) months. In surgical patients (n = 104), FCR was 16 (7.25-21), while in WW patients (n = 17), FCR was 18 (9-25), p = 0.464. The PHQ-9 score was 3 (1-10) in surgical patients and 5 (1-9) in WW patients, p = 0.669. SS was 31.7 (21.5-38.8) in surgical patients and 15.9 (12.1-38.6) in WW patients, p = 0.045. FS was 84 (61.3-87.8) in WW patients and 68.2 (61.1-78.4) in surgical patients, p = 0.045. When WW patients and pCR patients were also evaluated, no statistically significant difference was observed in terms of FCR and PHQ-9. SS was 15.9 (12.1-38.6) in WW patients and 31.8 (21.7-49.2) in pCR patients, p = 0.027. FS was 84 (61.3-87.8) in WW patients and 68.1 (50.7-78.2) in pCR patients, p = 0.027. pCR patients were evaluated according to the presence of a permanent stoma. In patients with a stoma (n:9), FCR was 19 (17.5-24.5), while in patients without a permanent stoma (n:18), FCR was 11.5 (3.75-20), p = 0.022. PHQ-9 was 12 (1.5-17) in those with a permanent stoma and 1.5 (1-8) in those without a permanent stoma, p = 0.020. There was no difference between these two groups in terms of SS and FS, p = 0.253. **Conclusions:** In WW patients, the fear of recurrence does not increase compared to those who underwent surgery after TNT; the level of depression is similar, but their symptoms are fewer, and their functional capacities are better. Considering both the fear of recurrence and the severe depression levels in patients who are particularly pCR and followed up with a permanent stoma, the decision to undergo WW should always be taken into account. Research Sponsor: None.

Post-treatment recovery patterns among patients with early-stage cancer who develop taxane-induced peripheral neuropathy (TIPN): SWOG S1714 (NCT03939481).

Meghna S. Trivedi, Joseph M. Unger, Daniel Louis Hertz, Cathie Till, Thomas Brannagan, Stephanie Reyes, Bryan P. Schneider, William Johnson Irvin Jr., Amanda Redden Hathaway, Amy C. Vander Woude, Vinay K. Gudena, Paula Anel Cabrera-Galeana, Mary Orsted, Michael LeBlanc, Michael Jordan Fisch, Norah Lynn Henry, Dawn L. Hershman; Columbia University Irving Medical Center, New York, NY; SWOG Statistics and Data Management Center, Fred Hutchinson Cancer Center, Seattle, WA; University of Michigan College of Pharmacy, Ann Arbor, MI; SWOG Statistics and Data Management Center, Fred Hutch Cancer Center, Seattle, WA; Columbia University Medical Center, New York, NY; Lewis Cancer & Research Pavilion at St. Joseph's Candler/GA NCORP, Savannah, GA; Indiana University School of Medicine, Indianapolis, IN; Bon Secours Saint Francis Medical Center Cancer Institute/Southeast Clinical Oncology Research (SCOR), Midlothian, VA; University Cancer & Blood Center, Athens, GA; Cancer & Hematology Centers of Western Michigan, Grand Rapids, MI; Cone Health Cancer Center, Greensboro, NC; Instituto Nacional de Cancerología, Mexico City, DF, Mexico; HealthPartners Cancer Center at Regions Hospital, St. Paul, MN; The University of Texas MD Anderson Cancer Center, Carelon Medical Benefits Management, Houston, TX; University of Michigan Rogel Cancer Center, Ann Arbor, MI; Herbert Irving Comprehensive Cancer Center, Columbia University Irving Medical Center, New York, NY

Background: The primary analysis of S1714 developed and validated a TIPN risk prediction model including 5 clinical risk factors. Recovery patterns of TIPN are not well described. Although some symptoms may improve with time, other symptoms may persist or worsen as a result of permanent nerve damage. We describe the incidence of TIPN over 3 years and report on the post-treatment patterns of TIPN in those individuals who report TIPN at the end of taxane treatment (EOT) as a secondary analysis of S1714. **Methods:** S1714 enrolled participants > 18 years with Stage I-III primary lung, breast, or ovarian cancer starting treatment with a taxane-based regimen for a planned duration of 8 to 18 weeks. Participants were followed over the course of 3 years and assessed for TIPN using the patient-reported EORTC QLQ-CIPN20, which is composed of 3 subscale scores reported from 0-100, with increasing scores representing worse TIPN. EOT TIPN was defined as an increase in the CIPN20 sensory subscale score of ≥ 8 points from pre-treatment to EOT. **Results:** Among 1336 enrolled patients, N = 1321 were evaluable: Median age 55.7 years (range 23-85), 98.9% female, 11.3% Black/4.5% Asian/10.5% Hispanic/Latino, 90.7% with breast cancer. Paclitaxel was administered to 60.3% and docetaxel to 39.7%; 98.4% planned to start treatment with full dose of taxane. EOT TIPN was reported in 553 participants (41.9%). We identified 3 patterns of TIPN in these 553 participants over the 3 year period using the EOT CIPN20 sensory score as the reference. Improvement in TIPN from EOT was seen in 268 participants (48.5%), defined as a decrease of ≥ 8 points from the EOT CIPN20 sensory score. Stable TIPN was seen in 187 participants (33.8%), defined as < 8 point increase or decrease from the EOT CIPN20 sensory score. Worsening of TIPN from EOT was seen in 98 participants (17.7%), defined as an increase of ≥ 8 points from the EOT CIPN20 sensory score. Of the 553 individuals with TIPN at EOT, 283 (51.2%) still had clinically meaningful TIPN at 3 years compared to the baseline pre-treatment CIPN20 sensory score (defined as increase in CIPN20 sensory score > 8 points from pre-treatment timepoint to final assessment). **Conclusions:** Among individuals experiencing TIPN at EOT, nearly half experienced clinically meaningful TIPN improvement but almost one fifth had worsening of TIPN by the final 3-year assessment. The identification of clinical and correlative risk factors for persistent or worsening TIPN after completion of taxane treatment will allow for more informed decision-making regarding the long-term risks of taxane treatment and prioritize selection of patients in the investigation of interventions for prevention and treatment of TIPN. Funding: NIH/NCI/NCORP grant UG1CA189974, The Hope Foundation for Cancer Research. Clinical trial information: NCT03939481. Research Sponsor: NIH/NCI/NCORP; UG1CA189974; The Hope Foundation for Cancer Research.

Untargeted baseline metabolomic profiling to identify candidate markers of long-term severe cancer-related fatigue (CRF) in breast cancer (BC) survivors.

Antonio Di Meglio, Jeremie Jacquemin, Julie Havas, Anne-Laure Martin, Claire Jouffroy-Zeller, Christelle Jouannaud, William Jacot, Claire Cheymol, Coureche Guillaume Kaderbhai, Anne Kieffer, Baptiste Sauterey, Olivier Tredan, Paul H. Cottu, François Cherifi Sr., Carole Tarpin, Melanie Petera, Stephanie Durand, Estelle Pujos-Guillot, Youenn Drouet, Ines Luis; Cancer Survivorship Program, Université Paris-Saclay, UVSQ, Gustave Roussy, Inserm, CESP, Villejuif, France; Prevention & Public Health Department, Centre Léon Bérard, Lyon, France; Université Paris-Saclay, UVSQ, Gustave Roussy, Inserm, CESP, Villejuif, France; Unicancer, Le Kremlin-Bicêtre, France; Unicancer, Paris, France; Jean Godinot Cancer Institute, Reims, France; Department of Medical Oncology, Institut du Cancer de Montpellier, Université de Montpellier, Montpellier, France; Centre Oscar Lambret, Lille, France; Georges François Leclerc Comprehensive Cancer Care Centre, Dijon, France; Institut de Cancerologie de Lorraine, Vandoeuvre, France; ICO Institut de Cancerologie de l'Ouest, Angers, France; Medical Oncology, Centre Léon Bérard and Cancer Research Center of Lyon, Lyon, France; Medical Oncology, Institut Curie, Université, Paris, France; Centre François Baclesse, Medical Oncology Department, Caen, France; Institut Paoli-Calmettes, Marseille, France; Université Clermont Auvergne, INRAE, UNH, Plateforme d'Exploration du Métabolisme, MetaboHUB Clermont, Clermont-Ferrand, France; Centre Léon Bérard, Lyon, France

Background: CRF is common and debilitating among BC survivors; however its predictors and underlying biology remain partially defined. We sought to identify baseline plasma metabolomic markers of subsequent CRF to inform risk prediction and symptom mechanisms.

Methods: Baseline (pre-treatment [tx]) plasma samples from women with stage I-III ER+/HER2- BC in the CANTO cohort (NCT01993498) underwent untargeted metabolomic profiling (liquid chromatography and high-resolution mass spectrometry with electrospray ionization), yielding metabolic features for analysis. CRF was measured using EORTC QLQ-C30 (severe CRF: score $\geq 40/100$). Three penalized regression approaches (lasso, adaptive lasso, elastic net) were used to select baseline metabolites associated with severe CRF, adjusting for clinical covariates, including pre-tx CRF, age, body mass index, comorbidities, socioeconomic status, psychological distress, health behaviors, and tx. The cohort was split 2/3:1/3 (train:test); penalization factor λ was tuned in the train set by cross-validation. Clinical-only and clinical+metabolite features models were compared using test-set AUC, with bootstrap confidence intervals from resampled predictions ($B = 1000$). Covariate missingness was addressed by multiple imputation on 15 datasets. Metabolite annotation was conducted computationally using W4M, with manual curation and interpretation of spectra to identify key metabolites relevant to CRF. **Results:** In the train set ($N = 645$), mean age was 58 years (SD 10), 44% received chemo- and 90% endocrine-tx, 20% reported severe pre-tx CRF (similar characteristics in the test set; $N = 325$). 1935 metabolic features were analyzed. For severe global CRF at year-4 (prevalence 31%) the adaptive lasso clinical+metabolite features model included a 51-feature signature and had AUC = 0.70, specificity = 0.89, and sensitivity = 0.39 (sensitivity difference vs. clinical-only +0.17 [95% CI +0.06 to +0.29; $p < .001$]). Features with the largest penalized coefficients were concordant with univariate associations (all in the same direction) and showed clear differences in standardized levels between severe vs non-severe CRF. Nineteen features belonged to the annotated reference dataset, enabling putative identification of metabolites spanning endogenous pathways (including glycine [inverse association] and chenodeoxycholic acid [positive association]) and a likely exogenous/xenobiotic-related feature (mandelonitrile [positive association]). **Conclusions:** Baseline untargeted metabolomics identified a 51-feature signature associated with severe global CRF at year-4, after ER+/HER2- BC. Adding features selected via adaptive lasso to clinical covariates increased model sensitivity, and putative pathway mapping highlighted candidates for targeted validation and mechanistic studies. Research Sponsor: None.

Social determinants of health and long-term outcomes in prostate cancer: Mortality, survival, and comorbidity risks in a propensity score–matched federated database analysis.

Ashu Singh, Victoria Barone, Alexandria Tarbell, Venu Pararath Gopalakrishnan, Roberto Pili, Satheesh Kumar Poolakkad Sankaran; Division of Hematology Oncology, Department of Medicine, Jacobs School of Medicine and Biomedical Sciences, Buffalo, NY; Hematology Oncology, Department of Medicine, Jacobs School of Medicine and Biomedical Sciences, University at Buffalo, Buffalo, NY; Division of Hematology Oncology, Department of Medicine, Buffalo, NY; Department of Hospital Medicine, University of Massachusetts Memorial Center, Worcester, MA; Division of Hematology-Oncology, Department of Medicine, Jacobs School of Medicine, University at Buffalo, Buffalo, NY; Division of Hematology and Oncology, University at Buffalo, Buffalo, NY

Background: Social determinants of health (SDOH) such as housing instability, food insecurity, and low income are known to influence health outcomes, but their long-term effects on prostate cancer (PCa) patients remain underexplored. To compare long-term outcomes, including mortality, sepsis, sexual dysfunction, and comorbidities across major organ systems, between prostate cancer patients with and without adverse SDOH. **Methods:** Retrospective cohort study using the TriNetX federated database (deprecated COVID-19 Research Network, 88 healthcare organizations). Cohort 1 included adults (≥ 18 years) with PCa (ICD-10-CM C61) and at least one adverse SDOH code ($n = 14,595$). Cohort 2 included PCa patients without SDOH codes ($n = 875,545$). Propensity score matching (1:1) balanced cohorts on demographics, external morbidity causes, ECOG status, and BMI (final $n = 12,626$ per cohort). The index event was the first prostate cancer diagnosis (with SDOH for Cohort 1). Outcomes assessed from 1-day post-index onward (up to 20 years prior exclusion). Risk ratios (RR), hazard ratios (HR) from Kaplan-Meier survival, and mean instances via t-tests for mortality, severe sepsis, sexual dysfunction, and diseases of genitourinary, circulatory, endocrine/metabolic, respiratory, digestive, and infectious systems. **Results:** After matching, cohorts were balanced (mean age ~ 72 years, $\sim 56\%$ White, $\sim 25\%$ Black). PCa with adverse SDOH had higher mortality risk (22.0% vs 17.3% ; RR 1.272 [95% CI, 1.209–1.338]; $p < 0.001$) and worse survival (median 2821 vs 5246 days; HR 2.018 [95% CI, 1.906–2.137]; $p < 0.001$). Severe sepsis risk was elevated (5.6% vs 4.7% ; RR 1.199 [95% CI, 1.074–1.339]; $p < 0.001$; HR 1.824 [95% CI, 1.626–2.047]; $p < 0.001$). Sexual dysfunction risk was lower (0.2% vs 0.4% ; RR 0.493 [95% CI, 0.305–0.794]; $p = 0.003$). For comorbidities, PCa with adverse SDOH showed mixed risks—genitourinary diseases had a lower risk but poorer survival (HR 1.113, 95% CI 1.017–1.218, $p = 0.020$); circulatory diseases showed equivalent risk but worse survival (HR 1.223, 95% CI 1.089–1.374, $p = 0.001$); endocrine/nutritional/metabolic conditions had similar risk but reduced survival (HR 1.277, 95% CI 1.151–1.418, $p < 0.001$); respiratory diseases had equivalent risk but poorer survival (HR 1.531, 95% CI 1.416–1.656, $p < 0.001$); digestive diseases demonstrated lower risk with worse survival (HR 1.308, 95% CI 1.200–1.425, $p < 0.001$). **Conclusions:** Adverse SDOH are associated with increased mortality and poorer survival in prostate cancer, alongside heightened sepsis risk and differential comorbidity patterns. Interventions targeting SDOH may improve long-term outcomes. Research Sponsor: Dr Roberto Pili, Hematology Oncology, Department of Medicine, Jacobs School of Medicine and Biomedical Sciences, University at Buffalo, Buffalo, NY, USA, 14203.

Correlative analysis between external and internal lymphedema in head and neck cancer survivors.

Jessica Abene, Barbara Murphy, Mary S. Dietrich, Jie Deng; University of Pennsylvania, Philadelphia, PA; Vanderbilt University Medical Center, Nashville, TN; Department of Biostatistics, Schools of Medicine and Nursing, Vanderbilt University Medical Center, Nashville, TN; University of Pennsylvania School of Nursing, Philadelphia, PA

Background: More than 75% of head and neck cancer (HNC) survivors develop lymphedema following cancer treatment. Lymphedema can affect both external (e.g., soft tissue of the face and neck) and internal (e.g., pharynx and larynx) structures. Early identification and timely referral are essential for maintaining functionality and minimizing symptom burden. Understanding the relationship between external and internal lymphedema may inform assessment and treatment strategies. However, data describing the association between external and internal lymphedema remains limited. The purpose of this report is to fill this gap. **Methods:** A prospective, longitudinal descriptive study included 117 patients with oral cavity and oropharyngeal cancer. External lymphedema was evaluated through physical examination using the validated Head and Neck External Lymphedema and Fibrosis Assessment Criteria. Internal lymphedema was evaluated using an endoscopic examination scored with the Modified Patterson Scale. Examinations were performed at baseline and every three months for 12 months post-treatment. Somers'd correlation coefficients were calculated to test associations between external and internal lymphedema measures. **Results:** Both the total number of sites with external lymphedema and the total external lymphedema severity score correlated with the presence of at least one site of internal lymphedema (both $d = 0.31$). The total number of external sites of lymphedema moderately correlated with internal lymphedema involving the following structures: epiglottis ($d = 0.31$), pharyngoepiglottic folds ($d = 0.35$), aryepiglottic folds ($d = 0.34$), and anterior commissure ($d = 0.32$). The total external lymphedema severity score correlated with internal lymphedema involving the following structures: the epiglottis ($d = 0.32$), pharyngoepiglottic folds ($d = 0.35$), and aryepiglottic folds ($d = 0.34$). External submental lymphedema correlated with internal lymphedema involving the buccal mucosa ($d = 0.27$), epiglottis ($d = 0.28$), pharyngoepiglottic folds ($d = 0.28$), and pyriform sinus ($d = 0.28$). External lymphedema of the neck correlated with internal lymphedema in the pharyngoepiglottic folds ($d = 0.28$), arytenoids ($d = 0.27$), and anterior commissure ($d = 0.29$). External cheek lymphedema failed to correlate significantly with internal lymphedema. **Conclusions:** HNC survivors with external lymphedema are likely to have concurrent internal lymphedema. The presence of external lymphedema should initiate evaluation for internal lymphedema, particularly in patients with dysphagia or shortness of breath. The site of external lymphedema correlates with the sites of internal lymphedema: this may help inform assessment and management. Research Sponsor: National Institute of Dental and Craniofacial Research of the National Institutes of Health; R01DE024982.

Estimation of the impact of chemotherapy-induced biological age acceleration on breast cancer survivorship using multi-scale simulation modeling.

Swarnavo Sarkar, Mina S. Sedrak, Judith Carroll, Clyde Schechter, Hyman Muss, Jeanne S. Mandelblatt; Georgetown Lombardi Comprehensive Cancer Center, Washington, DC; David Geffen School of Medicine at University of California, Los Angeles, Los Angeles, CA; UCLA Cousins Center for PNI, Los Angeles, CA; Department of Family & Social Medicine, Albert Einstein College of Medicine, Bronx, NY; Lineberger Comprehensive Cancer Center, The University of North Carolina at Chapel Hill, Chapel Hill, NC; Georgetown University, Washington, DC

Background: Treatment of breast cancer with chemotherapy improves breast cancer survival. But chemotherapy also increases the accumulation of senescent cells in breast cancer survivors, which induces more senescent cells through paracrine signaling. The increased accumulation of senescent cells increases inflammation and tissue damage, which leads to earlier onset of aging-related diseases in survivors. We developed a simulation model connecting the biology of aging with breast cancer epidemiology to estimate the impact of chemotherapy-induced biological age acceleration on breast cancer survivorship. **Methods:** We integrated a systems biology model of accumulation of senescent cells with chronological age and an established Cancer Intervention and Surveillance Modeling Network (CISNET) breast cancer simulation model to estimate the impact of biological age-acceleration on breast cancer survivorship outcomes. We used published clinical data on senescence biomarker expression level ($p16^{INK4a}$ mRNA expression) in chemotherapy recipient breast cancer survivors to simulate the elevated senescence expression level in the remaining lifetime of breast cancer survivors. The difference in the senescence expression level in the chemotherapy group was evaluated against the senescence expression level in the general female population to quantify the excess biological age, or the biological age acceleration, after chemotherapy. The modified biological age induced by chemotherapy was used to determine the hazard of non-breast cancer mortality in breast cancer survivors. We used the CISNET breast cancer simulation model to simulate multi-birth cohorts of US females diagnosed with breast cancer to estimate survivorship outcomes after chemotherapy. Outcomes included remaining life years after breast cancer diagnosis, absolute number of non-breast cancer deaths, and the time-point at which the risk non-breast cancer mortality starts to dominate breast cancer mortality. **Results:** Biological age acceleration after anthracycline-based regimes caused a greater loss of life years than anthracycline-free regimens for women diagnosed at ages 30–39 years (median of 11.7 years vs. 2.1 years lost). This loss in life years diminished with increasing age at diagnosis (median of 6.0 years vs. 1.4 years lost for 70–79 year old women). The risk of non-breast cancer mortality exceeded breast cancer mortality up to 10–15 years earlier than expected based on chronological age after anthracycline-based regimens. **Conclusions:** Integration of computational systems biology modeling with breast cancer population-level modeling helps to identify subgroups of breast cancer survivors who are likely to experience survivorship loss due to biological age acceleration and may need survivorship care targeting non-breast cancer mortality. Research Sponsor: National Cancer Institute at the National Institutes for Health Grant; U01CA253911.

The effectiveness of a multidisciplinary pain program in improving adherence to the use of aromatase inhibitors in breast cancer survivors.

Panuch Eiamprapaporn, Bharat R. Narapareddy, Yaohua Ma, Thiti Susiriwatananont, Pooja Prem Advani, Barbara Lubrano, Alejandra Cuartas-Abril, Allison R. Baird, Cristin S. Dobrowolski, Saranya Chumsri, Shehzad K. Niazi, Barbara K. Bruce; Department of Medical Oncology, Mayo Clinic Florida, Jacksonville, FL; Department of Psychiatry and Psychology, Mayo Clinic Florida, Jacksonville, FL; Mayo Clinic Florida, Jacksonville, FL; Jacoby Center for Breast Health, Mayo Clinic Florida, Jacksonville, FL; Department of Nursing, Mayo Clinic Florida, Jacksonville, FL

Background: Aromatase Inhibitors (AI) have become the standard of care to reduce breast cancer recurrence in hormone receptor-positive (HR+) breast cancer patients. AIs have been shown to be effective in reducing the risk of breast cancer recurrence by 47%. However, up to 52% of patients prematurely discontinue their use due to AI-associated musculoskeletal pain symptoms called Aromatase Inhibitor-associated musculoskeletal pain syndrome (AIMSS). No effective treatment exists to treat AIMSS. The present study examined the effectiveness of a multicomponent pain treatment program in reducing symptoms of AIMSS with the goal of improving adherence to AI medication. **Methods:** This trial enrolled breast cancer survivors with AIMSS in an intensive multicomponent pain treatment program. Pain, impact on functioning, fatigue, and mood were assessed with the Brief Pain Inventory, Center for Epidemiologic Studies of Depression- Revised Questionnaire, Pain Catastrophizing Scale, Symptom Impact Questionnaire Revised, and Fatigue Questionnaire at baseline, 3-month, 6-month, 9-month, and 12-month intervals. Adherence to AI medication was obtained from patients' self-reports. The treatment program consisted of a two-day structured intervention focused on Cognitive-Behavioral skills to address strategies to improve pain control, fatigue, sleep disturbance, and stress while educating patients on the efficacy of Aromatase Inhibitors in prolonging cancer-free survival. **Results:** A total of 73 patients were enrolled, with a median age of 63 years (range 31-79). Participants were primarily white, married, and highly educated. The measures showed elevated levels of pain, fatigue, and psychological distress at baseline with decrements in self-reported levels of functioning. Significant improvements across all measures were observed at the 3-month follow-up after participation in the multicomponent pain treatment program. Significant improvements in pain-related outcomes were observed at 3 months (WPI Δ -1.6; SS Δ -4.0; both $p < 0.001$), with sustained reductions in symptom severity through 6-month, 9-month, and 12-month follow-up. Self-report of AI medication adherence at one year showed that 77.9% of patients were still taking their prescribed medication. **Conclusions:** Patients with AIMSS experienced substantial emotional distress, pain, fatigue, and functional impairment at baseline. Following the intervention, significant improvements were observed across pain, physical functioning, fatigue, and psychological distress, with benefits sustained at one year. Importantly, the intervention was associated with high long-term adherence at one-year follow-up, highlighting its potential to improve both quality of life and treatment persistence. Research Sponsor: Linse Block Foundation Grant and the Mayo Women's Health Center Grant.

Cardiac substructure dose signatures as predictors of late cardiovascular events in childhood cancer survivors.

Hrushikesh Reddy Pamreddy, Panah Tushar Parab, Sharanya Tripathi, Akshat Saxena, Charmi Bhanushali, Vidit Majmundar; Saint Vincent Hospital, Worcester, MA

Background: Radiation-associated cardiovascular disease (CVD) remains a major late toxicity in childhood cancer survivors. Whole-heart dose may mask heterogeneous substructure exposure, limiting precision in survivorship surveillance and modern radiotherapy planning.

Methods: Using the Childhood Cancer Survivor Study (CCSS) open-access cardiac substructure dosimetry dataset (12 mean-dose structures; Gy), we modeled time from cancer diagnosis to CAD, CHF, valvular disease, and arrhythmia with elastic-net Cox ($\alpha=0.5$; 10-fold CV). Bootstrap stability selection (200 resamples) quantified reproducible substructure predictors; “core” structures were defined by selection frequency ≥ 0.80 . Parsimonious Cox models were fit using core structures (dose scaled per 5 Gy) and adjusted for sex, race, age at diagnosis, anthropometric category, and smoking. Model discrimination was assessed using the concordance index (C-index). Model-based predicted 20-year absolute risks were used to estimate dose thresholds for clinically interpretable risk targets (reference profile: median covariates; modal factor levels). **Results:** Among 25,481 survivors, events occurred for CAD (n=475), CHF (n=544), valvular disease (n=131), and arrhythmia (n=181). LAD and aorta emerged as reproducible, endpoint-specific predictors: LAD was core across CAD/CHF/valvular outcomes; aorta and LMCA were core for CAD/valvular; pericardium was core for CAD/CHF. In adjusted core models, aortic dose was associated with CAD (HR 1.59 per 5 Gy; 95% CI 1.14–2.21; C-index 0.796) and valvular disease (HR 1.96; 95% CI 1.15–3.32; C-index 0.773). LAD dose was associated with CAD (HR 1.26; 95% CI 1.05–1.53; C-index 0.796) and CHF (HR 1.23; 95% CI 1.02–1.47; C-index 0.818). Absolute risk translation identified interpretable thresholds: predicted 20-year CAD risk crossed ~1% at 13 Gy mean aortic dose and ~2% at 20 Gy; CAD risk crossed ~1% at 24 Gy mean LAD dose. Predicted 20-year CHF risk crossed ~0.5% at 21 Gy mean LAD dose. Predicted 20-year valvular risk crossed ~1% at 23 Gy mean aortic dose. **Conclusions:** Substructure-specific dosimetry yields reproducible radiation “signatures,” with LAD and aorta dose consistently linked to late CVD. These dose-risk thresholds provide actionable benchmarks for risk-stratified survivorship surveillance and may inform substructure-sparing dose constraints in contemporary radiotherapy planning moving beyond whole-heart dose to endpoint-specific substructure constraints. Research Sponsor: None.

Substructure-specific dose thresholds for 20-year cardiovascular risk.

Outcome	Core Substructure	HR per 5 Gy (95% CI)	20-Year Risk Target	Dose Threshold (Gy)
CAD	Aorta	1.59 (1.14–2.21)	1%	13
CAD	Aorta	1.59 (1.14–2.21)	2%	20
CAD	LAD	1.26 (1.05–1.53)	1%	24
CHF	LAD	1.23 (1.02–1.47)	0.5%	21
Valvular	Aorta	1.96 (1.15–3.32)	1%	23

Toxicity assessment clinic as an efficacious tool to provide fast care to oncology patients on systemic therapy by minimizing emergency department visits and streamlining admissions directly from the cancer clinics.

Andrew R. Maher, Jennifer Grando, Harman Bhatiani, Hannah Silk, Christine Piescic, Sara Rask, Rouslan Kotchetkov; Queen's University, Kingston, ON, Canada; Royal Victoria Health Center, Barrie, ON, Canada; Hudson Regional Cancer Program, Barrie, ON, Canada

Background: The Toxicity Assessment Clinic (TAC) at the Hudson Regional Cancer Centre was established to improve access to care for cancer patients experiencing treatment-related toxicities, ensuring timely access to oncology-specific symptom management. The TAC is nurse led and utilizes an evidence-based oncology assessment tool to determine the appropriate care pathway, ensuring symptom assessment and treatment in a timely and safe manner. **Methods:** We reviewed the volume and characteristics of patients seen in the TAC for one year (2024), including visit modality, primary causes for TAC consultation, and appropriateness of TAC referrals by identifying related vs. unrelated complaints and determining the proportion of patients without a family physician who utilized TAC services for unrelated concerns. **Results:** There were 15,387 total chemotherapy clinic visits. Among them, there were 692 visits to TAC (4.5%). In total, 94.8% of patients had a family physician. Majority (93.9%) called TAC directly, 4.6% were sent by chemo suite nurses and 1.4% were referred from outside the cancer center. In addition, there were 997 registered nurse phone calls to follow up on health issues occurring within the clinic hours. Median age was 69 years [range 19–93]; 61% of patients were over 65. 61.9% of TAC patients had a solid tumor diagnosis, 24.5% had a hematological malignancy, and 6.8% had gynecological cancers. Gastrointestinal malignancies (26.9%), breast (17.5%) and lung (12.3%) were most prevalent. 47.9% had stage IV cancer, 27.2% had stage III. 93.5% of patients were on active systemic therapy, with 80.8% on first line. In-person TAC visits composed 89.1% of consults, and 10.9% had assessments over the phone. Skin lesions (7.8%), diarrhea (6.9%), disease progression (6.5%), urinary tract infection (5.8%) and respiratory infections (5.6%) were the most common issues. In 92.3% of cases, the presenting complaint was considered directly related to the cancer or therapy. Consult assessment durations were the following: 30 minutes or less (23.2%), 30–60 minutes (71.8%), and ≥ 60 minutes (4.9%). Of note, 76% of phone calls required ≤ 30 minutes compared to 39% patients who attended TAC in person. 52.6% of admitted patients from TAC required ≥ 60 min of assessment time. In 85.7% of cases, medical problems were resolved during the TAC visit; 1.4% were sent to ED and 12.9% were directly admitted to hospital. **Conclusions:** The TAC model is feasible and provides rapid assessment of patients on systemic therapy, particularly in the front-line setting. It is a cost-effective alternative to ED visits and streamlines admissions directly from cancer clinics. TAC improves patient flow for vulnerable populations such as elderly and immunocompromised patients. Research Sponsor: None.

A prospective study of the early treatment of recombinant human thrombopoietin for chemoradiation-induced thrombocytopenia in cervical squamous cell carcinoma patients.

Lu Li, Ming Fan, Yueqian Guo, Yan Tan, Qian Peng, Fang Li, Xin Lai, Qingping Yin, Ke Yuan, Jinyi Lang, Mei Feng; Department of Radiation Oncology, Sichuan Cancer Hospital and Institute, Sichuan Cancer Center, School of Medicine, University of Electronic Science and Technology of China, Chengdu, China; Sichuan Cancer Hospital, Chengdu, China; Yibin Second People's Hospital, Yibin, China; Department of Medical Oncology, the Third People's Hospital of Sichuan, Chengdu, China

Background: To explore the early intervention timing of recombinant human thrombopoietin (rhTPO) for cancer treatment-induced thrombocytopenia (CTIT) in cervical squamous cell carcinoma (CSCC) patients during concurrent chemoradiotherapy. **Methods:** Patients with stage I-IVa CSCC who developed CTIT during radical concurrent chemoradiotherapy were prospectively enrolled in our study. rhTPO intervention was used at the first presentation of G1 or G2 CTIT during concurrent chemotherapy respectively. The key indexes, including nadir platelet count, platelet recovery time, platelet transfusion and incidence of G3-5 CTIT were recorded in two groups. χ^2 test was used for the effective analysis, and univariate and multivariate analyses logistic regression analysis was used to predict the potential factors for the G3-5 CTIT. **Results:** From February 2021 to June 2024, 204 CSCC patients who developed CTIT during radical chemoradiotherapy at Sichuan Cancer Hospital were prospectively enrolled. 75 patients who occurred G1 and G2 CTIT at the first presentation during concurrent chemoradiotherapy received rhTPO intervention. They were included in the intent-to-treat (ITT) population analysis. According to the timing of the rhTPO intervention, the patients were divided into G1 group ($100\times10^9/L > PLT > 75\times10^9/L$) and G2 group ($75\times10^9/L > PLT > 50\times10^9/L$). For effective analysis, the nadir platelet count in G1 group was greater than that in G2 group ($67\times10^9/L$ vs. $54\times10^9/L$, $p = 0.000$), and the platelet recovery time in G1 group was shorter than that in G2 group (8 days vs. 14 days, $p = 0.003$). Moreover, patients in G1 group had a significantly lower incidence of G3-5 CTIT than that in G2 group (14.3% vs. 35%, $p = 0.04$). In two groups, only 1 patient in G2 group received 4 apheresis platelet units transfusion. Univariate and multivariate analysis showed the early intervention of the rhTPO was a substantial factor for decreasing the incidence of G3-5 CTIT. The sensitivity was 0.67 and the specificity was 0.74. **Conclusions:** For CSCC patients received with radical concurrent chemoradiotherapy, the early intervention of rhTPO was a substantial factor for decreasing the incidence of G3-5 CTIT. It could significantly improve the nadir platelet count, shorten the platelet recovery time, and reduce the incidence of G3-5 CTIT, thereby ensuring the uninterrupted continuation of treatment. Research Sponsor: None.

Platelet recovery time and the degree of CTIT.				
Data	Baseline platelet count($\times10^9/L$)	Days with platelet count recover $\geq100\times10^9$ (Days)	Minimal mean platelet count ($\times10^9/L$)	Incidence of G3-5 CTIT(%)
G1	group	172 $\pm$ 64.92	8 $\pm$ 5.86	67 $\pm$ 15.81
14.3				
G2	group	166 $\pm$ 78.43	14 $\pm$ 9.59	54 $\pm$ 14.37
35				
P	value	0.76	0.003*	0.000*
0.04*				

*Statistically significant.

Comparison of prophylactic effects for chemotherapy-induced neutropenia between same-day versus next-day administration of pegteograstim in chemotherapy regimen composed of day 1 intensive myelosuppressive agent: A randomized clinical trial (CONCISE, KCSG PC22-11).

Kwonoh Park, Sang-Bo Oh, Jung Hoon Kim, Seok Jae Huh, Ilhwan Kim, Seong-Hoon Shin, Jiyun Jung; Division of Hematology & Medical Oncology, Department of Internal Medicine, Dongguk University Ilsan Hospital, Goyang, South Korea; Medical Oncology and Hematology, Department of Internal Medicine, Pusan National University Yangsan Hospital, Yangsan, South Korea; Division of Hematology/Oncology, Department of Internal Medicine, Pusan National University Yangsan Hospital, Yangsan, South Korea; Department of Internal medicine, Dong-A University College of Medicine, Busan, South Korea; Division of Oncology, Department of Internal Medicine, Haeundae Paik Hospital, Inje University College of Medicine, Busan, South Korea; Department of Internal Medicine, Kosin University Gospel Hospital, Busan, South Korea; Department of Biostatistics, Dongguk University College of Medicine, Goyang, South Korea

Background: Same-day administration of pegylated G-CSF is frequently used in clinical practice despite guideline recommendations favoring next-day administration. This study evaluated whether same-day administration of pegteograstim is noninferior to next-day administration with respect to the duration of grade (Gr) 4 chemotherapy induced neutropenia (CIN) in multi-day regimens containing day 1-intensive myelosuppressive agents. **Methods:** This multicenter, open-label, randomized, noninferiority trial (originally designed as a phase III study) enrolled patients receiving adjuvant/neoadjuvant or first-line palliative chemotherapy, including mFOLFIRINOX, ECb, EP, FOLFIRI, and FOLFOX. Patients were assigned in a 1:1 ratio to receive pegteograstim 6mg either within 4 hours after completion of chemotherapy (same-day group) or 24-36 hours (next-day group). The primary endpoint was Gr 4 CIN duration during cycle 1 (C1). A total sample size of 160 patients was calculated to verify noninferiority with a margin of 0.6 days; however, the trial closed prematurely after enrolling 90 patients. **Results:** Of the 90 enrolled patients, 81 were included in the analyses (37 same-day, 44 next-day). Mean Gr4 CIN duration was 0.43 days (95% CI, 0.13–0.74) in the same-day group and 0.09 days (95% CI, 0.00–0.29) in the Next-day group. The mean difference (Same-day minus Next-day) was 0.342 days (90% CI, 0.037 – 0.646). Because the upper bound exceeded the prespecified noninferiority margin of 0.6 days, noninferiority was not demonstrated (p -value = 0.080 for noninferiority). The incidence of Gr4 CIN was 21.1% (8 patients) of same-day group and 2.3% (1 patient) in the next-day group. During cycles 1-4, febrile neutropenia occurred in 1 patient (2.6%) in the same-day group and 3 patients (6.8%) in the next-day group. Two deaths occurred in each group: one FN-related death occurred in the same-day group. **Conclusions:** Same-day administration of pegteograstim did not meet the prespecified criterion for noninferiority compared with next-day administration. The incidence of grade 4 CIN, a key secondary outcome, favored next-day administration. These randomized data support maintaining next-day pegteograstim as standard practice in multi-day regimens with day 1-intensive myelosuppression. Clinical trial information: KCT0007694. Research Sponsor: GC Pharma.

Evaluating the impact of treatment timing with recombinant human thrombopoietin for cancer treatment–induced thrombocytopenia: A retrospective cohort study.

Xin Wang, Jun Bie, Mi Yang, Jianlin Liu; Department of Oncology, Nanchong Hospital, Beijing Anzhen Hospital Affiliated to Capital Medical University / Nanchong Central Hospital, Nanchong, China; Department of Medical Oncology, Nanchong Hospital, Beijing Anzhen Hospital Affiliated to Capital Medical University / Nanchong Central Hospital, Nanchong, China; Department of oncology, Nanchong Hospital, Beijing Anzhen Hospital Affiliated to Capital Medical University / Nanchong Central Hospital, Nanchong, China

Background: Recombinant human thrombopoietin (rhTPO) is utilized for cancer treatment–induced thrombocytopenia (CTIT) to ensure timely and full-dose chemotherapy delivery. This study investigated the differential clinical benefits of platelet-guided intervention timing strategies to provide evidence-based support for early initiation protocols. **Methods:** This single-center retrospective cohort study enrolled CTIT patients receiving rhTPO therapy. Participants were stratified into three groups based on platelet count at rhTPO initiation: early intervention group 1 (platelets $75- <100 \times 10^9/L$), early intervention group 2 ($50- <75 \times 10^9/L$), and salvage therapy group ($<50 \times 10^9/L$). Comparative analyses among the three groups encompassed time to platelet recovery and recovery rates, severe CTIT incidence, platelet transfusion requirements, bleeding event rates, chemotherapy continuity parameters (dose reduction, delay, or discontinuation), and safety profiles. **Results:** Among 456 solid tumor patients with CTIT, 159 (34.9%) were in early intervention group 1, 172 (37.7%) in early intervention group 2, and 125 (27.4%) in the salvage therapy group. Median time to platelet threshold achievement was significantly shorter in group 1 (7.0 d) versus group 2 and salvage therapy (both 11.0 d; $P < 0.001$), with concomitantly shorter rhTPO treatment duration (5.0 d vs. 7.0 d vs. 7.0 d; $P < 0.001$). Severe CTIT incidence was significantly reduced in early intervention groups (12.6% in group 1 and 19.2% in group 2 vs. 56.0% in salvage therapy; both $P < 0.001$). Platelet recovery rates were superior in early intervention groups (81.1% in group 1 and 75.0% in group 2 vs. 59.2% in salvage therapy; $P < 0.001$ and $P = 0.004$, respectively). Platelet transfusion requirements were significantly lower (0.6% in group 1 and 1.2% in group 2 vs. 12.0% in salvage therapy; both $P < 0.001$). Chemotherapy continuity was significantly improved, with lower rates of delay/discontinuation (18.9% in group 1 and 33.1% in group 2 vs. 46.4% in salvage therapy; all $P < 0.05$). No significant inter-group differences in bleeding incidence were observed, and no rhTPO-related serious adverse events or thromboembolic events occurred. **Conclusions:** rhTPO therapy for CTIT exhibits a pronounced threshold effect, with early intervention (platelet count $\geq 50 \times 10^9/L$) conferring substantially greater clinical benefit than salvage therapy. Initiation at $50- <75 \times 10^9/L$ effectively preserves chemotherapy continuity and reduces transfusion burden, while initiation at $75- <100 \times 10^9/L$ optimizes platelet recovery kinetics and cost-effectiveness. Research Sponsor: None.

AQP4 and MOG as definers of distinct autoantibody signatures in immune checkpoint inhibitor–induced optic neuritis.

Jingyao Zhang, Ma Yifei, Yongluo Jiang, Jiakai Lin, Ao Zhang, Guanqing Zhong, Guangmin Jian, Yi-Wei Xu, Pengfei Zhu, Youlong Wang, Xinjia Wang, Weidong Wang, Jun Lu, Ruijie Yao, Xiaoping Hong, Chenyu Yang, Rui Wang, Shangeng Weng, Rui Li, Tong Wu; Department of Medicine, Nuvance Health/Northwell Health Danbury Hospital, Danbury, CT; Institute of Abdominal Surgery, the First Affiliated Hospital of Fujian Medical University, Fuzhou, China; Department of Nuclear Medicine, State Key Laboratory of Oncology in South China, Collaborative Innovation Center for Cancer Medicine, Sun Yat-sen University Cancer Center, Guangzhou, China; Department of Neurology, Hainan Hospital of Chinese PLA General Hospital, Sanya, China; State Key Laboratory of Oncology in South China, Guangdong Key Laboratory of Nasopharyngeal Carcinoma Diagnosis and Therapy, Guangdong Provincial Clinical Research Center for Cancer, Sun Yat-sen University Cancer Center, Guangzhou, China; Department of Clinical Laboratory & Key Clinical Laboratory of Henan province, The First Affiliated Hospital of Zhengzhou University, Zhengzhou, China; Department of Clinical Laboratory Medicine, Cancer Hospital of Shantou University Medical College, Shantou, China; Department of General Surgery, Hainan Hospital of People's Liberation Army General Hospital, Sanya, China; Department of Orthopedics and Spine Surgery, Cancer Hospital of Shantou University Medical College, Shantou, China; Department of Hepatobiliary Surgery, the First Affiliated Hospital of Shantou University Medical College, Shantou, China; Shengli Clinical Medical College of Fujian Medical University, Department of Urology, Fujian Provincial Hospital, Fuzhou University Affiliated Provincial Hospital, Fuzhou, China; Department of Ophthalmology, the Second Affiliated Hospital of Fujian Medical University; Fujian Medical University, Quanzhou, China; Cancer Hospital of Shantou University Medical College, Shantou, China; Department of Ophthalmology, Hainan Hospital of Chinese PLA General Hospital, 80th Jianglin Road, Sanya, China; Department of Neurology of First Affiliated Hospital, Institute of Neuroscience, Fujian Medical University, Fuzhou, China

Background: Checkpoint blockade–induced optic neuritis (CBON) is a rare but vision-threatening immune-related adverse event with limited response to standard immunosuppression and no established diagnostic biomarkers. The humoral immune mechanisms underlying CBON remain poorly characterized, limiting early recognition and mechanistic understanding. **Methods:** We conducted a multicenter study integrating three independent CBON cohorts (n=25, 29, and 34) and 49 ICI-treated controls without neuro-ophthalmic complications, enrolled between January 2020 and June 2025. CBON cases were identified from a prospective biospecimen bank of >2,300 ICI-treated patients. Leveraging pre-ICI baseline, prodromal-phase, onset, and follow-up serum samples (>2,300 total samples), IgG autoantibodies against 25 neural surface antigens were assessed using cell-based assays. Longitudinal antibody dynamics and associations with clinical and oncologic features were evaluated. **Results:** Across 88 CBON patients, the autoantibody response was highly antigen-specific and dominated by aquaporin-4 (AQP4) and myelin oligodendrocyte glycoprotein (MOG). AQP4-IgG or MOG-IgG was detected in 32–48% of CBON cases across cohorts, while paraneoplastic, synaptic, and other neural autoantibodies were rare (<12%). AQP4-IgG and MOG-IgG were largely mutually exclusive, suggesting distinct immunologic subtypes of CBON. These antibodies were virtually absent in ICI-treated controls (0–2%). Longitudinal analyses demonstrated consistent seronegativity prior to ICI exposure, followed by seroconversion at symptom onset with persistent antibody titers during follow-up despite corticosteroid therapy, consistent with a sustained humoral immune response. Autoantibody status showed limited and inconsistent associations with demographic, oncologic, or clinical characteristics. **Conclusions:** CBON is characterized by a distinct, antigen-specific humoral immune response targeting AQP4 or MOG that emerges following ICI exposure. These findings support an ICI-triggered breakdown of immune tolerance and establish a serologic framework for CBON diagnosis and classification. Incorporation of AQP4-IgG and MOG-IgG testing may aid early recognition and risk stratification of visual immune-related adverse events during immunotherapy. Research Sponsor: None.

Prevention of paclitaxel-induced neurotoxicity with lithium: Results from a multicenter, randomized, double-blind, placebo-controlled phase 2 trial (PREPARE).

Wolfgang Boehmerle, Jens U. Blohmer, Verena Imke Isabel Kiver, Nikola Bangemann, Sophie Adam, Oliver Hoffmann, Tjalf Ziemssen, Agnes Flöel, Alice Schneider, Rainer Hellweg, Matthias Endres, Petra Huehnchen; Charité Universitätsmedizin Berlin, Department of Neurology, Berlin, Germany; Charité Universitätsmedizin Berlin, Department of Gynecology with Breast Center, Berlin, Germany; Medizinische Universität Lausitz - Carl Thiem, Cottbus, Germany; Mammazentrum Hamburg, Hamburg, Germany; Department of Obstetrics and Gynecology, University Hospital Essen, Essen, Germany; Universitätsklinikum Carl Gustav Carus, Dresden, Germany; Universitätsmedizin Greifswald, Greifswald, Germany; Charité Universitätsmedizin Berlin, Institute of Biometry and Clinical Epidemiology, Berlin, Germany; Charité Universitätsmedizin Berlin, Department of Psychiatry, Berlin, Germany

Background: Chemotherapy-induced neurotoxicity is a frequent adverse effect of paclitaxel (PTX). It reduces quality of life and often necessitates treatment modifications. The objective of this clinical trial was to determine the safety and efficacy of lithium (Li^+) co-treatment on chemotherapy-induced neurotoxicity in breast cancer patients treated with PTX. **Methods:** Multicenter, randomized, double-blind, placebo-controlled phase-2 trial (parallel-group design) conducted in eight primary care centers in Germany between August 2022 and July 2024. Eligible breast cancer patients aged 18–70 years, with no pre-existing polyneuropathy and to be treated with PTX were randomized 1:1 to either oral Li^+ or placebo with sham dose adjustments. The intervention started 10–14 days prior to the first and lasted until three days after the last PTX infusion. **Results:** A total of 94 patients were enrolled, 86 patients were randomized and 78 were analyzed according to the intention-to-treat principle. Targeted Li^+ trough serum concentrations of 0.5 to 0.8 mmol/l were reliably reached prior to PTX therapy. The total neuropathy score reduced (TNSr) was 0.5 points higher in the placebo group than in the Li^+ group (95% CI 1.6 to -0.6, not significant), while serum neurofilament light chain levels showed no difference. Structural MRI showed slightly higher total intracranial volume in the Li^+ group, but no difference in hippocampal volume. Cognitive testing using the CANTAB indicated a strong trend towards better performance in hippocampus-dependent tasks, including delayed matching to sample and spatial working memory for the Li^+ group. The patient-reported outcome measures (PROM) completion rates were high (baseline 99%, endpoint 95%). Patients receiving Li^+ consistently reported higher quality of life and less pain scores on the EORTC QLQ-C30 during and after therapy, with between-group differences of 11 AU (95% CI 18 to 4) for global health status and -14 AU (95% CI -27 to -0.2) for pain, exceeding established minimal clinically important differences. The latter finding was supported by a lower reported intake of pain medication in the Li^+ group of 54% vs 70% in the placebo group. Eleven serious adverse events were reported in the trial, six in the placebo group and five in the Li^+ group. Patients in the Li^+ group experienced fewer adverse events compared to patients in the placebo group with a relative risk reduction of 26% for any CTCAE grade and 45% for grade ≥ 3 . **Conclusions:** Among breast cancer patients receiving PTX chemotherapy co-treatment with Li^+ was not superior to placebo for the development of polyneuropathy as measured by TNSr. However, there were better patient-reported outcomes including quality of life and pain, as well as lower rates of adverse events. These observations warrant confirmation in a larger phase-3 interventional trial. Clinical trial information: DRKS00027165. Research Sponsor: Federal Ministry of Research, Technology and Space; 01KG2123.

Hetrombopag plus caffeic acid tablets for the treatment of chemotherapy-induced thrombocytopenia in solid tumors: A single-center, open-label, phase II trial.

Xiao Li Xiao, Fanzhuoran Lou, Xintian Huang, Kaiyi Rong, Yongxiang Hong, Jun Zhang; Department of Oncology, Zhongshan Hospital of Xiamen University, School of Medicine, Xiamen, Fujian, China; Department of Oncology, Zhongshan Hospital of Xiamen University, School of Medicine, Xiamen University, Xiamen, Fujian, China; Department of Oncology, Zhongshan Hospital of Xiamen University, School of Medicine, Xiamen University, Xiamen, China; Department of Oncology, Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China

Background: Chemotherapy-induced thrombocytopenia (CIT) frequently complicates cancer therapy, resulting in treatment delays, dose reductions, and premature discontinuation. However, no widely approved therapies are currently available to address this clinical gap. This phase II trial was designed to evaluate the efficacy and safety of the thrombopoietin receptor agonist hetrombopag combined with caffeic acid tablets in this patient population. **Methods:** This is a single-arm, single-center, prospective phase II trial (ChiCTR2400086043) designed to enroll patients with malignancies experiencing thrombocytopenia (platelet count $\leq 75 \times 10^9/L$) during anti-cancer therapy. Eligible participants received hetrombopag 5 mg once daily (QD) plus caffeic acid tablets 0.3 g three times daily (TID) for 14 consecutive days. The primary endpoint is the proportion of patients achieving a platelet count $\geq 100 \times 10^9/L$ after treatment; secondary endpoints included time to first response (platelet count $\geq 100 \times 10^9/L$), proportion of patients with platelet recovery to $\geq 75 \times 10^9/L$, and safety profile of the regimen. **Results:** A total of 65 patients were enrolled between 24 June 2024 and 25 December 2025. The median age of enrolled patients was 60.0 years, and 70.8% of patients had a baseline platelet count of $\geq 50 \times 10^9/L$. The most common tumor types were colorectal cancer (23.1%) and gastric cancer (13.8%). The majority (41.5%) received oxaliplatin-based chemotherapy, 26.2% received immunotherapy plus chemotherapy, and 18.5% received targeted therapy plus chemotherapy. After treatment with hetrombopag plus caffeic acid tablets, 84.6% (55/65) of patients achieved platelet counts $\geq 100 \times 10^9/L$ and 87.7% (57/65) achieved $\geq 75 \times 10^9/L$. The median durations from the first dose of hetrombopag plus caffeic acid tablets platelet response $\geq 100 \times 10^9/L$ was 7 days (range: 5–9). Adverse drug reactions were reported in 17 patients; no drug-related adverse events of grade ≥ 3 occurred. **Conclusions:** Hetrombopag plus caffeic acid tablets confer outstanding therapeutic efficacy in CIT while maintaining a well-tolerated safety profile. This oral regimen fulfills an unmet clinical need and provides a practical, non-invasive therapeutic option for CIT management. Clinical trial information: ChiCTR2400086043. Research Sponsor: None.

Efficacy of surgical glove-compression therapy as a prevention of paclitaxel-induced peripheral neuropathy: Randomized controlled trial.

Saowani Thantaviraya, Sunatee Sa-nguansai, Kunlatida Maneenil, Piyawan Tienchaiananda; Oncology Unit, Department of Medicine, Rajavithi Hospital, Thailand, Bangkok, Thailand; Oncology Unit, Department of Medicine, Rajavithi Hospital, College of Medicine, Rangsit University, Bangkok, Thailand

Background: Paclitaxel is a common cause of chemotherapy-induced peripheral neuropathy (CIPN), a dose-limiting toxicity for which no preventive intervention is currently recommended. This randomized controlled trial evaluated the efficacy of surgical glove-compression therapy (SGCT) in preventing paclitaxel-induced peripheral neuropathy. **Methods:** Patients with solid malignancies scheduled to receive paclitaxel every three weeks were randomized 1:1 to SGCT or placebo. SGCT consisted of bilateral double-layer surgical gloves one size smaller than patient's hand size, covered with outer cotton gloves, worn from 30 minutes before paclitaxel infusion until 30 minutes after completion. The placebo group wore non-compression gloves with identical cotton gloves for the same duration. Patients were followed for four cycles of paclitaxel. The primary endpoint was the incidence of paclitaxel-induced sensory neuropathy of Common Terminology Criteria for Adverse Events (CTCAE) version 6.0 grade ≥ 2 . Secondary endpoints included Patient Neurotoxicity Questionnaire (PNQ) grade $\geq D$, Functional Assessment of Cancer Therapy-Gynecologic Oncology Group-Neurotoxicity (FACT/GOG-NTX) scores, and loss of protective sensation assessed by monofilament testing. Analyses were conducted using the intention-to-treat approach. Sensitivity analyses included per-protocol analysis and treatment effect adjustment for important prognostic factors for CIPN. **Results:** Between November 2024 and November 2025, 39 patients were randomized to SGCT (n=19) or placebo (n=20). Most patients were female, had breast cancer, and received single-agent paclitaxel. In the intention-to-treat analysis, sensory CIPN grade ≥ 2 occurred significantly less frequently in the SGCT group than in the placebo group (26.3% vs. 60.0%; $p=0.034$). This finding was consistent in the per-protocol analysis (27.8% vs. 66.7%; $p=0.019$). The protective effect of SGCT remained statistically significant after adjustment for sex, cancer type, and chemotherapy regimen (adjusted OR 0.10; 95% CI, 0.02 to 0.58; $p=0.010$). No significant differences were observed in secondary outcomes, including motor CIPN, PNQ grade $\geq D$, monofilament test abnormalities, or FACT/GOG-NTX scores. Any-grade sensory CIPN was common and did not differ between groups. SGCT was well tolerated, with no serious adverse events and high adherence. **Conclusions:** SGCT significantly reduced the incidence of clinically meaningful paclitaxel-induced sensory neuropathy and was safe and well-tolerated. These findings support SGCT as a simple, low-cost preventive strategy for CIPN. Clinical trial information: NCT06763575. Research Sponsor: Rajavithi Hospital.

Natural language processing chatbot and continuous activity monitoring in a phase II randomized trial: Impact on hospitalizations and quality of life.

Casey Hollawell, Abigail Pepin, Scott Appel, Jonathan Fu, Karen Tang, Joshua Bryer, Amanda Munter, Nishant Shah, Kristine Kim, Steven J. Feigenberg, Jeffrey D. Bradley, William C. Levin, Russell Maxwell, Alexander Lin, Karishma Khullar, James M. Metz, John Peter Plastaras, Arun Goel; Hospital of the University of Pennsylvania Radiation Oncology, Philadelphia, PA; Hospital of the University of Pennsylvania, Philadelphia, PA; Astera Cancer Care, Flemington, NJ; Columbia University Radiation Oncology, New York, NY; University of Pennsylvania, Philadelphia, PA

Background: Toxicities associated with concurrent chemoradiotherapy (CRT) can lead to hospitalizations and impaired quality of life (QoL). This study reports on secondary endpoints investigating whether combining continuous activity monitoring (CAM) with an AI-driven chatbot can support symptom identification, triage, reduce hospitalizations, and improve QoL. **Methods:** Patients receiving CRT for head and neck (H&N), gastrointestinal (GI) or thoracic cancers were recruited from radiation oncology clinics at a single, urban institution. Subjects were randomized to: (1) CAM with nursing triage or (2) CAM with chatbot triage with as needed symptom assessments. A Fitbit device monitored the step count and heart rate (HR) relative to baseline. Triage was triggered when the daily average HR was >100 or 20% above their resting average or if there was a decrease of >1000 steps from baseline. In the control arm, triage prompted a nursing assessment within 1 business day. In the intervention arm, triage visits were triggered based on a low-, intermediate-, or high-risk symptom algorithm determined by the chatbot (next OTV, next business day, within 24 hrs, respectively). Hospitalizations during CRT and one month post treatment were counted. Logistic regression controlled for ECOG and sex. EORTC C30 QoL instruments were administered at baseline, during OTVs, and during follow-up. A mixed method for repeated measures model assessed global health status/QoL, fatigue, and physical, role, emotional, cognitive, and social functioning scales adjusting for ECOG, race, and stage. All statistical tests were completed on SAS 9.4. **Results:** From June 2023 to January 2025, 77 patients undergoing CRT for their H&N ($n=30$, 39%), GI ($n=29$, 38%), or thoracic cancers ($n=18$, 23%) were enrolled. The median age at consent was 59 years (range 28–81 years). Subjects were randomized to either nursing ($N = 36$, 50%) or chatbot triage ($N = 36$, 50%). There were no statistically significant demographic or clinical differences between arms. Subjects in the chatbot arm had significantly fewer hospitalizations (11%, $n=4$ chatbot; 39%, $n=14$ nursing triage, $p=0.01$). On logistic regression, subjects on the chatbot arm ($p=0.0125$) and those who had ECOG 0 ($p=0.0131$) were less likely to be hospitalized. In both arms, global QoL/health, fatigue, and physical, social, cognitive, and emotional functioning declined during CRT. Chatbot subjects had significantly inferior global QoL/Health status ($p=0.049$), cognitive functioning ($p=0.005$), and physical functioning ($p=0.02$) vs nursing triage. **Conclusions:** Patients undergoing CRT experience functional decline. While AI-driven chatbots may reduce hospitalizations, they are not a perfect substitute for a compassionate healthcare team. An analysis of alerts and triage visits will be reported with our primary endpoint. Research Sponsor: GI Cancer Service Line.

Applying a large language model to detect immune-related adverse events in electronic health records: Effect of integrating prescription and laboratory data on accuracy.

Yukiko Shimoda Igawa, Hidehito Horinouchi, Toshiki Takeuchi, Kunihiro Nishimura, Masaaki Komatsu, Nobuji Kouno, Satoshi Takahashi, Masami Mukai, Tatsuya Yoshida, Yasushi Goto, Ryuji Hamamoto; Department of Thoracic Oncology, National Cancer Center Hospital, Tokyo, Japan; Xcoo, Inc., Tokyo, Japan; Division of Medical AI Research and Development, National Cancer Center Research Institute, Tokyo, Japan; Division of Medical Informatics, National Cancer Center Hospital, Tokyo, Japan; National Cancer Center Hospital, Department of Thoracic Oncology, Tokyo, Japan

Background: Accurate identification of immune-related adverse events (irAEs) is essential; however, manual review of electronic health records poses a significant burden on clinicians. Furthermore, conventional text-only approaches may fail to capture clinically important events. In this study, we evaluated whether a Large Language Model (LLM) with a multimodal approach could improve patient-level identification of irAEs. **Methods:** Among patients who received immune checkpoint inhibitors (ICIs) monotherapy at National Cancer Center Hospital, Tokyo, Japan between October 2014 and July 2023, a subset of patients was randomly sampled for analysis. A zero-shot prompt was designed to identify irAEs. Using a standalone local LLM (gpt-oss-20b), single-modal analysis utilized clinical notes alone, whereas multimodal analysis additionally incorporated systemic steroid prescriptions and laboratory data. Patient-level predictions were aggregated, using the threshold that maximizes the micro-averaged F1-score. The irAEs were clinically adjudicated by board-certified oncologists. Analyses were limited to major irAEs, and performance was evaluated using precision, recall, and the F1-score ($\alpha = 0.05$). **Results:** The median number of cases reviewed per day by physicians was 18, whereas the LLM processed 25. During the study period, 296 patients (207 with irAEs and 89 without irAEs) were randomly sampled. Among patients with irAEs, irAE types included rash, pneumonitis, endocrine disorders, colitis, and hepatitis. For the identification of irAE occurrence, the precision of the multimodal approach was significantly higher than that of the single-modal approach (88.7% to 83.7%, $p = 0.01$). In organ-specific analyses, precision for colitis and rash and recall for endocrine were significantly improved. In addition, the multimodal approach reduced false-positive classifications from 33% to 22% and false-negative classifications from 37% to 35%. irAE onset timing also differed significantly between the two approaches, with earlier identification by the multimodal LLM (-21.9 vs -17.7 days, $p = 0.04$); both approaches detected onset earlier than clinical adjudication. **Conclusions:** A multimodal LLM framework improves irAE detection accuracy and may reduce clinician workload. Research Sponsor: National Cancer Center Hospital "Mirai Project".

irAEs with significant differences between single-modal and multimodal analyses.

		Precision			Recall			F1-score
		%	95%CI	P	%	95%CI	P	%
Any irAE	Multi	88.7	84.2-93.1	0.01	83.1	78.0-88.2	0.62	85.8
	Single	83.7	78.7-88.8		82.1	76.9-87.3		82.9
Rash	Multi	64.5	53.7-75.2	0.03	60.5	49.8-71.1	0.10	62.4
	Single	58.9	48.7-69.1		65.4	55.1-75.8		62.0
Colitis	Multi	80.4	69.5-91.3	<0.01	77.4	66.1-88.6	0.32	78.8
	Single	61.8	50.2-73.3		79.2	68.3-90.2		69.4
Endocrine	Multi	71.2	59.6-82.7	0.37	75.0	63.7-86.3	0.03	73.0
	Single	76.6	64.5-88.7		64.3	51.7-76.8		69.9

Prophylactic vedolizumab to facilitate use of immune-checkpoint inhibitors in cancer patients at high risk of immune-mediated colitis.

Hemant Khandelia, David Hockenbery, Daniel S. Hippe, Evan Thomas Hall, Sylvia Lee, Lisa May Ling Tachiki, Joshua Veatch, Natalie J. Miller, Andrea M. Perdue, Julia K. Majovski, Chloe Thorup, Zach Herrin, Kristin A. Province, Shailender Bhatia; Department of Medicine/Division of Hematology and Oncology, University of Washington, and Clinical Research Division, Fred Hutchinson Cancer Center, Seattle, WA; Gastroenterology/Hepatology and Divisions of Translational Science and Therapeutics, Human Biology, Public Health Sciences, Fred Hutchinson Cancer Center, Seattle, WA; Clinical Research Division, Fred Hutchinson Cancer Center, Seattle, WA; University of Washington, Fred Hutchinson Cancer Center, Seattle, WA; Fred Hutch Cancer Center, Seattle, WA; University of Washington, Seattle, WA; Division of Translational Science and Therapeutics, Fred Hutchinson Cancer Center, Seattle, WA; Department of Medicine/Division of Hematology and Oncology, University of Washington and Clinical Research Division, Fred Hutchinson Cancer Center, Seattle, WA; Division of Medical Oncology, Department of Medicine, University of Washington and Fred Hutchinson Cancer Center, Seattle, WA

Background: Inflammatory diarrhea/colitis is a frequent immune-related adverse event (IRAE) associated with immune checkpoint inhibitors (ICIs). Treatment with ICI is relatively contraindicated in patients with history of severe ICI-colitis or those with pre-existing severe inflammatory bowel diseases (IBD). Vedolizumab (VDZ), an anti- $\alpha 4\beta 7$ integrin antibody associated with selective immune suppression in the gastrointestinal (GI) tract, is approved for IBD treatment and is also effective in treating steroid-refractory ICI-colitis. However, limited data exist for its utility as a prophylactic treatment for primary or secondary prevention of ICI-colitis in high-risk patients. **Methods:** We conducted a single-center, retrospective study of patients with advanced skin cancers, who were deemed "high-risk" due to prior severe ICI colitis or IBD, and received VDZ prophylaxis prior to ICI (re)treatment. VDZ efficacy was assessed by analyzing the frequency, severity, duration and treatment details of GI symptoms. In patients with prior ICI-colitis, outcomes with and without VDZ prophylaxis were compared using descriptive statistics. ICI efficacy in the presence of VDZ was evaluated by objective response rate (ORR) per RECIST v1.1. **Results:** We identified 16 high-risk patients (11- prior ICI colitis, 5 - IBD) who received VDZ prophylaxis (typically 300 mg at weeks 0, 2, and 6 initially, then q8 weeks) prior to ICI (re)treatment, between 2015-2025. Median number of VDZ doses before (re)introducing ICI was 2 (range, 1-3). In the ICI-colitis cohort, VDZ prophylaxis prior to ICI re-treatment resulted in less frequent and milder GI symptoms not needing corticosteroids, than previously observed with initial ICI treatment without VDZ prophylaxis (see Table). Among 14 patients with evaluable disease (measurable and progressing at the time of VDZ treatment), ORR was 33% (3/9) in the ICI-colitis cohort and 80% (4/5) in the IBD cohort. **Conclusions:** Use of prophylactic VDZ can facilitate successful, long-term ICI treatment in high-risk patients with prior ICI-colitis or IBD, while mitigating GI symptoms, reducing corticosteroid usage and preserving anti-tumor responses. Research Sponsor: None.

	ICI-colitis cohort, without VDZ prophylaxis (N = 11)	ICI-colitis cohort, with VDZ prophylaxis (N = 11)	IBD cohort, with VDZ prophylaxis (N = 5)
Diarrhea (any grade), n (%)	11 (100)	3 (27)	4
Diarrhea ($\geq$ grade 3), n (%)	8 (73)	0	2 (40)
Symptom duration in days, Median (range)	75 (13, 251)	46 (8, 54)	39 (17, 129)
Corticosteroid use, n (%)	11 (100)	0	2 (40)
Corticosteroid use in days, Median (range)	54 (7, 102)	N/A	59 (59, 59)
Additional biologic therapy, n (%)	10 (91)	0	3 (60)
ICI discontinuation due to diarrhea, n (%)	11 (100)	2 (18)	3 (60)
ICI treatment duration in months, Median (range)	2.1 (1.4, 17.5)	7.7 (1.1, 49.0)*	7.4 (6.7, 20.8)

*4 patients had ongoing ICI treatment.

Gabapentin plus intranasal ketamine for the prevention and treatment of pain in patients undergoing radiotherapy for head and neck cancer: Phase II trial results.

Natalie A. Lockney, Lindsay Mundy, Phyllis Kilpatrick, Taylor Butler, Zachary Kohutek, Anthony Cmelak, Sean All, Barbara Murphy, Derek Smith; Vanderbilt University Medical Center, Nashville, TN

Background: Prophylactic gabapentin decreases pain, opioid use, and weight loss in head and neck (HNC) patients treated with chemoradiotherapy. Nonetheless, significant symptom burden remains. Ketamine is an NMDA receptor antagonist which has neuromodulator and anti-inflammatory properties. We undertook a phase I/II study to explore safety, feasibility, and obtain preliminary efficacy data pertaining to the combination of ketamine and gabapentin in HNC patients undergoing radiation +/- chemotherapy. Results of the phase I study were previously reported. Herein we report preliminary results of the phase II portion of the study.

Primary outcomes were toxicity and feasibility; secondary outcomes were symptom burden.

Methods: Eligibility: locally advanced HNC patients planned for primary or adjuvant radiotherapy +/- chemotherapy. Treatment: Day 1: gabapentin 100 mg PO TID; Day 8: increase gabapentin to 300 mg PO TID; Day 15: continue gabapentin and start intranasal ketamine 30 mg TID. Dose modifications were allowed for both agents. Toxicity: assessed using CTCAE 5.0.

Feasibility: data capture by pill counts and patient medication logs. Efficacy: patient reported outcomes measures completed at baseline, weekly during radiation and 1-, 2-, and 3-months post-radiation.

Results: Patient characteristics: median age 60 yrs, 85% males, 67% p16-positive, 21 post-operative. Toxicity: Of 45 patients who completed treatment, 7 patients (16%) experienced a grade 2+ toxicity (5 were probably related to ketamine). Four patients required ketamine dose de-escalation due to dizziness. Six patients (13%) eventually discontinued ketamine due to toxicity. Feasibility: 41 (91%) patients missed <5% of gabapentin doses; 35 (78%) patients missed <5% of ketamine doses. Preliminary Efficacy: Eight patients (18%) required PEG placement. median score on the pain subscale of the Vanderbilt Head and Neck Symptom Survey 2.0 was highest at the end of treatment (4.3/10) and decreased rapidly (2.4/10 at 1 month and 1.7/10 at 2 months post-treatment). During treatment, 8 patients (18%) required no opioids, and 24 patients (55%) required immediate-release (IR) opioids only. The median of the maximum morphine milligram equivalent (MME) per day for IR opioids alone was 90 MME/day (range 10 – 180 MME/day). The median duration of IR prescription alone was 30 days (range 10 – 347 days). Twelve patients (27%) required addition of extended-release (ER) opioids with a median duration 35 days (range 28 – 220 days). Only 3 patients (7%) required ER opioids for >90 days.

Conclusions: The combination of gabapentin and ketamine was safe and feasible. Preliminary data indicates the majority of patients experienced low to moderate levels of pain with minimal use of opioids. Larger, randomized studies are warranted to confirm the benefit of the combination of gabapentin and ketamine. Clinical trial information: NCT05156060. Research Sponsor: NCATS/NIH Grant Support for REDCAP use (UL1 TR000445); Ingram Industries Pain & Symptom Management Program Endowment.

The role of pretreatment vitamin D insufficiency in racial disparity in taxane-induced peripheral neuropathy: Results from the SWOG S0221 trial.

Nam Nguyen-Hoang, Ciao-Sin Chen, Gary Zirpoli, George Thomas Budd, Lajos Pusztai, Gabriel N. Hortobagyi, Kathy S. Albain, Andrew K. Godwin, Alastair Mark Thompson, Norah Lynn Henry, Christine B. Ambrosone, Kathleen A. Stringer, Daniel Louis Hertz; University of Michigan, Ann Arbor, MI; Boston University Slone Epidemiology Center, Boston, MA; Cleveland Clinic, Cleveland, OH; Yale Cancer Center, New Haven, CT; The University of Texas MD Anderson Cancer Center, Houston, TX; Loyola University Chicago Stritch School of Medicine, Cardinal Bernardin Cancer Center, Maywood, Chicago, IL; Department of Pathology and Laboratory Medicine, University of Kansas Medical Center, Kansas City, KS; Baylor College of Medicine, Houston, TX; University of Michigan Rogel Cancer Center, Ann Arbor, MI; Roswell Park Comprehensive Cancer Center, Buffalo, NY; University of Michigan College of Pharmacy, Ann Arbor, MI

Background: Taxane-induced peripheral neuropathy (TIPN) affects up to 70% of patients receiving taxanes and can lead to severe, irreversible symptoms that impair daily functioning and quality of life. Approximately 25% of patients require taxane dose modification or discontinuation to prevent TIPN, compromising treatment effectiveness and survival. Self-reported Black patients experience nearly two times greater incidence of TIPN compared to White patients, contributing to treatment alterations and worse cancer outcomes. Vitamin D insufficiency, which is more common among Black patients, has been implicated as a modifiable risk factor for TIPN. This study assessed the extent to which vitamin D insufficiency mediates the racial disparity in TIPN. **Methods:** This secondary analysis included self-reported Black or White female patients with early-stage breast cancer treated with paclitaxel-based chemotherapy on the SWOG S0221 phase III trial. The primary endpoint was clinician-assessed grade ≥ 3 sensory neuropathy per NCI CTCAE attributed to paclitaxel. The mediator was pre-treatment vitamin D insufficiency, defined as total 25-hydroxyvitamin D ≤ 20 ng/mL. Causal mediation analysis decomposed the total effect of race on TIPN into its direct effect and an indirect effect mediated through vitamin D insufficiency, adjusted for age and paclitaxel regimen (weekly or every other week). Log-linear model with modified Poisson regression and weighted logistic regression were used for the outcome model and the mediator model, respectively. Confidence intervals were computed via bootstrapping, and significance was set at $\alpha=0.05$. **Results:** A total of 1,106 participants (mean age 51.2 [SD 10] years) were included, of whom 109 were Black and 997 were White. Black patients had a higher prevalence of vitamin D insufficiency (77% vs. 28%, $p < 0.001$) and a higher incidence of grade ≥ 3 sensory TIPN (29% vs. 14%, $p < 0.001$). The adjusted risk ratio (RR) for TIPN comparing Black to White patients was 2.24 (95% CI, 1.54–3.19; $p < 0.001$). Vitamin D insufficiency statistically mediated this association, with an indirect effect RR of 1.18 (95% CI, 1.01–1.38; $p = 0.048$), accounting for 27% of the racial disparity in TIPN. The direct effect of race on TIPN, independent of vitamin D status, remained significant (RR 1.90; 95% CI, 1.30–2.85; $p < 0.001$). **Conclusions:** Vitamin D insufficiency contributes to, but does not entirely explain, the racial disparity in TIPN. While other unaccounted factors may interact with or modify this association, vitamin D supplementation in insufficient patients could partially reduce racial disparities in TIPN and improve pharmacoequity. Research Sponsor: American Cancer Society; N030566-497333; National Cancer Institute of the National Institutes of Health, Amgen; U10CA180888, U10CA180819, R01CA116395, R01CA139426; Amgen.

Value of risk-directed thromboprophylaxis in ambulatory lung and gastrointestinal cancer care: Economic evaluation of the TARGET-TP randomized trial.

Marliese Alexander, Antonio Ahumada-Canale, Kate Hadfield, Dan Liu, Michael Michael, Jeanne Tie, Benjamin J. Solomon, Samuel J. Harris, Craig R. Underhill, Richard De Abreu Lourenço, Kate Burbury; Pharmacy Department, Peter MacCallum Cancer Centre & Sir Peter MacCallum Department of Oncology, University of Melbourne, Melbourne, VIC, Australia; Centre for Health Economics Research and Evaluation, University of Technology Sydney, Sydney, Australia; Department of Medical Oncology, Peter MacCallum Cancer Centre and Sir Peter MacCallum Department of Oncology, University of Melbourne, Melbourne, Australia; Peter MacCallum Cancer Centre, Melbourne, VIC, Australia; Bendigo Cancer Centre, Bendigo Health, Bendigo, VIC, Australia; Border Medical Oncology, East Albury, Australia; Tasmanian Health Service & Sir Peter MacCallum Department of Oncology, The University of Melbourne, Hobart, Australia

Background: Thromboembolism (TE) is a major and preventable hematological complication in patients with cancer, contributing to substantial adverse health impacts for patients and the health system. Targeted Thromboprophylaxis in Ambulatory Patients Receiving Anticancer Therapies (TARGET-TP; ACTRN12618000811202) was an Australian phase III randomized trial of biomarker risk-directed enoxaparin thromboprophylaxis. The TARGET-TP intervention reduced TE (HR 0.31, $p = 0.005$) and six-month mortality (HR 0.48, $p = 0.03$) versus usual care (no prophylaxis). This study evaluated the value for money of the TARGET-TP intervention versus usual care. **Methods:** A within-trial and modelled economic evaluation was conducted from the Australian health system perspective. Resource use collected within the trial reflected risk stratification, thromboprophylaxis, side-effect management, and treatment of TE events. Health benefits were quantified as quality-adjusted life years (QALYs), utilities derived from SF-12v2 data. Bootstrapping was used to evaluate sampling uncertainty. A Markov model estimated long-term costs and outcomes over a 5-year horizon. Scenarios assessed the use of oral anticoagulants and stewardship, while probabilistic sensitivity analysis (PSA) tested parameter uncertainty. **Results:** Within-trial analysis showed the TARGET-TP intervention was associated with lower costs, while being more effective (i.e., dominant), reducing costs by \$1,095 per patient and generating an additional 0.0097 QALYs, driven mainly by fewer hospitalizations. The TARGET-TP intervention was dominant in $> 83\%$ of bootstrap iterations. Modelled analyses supported these findings, with cost savings of \$3,551 per patient and a gain of 0.4 QALYs. PSA demonstrated dominance in $> 95\%$ of iterations (Figure 1). The oral anti-coagulant and stewardship scenarios remained dominant for rivaroxaban, while apixaban was highly cost-effective, driven by bleeding events and drug costs. **Conclusions:** Biomarker-driven primary thromboprophylaxis in patients with lung and gastrointestinal cancer was less costly and more effective from the healthcare system perspective, supporting its implementation in routine care. Clinical trial information: ACTRN12618000811202. Research Sponsor: Victorian Cancer Agency; ECHSRF18006; Australian National Health and Medical Research Council; 1196211.

Pharmacokinetic variability with pembrolizumab dosage switching and its impact on immune-related adverse events in patients with non-small cell lung cancer.

Yoshihiro Masui, Tatsuya Yoshida, Ryoko Inaba Higashiyama, Shigehiro Yagishita, Mayu Ohuchi, Ken Masuda, Yuki Shinno, Yuji Matsumoto, Tomonori Mizutani, Yusuke Okuma, Hidehito Horinouchi, Shohei Koyama, Noboru Yamamoto, Akinobu Hamada, Yasushi Goto; Department of Thoracic Oncology, National Cancer Center Hospital, Tokyo, Japan; Division of Molecular Pharmacology, National Cancer Center Research Institute, Tokyo, Japan; Department of Pharmacology and Therapeutics, Fundamental Innovative Oncology Core, National Cancer Center Research Institute, Tokyo, Japan; Department of Immunogenomic Medicine, National Cancer Center Research Institute, Tokyo, Japan

Background: Pembrolizumab 400 mg every 6 weeks (Q6W) was approved based on population pharmacokinetic (pop-PK) modeling rather than direct pharmacokinetic measurements, leaving its real-world concentrations insufficiently characterized. The impact of concentration changes when switching from 200 mg every 3 weeks (Q3W) to Q6W on immune-related adverse events (irAEs) remains unclear. **Methods:** We retrospectively identified patients with advanced non-small cell lung cancer who switched pembrolizumab from Q3W to Q6W between March 2017 and September 2023. Serum concentrations were quantified by liquid chromatography–tandem mass spectrometry; pop-PK analysis estimated maximum concentration (eC_{max}) and trough concentration (eC_{trough}). Inter-cycle variability was expressed as percentage coefficient of variation (%CV) using all available Q3W cycles. Early irAEs were defined as events within 126 days. In exploratory analysis, associations between pop-PK metrics and after switching irAEs (including pneumonitis) were evaluated using Wilcoxon rank-sum tests and multivariable logistic regression. Clinical correlates of %CV–eC_{max} were examined using multivariable stepwise linear regression. **Results:** Seventy-nine patients switched, and pop-PK analysis was feasible in 66. Median age was 70 years, 50 were male and 62 had a smoking history. Median Q3W cycles were 6 (range, 1–37) and median follow-up after switching was 463 days. After switching, 42 patients developed new or worsened irAEs, with 16 pneumonitis, and 22 had early irAEs, with 12 early pneumonitis. First-dose 400 mg eC_{max} and cross-regimen exposure ratios were not associated with the occurrence of irAEs. Among 64 patients who received ≥ 2 cycles of Q3W, those who developed irAEs after switching showed higher %CV–eC_{max} during Q3W ($p = 0.036$). Similar associations were observed for early irAEs ($p = 0.024$), pneumonitis ($p = 0.023$), and early pneumonitis ($p = 0.007$). %CV–eC_{trough} during Q3W was not associated with irAEs after switching (irAEs, $p = 0.24$; early irAEs, $p = 0.13$; pneumonitis, $p = 0.16$), with an association observed only for early pneumonitis ($p = 0.044$). High %CV–eC_{max} during Q3W was associated with increased odds of irAEs (odds ratio [OR] 8.4, $p = 0.02$), pneumonitis (OR 14.3, $p = 0.03$), early irAEs (OR 15.2, $p = 0.017$), and early pneumonitis (OR 30.0, $p = 0.03$). No significant associations were observed between %CV–eC_{trough} and irAEs or early irAEs. Higher platelet count and renal dysfunction were independently associated with increased %CV–eC_{max}. **Conclusions:** Higher inter-cycle variability in eC_{max} during 200 mg Q3W was associated with an increased risk of new or worsened irAEs, particularly pneumonitis, after switching to 400 mg Q6W. These findings suggest that inter-cycle variation in C_{max} may be an important safety consideration when transitioning to a 400 mg Q6W regimen. Research Sponsor: None.

Impact of synbindin deficiency on immune checkpoint blocker–induced systemic inflammation and multi-organ damage.

Zhenghang Xu, Luoyan Ai; Zhongshan Hospital, Fudan University, Shanghai, China; Department of Medical Oncology, Zhongshan Hospital, Fudan University, Shanghai, China

Background: Immune-related adverse events (irAEs) are a major safety limitation for the broad application of immune checkpoint blockade (ICB) in oncology, yet their precise molecular mechanisms remain unclear. Synbindin, a tethering-associated protein involved in vesicular trafficking and related processes, plays a key role in immune-cell activation and activation of inflammatory signaling pathways and therefore may represent an important initiator and predictive factor for irAEs. **Methods:** We generated constitutive whole-body Trappc4 knockout (Trappc4-KO) C57BL/6 mice and administered either anti-PD-1 monotherapy or combined anti-PD-1 plus anti-CTLA-4 immune checkpoint blockade via intraperitoneal injection. Plasma biochemical indices and the extent of organ injury were assessed following treatment. **Results:** Trappc4-KO mice receiving combined anti-PD-1/anti-CTLA-4 treatment exhibited markedly more severe immune-related toxicity and multi-organ injury than wild-type controls. Biochemically, markers of hepatic injury (AST, ALT) were substantially elevated, indicating liver dysfunction; renal function markers (serum creatinine and blood urea nitrogen) were significantly increased, consistent with kidney injury; and cardiac markers (CK-MB, cTnT, cTnI) were also markedly raised. A similar trend, although less pronounced, was observed following anti-PD-1 monotherapy. Histopathological examination corroborated these findings: H&E sections of affected organs showed prominent focal immune cell infiltration, cellular swelling, and areas of necrosis. **Conclusions:** These data demonstrate that Trappc4 deficiency significantly exacerbates ICB-induced systemic inflammation and multi-organ damage, suggesting that Synbindin plays a critical protective role in the development of irAEs. Research Sponsor: None.

A randomized controlled pilot study of aromatherapy to reduce anxiety and pain during bone marrow aspiration and biopsy.

Kristina Gowin, Ali Derakhshani, Maggie Goodson, Jeffrey Li, Aaron Fisher, Phi Tran, Ashley Larsen, Natasha Bahri, Richard T. Lee; City of Hope, Irvine, CA; City of Hope, Orange County, CA

Background: Bone marrow aspiration and biopsy (BMAB) is associated with substantial anxiety and pain among patients with hematologic malignancies. Nonpharmacologic strategies to improve procedural tolerance are needed. Aromatherapy with lavender essential oil and its primary active constituent, linalool, has demonstrated anxiolytic effects in preclinical and peri-procedural settings but has not been rigorously evaluated during BMAB. **Methods:** We conducted a single-center, randomized pilot study of adult patients with cancer receiving a BMAB. Subjects were randomized (1:1:1) to lavender essential oil ($\geq 25\%$ linalool), pure linalool oil ($\geq 97\%$), or placebo (jojoba oil). Aromatherapy was administered via inhalation prior to and throughout the procedure. Primary outcomes included feasibility ($>70\%$ completion) and patient satisfaction. Secondary outcomes included anxiety and pain assessed by visual analog scales (VAS) before, during, and after BMAB. Exploratory physiologic outcomes included bispectral index (BIS), an electroencephalogram-based measure of cortical arousal. **Results:** Forty-five patients were enrolled, with 43 (96%) completing the study, meeting feasibility criteria. Most participants (88%) agreed or strongly agreed that aromatherapy was relaxing and enjoyable. All groups demonstrated significant within-group reductions in VAS-anxiety from pre- to post-procedure, with the largest reduction observed in the linalool arm (-3.1 ± 0.70 (mean $\pm$ SE); $p < 0.01$), compared with lavender (-1.8 ± 0.67 ; $p = 0.02$) and placebo (-2.4 ± 0.61 ; $p < 0.01$). During BMAB, anxiety reduction favored the lavender and linalool arms, with a trend toward between-group significance ($p = 0.053$). Pain increased during BMAB across all groups; however, the linalool arm demonstrated the smallest increase (2.6 ± 0.69 ; $p < 0.01$) compared with lavender (3.8 ± 0.93 ; $p < 0.01$) and placebo (4.0 ± 1.3 ; $p < 0.01$). Post-BMAB, between group analysis trended toward significantly less pain with lavender and linalool compared to placebo ($p = 0.057$). Exploratory within-group BIS scores analyses demonstrated significant reductions in average BIS after aromatherapy treatment prior to BMAB with lavender showing the greatest reductions (-6.0 ± 2.0 ; $p = 0.01$), as compared to linalool (-3.6 ± 1.6 ; $p = 0.047$) and placebo (-1.6 ± 1.3 , $p = 0.27$). No serious adverse events occurred. **Conclusions:** Aromatherapy using lavender and linalool during BMAB is feasible, safe, and potentially associated with meaningful reductions in procedural anxiety and pain. These preliminary findings support a larger randomized control trial to confirm efficacy and explore integration into routine supportive oncology care. Clinical trial information: NCT06581211. Research Sponsor: None.

Cumulative toxicity assessed by area-under-the-curve (AUC) in targeted therapy versus chemotherapy for advanced *EGFR*-mutant NSCLC.

William J. Phillips, Vida Alami, Dexiang Gao, Alexander S. Watson, David Ross Camidge; University of Colorado Denver, Anschutz Medical Campus, Aurora, CO; University of Colorado Cancer Center, Aurora, CO; University of Colorado, Aurora, CO; Arthur J.E. Child Comprehensive Cancer Center, Calgary, AB, Canada

Background: Current adverse event (AE) reporting standards emphasize peak toxicity, which may inadequately capture the cumulative burden of persistent low-grade AEs characteristic of targeted therapies. We conducted a post-hoc analysis of the LUX-Lung 3 trial to compare longitudinal toxicity patterns of targeted therapy and chemotherapy over time. **Methods:** This post-hoc analysis used individual, de-identified patient-level data from the phase III LUX-Lung3 clinical trial comparing afatinib with platinum-based chemotherapy as first-line treatment for advanced *EGFR*-mutant NSCLC, accessed through Vivli. Select treatment-related AEs were evaluated longitudinally by grade. Cumulative toxicity burden was quantified using the area-under-the-curve (AUC) of AE grade prevalence over time. Pearson correlation was used to assess temporal trends in AUC. **Results:** A total of 340 patients had evaluable AE data, including 229 (67%) treated with afatinib and 111 (33%) treated with chemotherapy. The median onset of grade 1-2 AEs generally occurred earlier with chemotherapy than afatinib. The median onset of chemotherapy-related fatigue was 4 days and nausea 2 days, whereas median onset of afatinib-related diarrhea was 4 days, rash 8 days, and paronychia 37 days. Longitudinal AUC analysis (Table 1) demonstrated a significant improvement in grade 1-2 chemotherapy-related nausea ($p=0.003$) and stomatitis ($p=0.05$), and a trend towards improvement in fatigue ($p=0.2$) by 12-months. In contrast, grade 1-2 afatinib-related rash ($p=0.4$) and diarrhea ($p=0.99$), remained stable, while paronychia increased over time ($p=0.004$). For grade 3+ AEs, the AUC improved over time for both the chemotherapy ($p=0.04$) and afatinib ($p=0.02$) groups. **Conclusions:** Assessment of time to onset and longitudinal AUC reveal distinct temporal AE patterns for targeted therapy and chemotherapy. Longitudinal toxicity reporting is feasible and highlights the sustained burden of chronic AEs associated with targeted therapies that are clinically meaningful yet underrepresented by conventional peak toxicity reporting. Research Sponsor: Thoracic Oncology Research Initiative (TORI), University of Colorado.

Cumulative toxicity of afatinib and chemotherapy was quantified using the area under the curve of grade 1-2 adverse events prevalence at landmark time points.*

Adverse event	Month 1	Month 3	Month 6	Month 12	Pearson's coefficient	p-value
Afatinib (%)						
Rash	0.24	0.39	0.44	0.45	0.24	0.4
Diarrhea	0.30	0.44	0.47	0.45	-0.002	0.99
Paronychia	0.02	0.20	0.32	0.39	0.74	0.004
Chemotherapy (%)						
Fatigue	0.05	0.09	0.09	0.07	-0.36	0.2
Nausea	0.07	0.17	0.17	0.10	-0.60	0.03
Stomatitis	0.02	0.02	0.02	0.01	-0.56	0.05

*Trends were assessed using Pearson's correlation coefficient and corresponding p-value.

The price of a breath: The economic and mortality burden of checkpoint inhibitor pneumonitis (2016–2020).

Milan Regmi, Abdelrahman Shehata, Bibek Man Shrestha, Danyal Butt, Mohamed Fouad Elganainy, Mina Arnist Ghaly; Southeast Health Medical Center, Dothan, AL; University of Toledo, Toledo, OH; East Carolina University, Greenville, NC; Jefferson Health, Somerdale, NJ

Background: The landscape of oncologic toxicity has drastically changed because of the rapid introduction of Immune Checkpoint Inhibitor (ICI) indications, ranging from the treatment of melanoma to thoracic cancers. Immune-related adverse events (irAEs) are a novel range of toxicities brought about by the rapid growth of ICI. The overall national burden of severe inpatient toxicities is still unknown, despite the well-described outpatient care of irAEs. We measured the prevalence, mortality, and financial impact of severe irAEs necessitating hospitalization using the Nationwide Inpatient Sample (NIS). **Methods:** We evaluated adult hospitalizations secondary to major irAEs (pneumonitis, colitis, hepatitis, and endocrinopathies) using ICD-10-CM codes for a retrospective cohort analysis of the National Inpatient Sample database from 2016 to 2020. Only patient with cancer diagnosis associated complications were included to reduce confounders. Statistical evaluations and outcomes were generated using STATA version 19. The use of mechanical ventilation, total hospital charges, and in-hospital mortality were the major outcomes. Temporal trends and mortality factors were examined using survey-weighted regression models. **Results:** We identified a weighted national cohort of 109,225 irAE-related hospitalizations from 2016 to 2020. **Epidemiology:** Immune-mediated Colitis was the dominant driver of volume (54.6%) for inpatient admission, followed by Pneumonitis (22.2%) and Hepatitis (18.2%). The proportion of admissions attributable to Pneumonitis was increased from 21.1% in 2016 to 24.0% in 2020 ($p < 0.001$), coincident with expanded ICI use in lung cancer. **Outcomes & Acuity:** Pneumonitis was associated with the longest mean length of stay (LOS) of 6.9 days and the highest raw mortality (7.8%) compared to Colitis (1.6%). In multivariable analysis, Pneumonitis was the strongest independent predictor of in-hospital mortality (aOR 4.98; 95% CI 4.12–6.02; $p < 0.001$) relative to Colitis. Conversely, female sex was associated with a significant survival advantage (aOR 0.76; $p = 0.001$). **Economic Burden:** Pneumonitis was the most resource-intensive toxicity (Mean Charge: \$74,298 vs. \$43,831 for Colitis). The aggregate national hospital bill for irAEs rose from \$1.14 Billion in 2016 to a peak of \$1.75 Billion in 2020. **Conclusions:** Pneumonitis is the primary cause of death and economic expense, whereas colitis is the primary cause of irAE hospitalizations. Between 2016 and 2020, the total cost of hospitalization in the United States almost doubled, reaching approximately \$1.75 billion per year. Health systems need to prepare for an increase in high-acuity, resource-intensive pulmonary toxicity as ICI indications spread into the adjuvant environment. **Research Sponsor:** None.

A risk prediction model for severe, life-threatening, and fatal treatment-related toxicity.

Joseph M. Unger, Norah Lynn Henry, Michael Jordan Fisch, Dawn L. Hershman; SWOG Statistics and Data Management Center, Fred Hutchinson Cancer Center, Seattle, WA; University of Michigan Rogel Cancer Center, Ann Arbor, MI; The University of Texas MD Anderson Cancer Center, Carelon Medical Benefits Management, Houston, TX; Herbert Irving Comprehensive Cancer Center, Columbia University Irving Medical Center, New York, NY

Background: Adverse events are major contributors to morbidity and mortality in patients receiving systemic cancer therapy. Accurate prediction of high-grade toxicity could inform risk-adapted treatment strategies. **Methods:** This cohort study included data from 18 SWOG adult phase 2 and 3 treatment trials conducted from 1990 to 2022. Baseline patient-reported symptoms (fatigue, pain, and anxiety, classified as clinically meaningful yes vs. no), baseline sociodemographic (age, sex, race, ethnicity), and performance status (PS) variables were used. The aim was to develop a unified risk score applicable across multiple toxicity severity thresholds; adverse events were classified using the Common Terminology Criteria for Adverse Events. The primary outcomes were severe (Grade ≥ 3), life-threatening (Grade ≥ 4), and fatal toxic events. A training set was derived using a random 60% sample, balanced by study and arm; validation will occur in the remaining 40%. Best-subsets logistic regression was used for variable selection; final models were stratified by cancer type (hematologic, hormone-driven solid tumor, or other solid tumor) and treatment status (untreated vs refractory). Model discrimination was assessed using the concordance (c) statistic. Patients were divided into tertiles according to their total risk score. Toxicity rates and odds ratios were evaluated across tertiles (Ts). **Results:** Of 7,936 patients, 4,776 (60.2%; median age 64.9 (range, 18–95.3); female 28.0%; Black 10.8%) formed the training cohort. Increased toxicity was associated with age ≥ 60 years, fatigue, female sex, and PS ≥ 1 . The multivariable risk models demonstrated good discrimination for grade ≥ 3 (c=0.76), grade ≥ 4 (c=0.77), and grade 5 toxicity (c=0.77). Severe toxicity increased from 15.8% in the lowest risk tertile (T1) to 64.6% in T3; life-threatening toxicity increased from 2.7% in T1 to 26.2% in T3 (Table). Compared with the lowest tertile, the highest risk tertile had markedly higher odds of grade ≥ 3 (OR 9.76), grade ≥ 4 (OR 12.96), and grade 5 toxicity (OR 7.15; all $p < .001$). Model validation results will be presented. **Conclusions:** This risk model accurately identified patients with substantially elevated risk for severe, life-threatening, and fatal toxicities. Risk stratification may support individualized treatment counseling, risk-guided monitoring, and proactive toxicity management. Research Sponsor: The Hope Foundation; National Cancer Institute/U.S. National Institutes of Health; U10CA180888; National Cancer Institute/U.S. National Institutes of Health; U10CA180819; National Cancer Institute/U.S. National Institutes of Health; UG1CA189974.

Observed toxicity rates and odds ratios by predicted-risk tertile.

	Observed Toxicity			Odds Ratios by Model (95% CI, p-value)		
	T1 (n=1536)	T2 (n=1646)	T3 (n=1594)	Increase per risk level	T2 vs. T1	T3 vs. T1
Grade ≥ 3	15.8	37.7	64.6	3.11 (2.86-3.39, $p < .0001$)	3.23 (2.73-3.83, $p < .0001$)	9.76 (8.23-11.59, $p < .0001$)
Grade ≥ 4	2.7	9.1	26.2	3.58 (3.12-4.11, $p < .0001$)	3.66 (2.57-5.20, $p < .0001$)	12.96 (9.32-18.02, $p < .0001$)
Grade ≥ 5	0.2	0.6	1.4	2.54 (1.54-4.18, $p < .0001$)	3.12 (0.86-11.37, $p = .08$)	7.15 (2.14-23.94, $p = .001$)

Dentist-led systematic oral education programs in the prevention of radiation-induced oral toxicities in patients with head and neck cancer (BRIGHT): A randomized clinical trial.

Yu Min, Kun Gao, Mao Ye, Yiyan Pei, Zhigong Wei, Zheran Liu, Huaju Yang, Lei Cai, Meiyang Shao, Xingchen Peng; Department of Biotherapy, Cancer Center, West China Hospital, Sichuan University, Chengdu, China; West China School of Public Health and West China Fourth Hospital, Chengdu, China; West China Hospital, Chengdu, China; Cancer Center and State Key Laboratory of Biotherapy, West China Hospital, Sichuan University, Chengdu, China; Institute of Hepatopancreatobiliary Surgery, Chongqing General Hospital, Chongqing University, Chongqing, Chongqing, China

Background: Radiotherapy-induced oral toxicity (RIOT) is a common complication in patients with head and neck cancer (HNC). International guidelines have recognized the role of oral-health education in preventing RIOT. However, most recommendations remained at the level of general principles and lacked a detailed, systematic and operationalized process, which hinders effective clinical delivery of oral-health education. Given that dentists are uniquely positioned to manage oral health, this study aims to evaluate the effectiveness of a dentist-led systematic oral-health education program (OHEP) on RIOT and provide a standard operating procedure (SOP) for its implementation. **Methods:** In this single-centre, assessor-blinded, randomised controlled trial, 150 patients with non-metastatic HNC scheduled for definitive radiotherapy (60–72 Gy) were enrolled at West China Hospital in China. Participants were randomly assigned (1:1) to receive either a dentist-led oral health education program (OHEP) or routine oral health care. The primary endpoint was the incidence of oral mucositis (OM), assessed by the WHO Oral Mucositis Grading Scale. Secondary endpoints included the incidence of severe oral mucositis (SOM, defined as WHO grade 3–4) as well as the time to onset and duration of OM (SOM). Outcome assessments were conducted by trained research assistants blinded to group allocation. Analyses were performed in both intention-to-treat and per-protocol populations, with two-sided $P < 0.05$ considered statistically significant. This study is registered with ClinicalTrials.gov, NCT06690346, and is now complete. **Results:** Of 150 randomised patients, 75 were allocated to each arm, and 142 (94.7%) completed the trial and were included in the intention-to-treat analysis. The incidence of OM was significantly lower in the OHEP arm than in the control arm (70.7% [53/75] vs. 88.0% [66/75] $P = 0.016$), with a significantly delayed onset (median 17 vs. 14 days; $P = 0.006$) and shorter duration (median 39 vs. 60 days; $P < 0.001$). Consistent results were observed in the per-protocol population. However, no significant difference was observed in the incidence, onset, or duration of SOM between arms. **Conclusions:** Dentist-led OHEP significantly reduced the incidence and delayed the onset of radiotherapy-induced OM. These results support dentist-led OHEP as a feasible, non-pharmacological approach to mitigate oral toxicity and improve supportive care in patients receiving radiotherapy for HNC. Clinical trial information: NCT06690346. Research Sponsor: Ministry of Science and Technology of the People's Republic of China; 2023ZD0503000, 2023ZD0503004; National Natural Science Foundation of China; U24A20735; Ministry of Education of the People's Republic of China; 82473434.

Efficacy and safety of Meilian Fuxin liquid for radiation-induced oral mucositis in head and neck cancer: A multicenter randomized clinical trial.

Huaju Yang, Zhihui Li, Zhigang Liu, Lei Cai, Zhigong Wei, Kun Gao, Zheran Liu, Yiyan Pei, Yu Min, Ruidan Li, Xingchen Peng; Cancer Center and State Key Laboratory of Biotherapy, West China Hospital, Sichuan University, Chengdu, China; Department of Oncology, The General Hospital of Western Theater Command, Chengdu, China; Dongguan People's Hospital, Dongguan, China; Institute of Hepatopancreatobiliary Surgery, Chongqing General Hospital, Chongqing University, Chongqing, Chongqing, China; Department of Biotherapy, Cancer Center, West China Hospital, Sichuan University, Chengdu, China

Background: Radiation-induced oral mucositis (RIOM) is common during head and neck radiotherapy (> 90% incidence), and 40–70% of patients develop severe oral mucositis (SOM; WHO grade 3–4), which markedly impairs quality of life and may lead to radiotherapy interruptions. Given the limited effective therapies and the lack of evidence-based standard of care, we assessed the efficacy and safety of MeiLianFuXin Liquid (*Periplaneta americana* extract) for reducing SOM incidence. **Methods:** This multicenter, randomized, double-blind, placebo-controlled phase II trial was conducted across 7 hospitals in China from June 12, 2024, through October 31, 2025. Eligible patients (18–80 years) had non-metastatic head and neck cancer planned for radiotherapy (planned total dose ≥ 60 Gy), with cisplatin as the only allowed concurrent agent. Following investigator-confirmed WHO grade 1 oral mucositis, patients were randomized (1:1:1) via a centralized interactive web response system (IWRS) using a dynamic minimization algorithm to receive low-dose MeiLianFuXin Liquid, high-dose MeiLianFuXin Liquid, or a matched placebo. The study drug was administered three times daily until 14 days post-radiotherapy. The primary endpoint was SOM incidence. Adjusted proportion differences were estimated using logistic regression. Adverse events were graded according to the Common Terminology Criteria for Adverse Events (CTCAE), version 5.0. **Results:** In the full analysis set (FAS), 215 patients received treatment (low-dose, $n = 72$; high-dose, $n = 72$; placebo, $n = 71$). The incidence of SOM was 22.2% (95% CI, 13.3 to 33.6) in the low-dose group, 29.2% (95% CI, 19.0 to 41.1) in the high-dose group, and 43.7% (95% CI, 31.9 to 56.0) in the placebo group. Compared with placebo, adjusted proportion differences were –22.5% (95% CI, –37.3 to –7.8; $P = .0042$) for the low-dose group and –16.4% (95% CI, –32.2 to –0.5; $P = .0463$) for the high-dose group. Adverse events and serious adverse events were generally similar across groups. **Conclusions:** To our knowledge, this is the first randomized, double-blind, placebo-controlled trial of a traditional Chinese medicine for RIOM showing that MeiLianFuXin Liquid reduces SOM incidence versus placebo with a favorable safety profile. These findings support MeiLianFuXin Liquid as a promising treatment strategy to mitigate RIOM. Clinical trial information: ChiCTR2400084288. Research Sponsor: the Noncommunicable Chronic Diseases–National Science and Technology Major Project (2023ZD0503000, 2023ZD0503004); the Regional Innovation and Development Joint Fund Key Project of the National Natural Science Foundation of China (U24A20735); the National Natural Sciences Foundation of China (82473434); the Fundamental and Interdisciplinary Disciplines Breakthrough Plan of the Ministry of Education of China, the Institutional Joint Innovation Fund from Sichuan University and Nuclear Power Institute of China (1-KJ-FWHT-WU-20240150).

Oral mannitol for chemotherapy-induced constipation (CIC): A randomized, multicenter, controlled study.

Chaomin Liu, Yanru Liu, Mingxiang Gao, Ke Xu, Pengcheng Li, Jiang Zhu, Lei Cao, Tao Ren; The First Affiliated Hospital of Chengdu Medical College, Chengdu, China; West China Hospital of Sichuan University, Chengdu, China; Qingbaijiang District People's Hospital, Chengdu, China

Background: Chemotherapy-induced constipation (CIC) is a common yet frequently overlooked supportive care issue, currently, there is still a lack of efficient and affordable methods. This trial was designed to compare the efficacy and safety of orally administered mannitol injection versus lactulose in cancer patients with CIC. **Methods:** An open-label, multicenter, prospective RCT (ChiCTR2200056847) planned to enroll 114 adults. Participants were randomized 1:1 to oral mannitol 50 mL post-meal 3–5×/day or lactulose 30 mL once daily for 3 days. Primary endpoint: time to first spontaneous defecation (TFSD). Secondary endpoints included weekly complete spontaneous bowel movements (CSBMs), Bristol Stool Form Scale, PAC-QOL, and CTCAE v5.0 adverse events (AEs). Interim analysis was performed when 112 participants had completed the 7-day assessment; database was locked on 30 January 2026. **Results:** A nationwide survey (14 provinces, n=1,174) revealed significantly higher constipation rates in stage IV cancer patients ($p<0.05$), and found that the managements vary in effectiveness. In an RCT interim analysis (112 patients), baseline demographics were balanced between mannitol (n=56) and lactulose (n=56) groups. Median time to first defecation was significantly shorter in mannitol group with 5.5 hours (IQR 3.0–15.8) than in lactulose with 16.0 hours (IQR 5.3–27.5) ($p=0.003$)(Fig. 1). Secondary outcomes were comparable: weekly mCSBMs (3.0 vs. 3.0, $p=0.083$); Bristol Scale improvement ≥ 1 category (60.7% vs. 58.9%, $p=0.847$); and PAC-QOL score (–26 vs. –18 points, $p=0.105$). Both treatments were safe, with only mild, transient adverse events at similar rates (3.6% vs. 5.4%, $p=0.647$)(Table 1). **Conclusions:** Survey data confirm under-recognition of CIC and therapeutic gaps for advanced-stage patients. In this interim analysis, oral mannitol significantly shorten TFSD than lactulose, with mild adverse events, which is a rapid-onset, low-cost option for CIC management. Clinical trial information: ChiCTR2200056847. Research Sponsor: None.

TFSD, weekly CSBMs, adverse events, PAC-QOL.			
Outcome	Mannitol (n=56)	Lactulose (n=56)	p-value
TFSD (median, IQR)	5.5 (3.0–15.8) hrs	16.0 (5.3–27.5) hrs	0.003
Weekly CSBMs (median, IQR)	3.0 (3.0–4.0)	3.0 (2.0–3.0)	0.083
Stool form improvement (≥ 1 Bristol)	34 (60.7%)	33 (58.9%)	0.847
PAC-QOL change (Δ , mean)	-26 (18.3–40.5)	-18 (12.5–37.5)	0.105
Any AE (%)	2 (3.6%)	3 (5.4%)	0.647

Efficacy and safety of mixed formulation aprepitant and palonosetron (QLM2010) for prevention of cisplatin-based highly emetogenic chemotherapy-induced nausea and vomiting: A multicenter, randomized, double-blind, double-dummy, positive-controlled phase III study.

Jieer Ying, Qingshan Li, Shuang Leng, Na Li, Chunling Liu, Lin Lai, Tienan Yi, Kaijian Lei, Xisheng Fang, SongNan Zhang, Hailong Wei, Honglin Hu, Qiong Wang, Yanxia Zhang, Xingli Gu, Yue Wang, Xiaojie Du, Yuanyuan Li, Xiangdong Cheng; Department of Hepatobiliary, Pancreatic and Gastric Medicine, Zhejiang Cancer Hospital, Chinese Academy of Sciences, Hangzhou, Zhejiang, China; Oncology Department, Affiliated Hospital of Chengde Medical University, Chengde, China; Oncology Center, Meihokou Central Hospital, Meihokou, China; Oncology Department, Sui Ning Central Hospital, Suining, China; Pulmonar Medicine Ward II, The Affiliated Tumour Hospital of Xinjiang Medical University, Urumqi, China; Department of Abdominal Oncology, Enshi Tujia and Miao Autonomous Prefecture Central Hospital, Enshi, China; Oncology Department, Xiangyang Central Hospital, Xiangyang, China; Oncology Center, The Second People's Hospital of Yibin, Yibin, China; Oncology Department, Guangzhou First People's Hospital, Guangzhou, China; Oncology Department, Affiliated Hospital of Yanbian University, Yanji, Jilin, China; Pulmonar Medicine, Leshan People's Hospital, Leshan, China; Tumor Center, Sichuan Provincial People's Hospital, Chengdu, China; Oncology Department, Jiangyin People's Hospital, Jiangyin, China; Oncology Department, Linyi People's Hospital, Linyi, China; Qilu Pharmaceutical Co., Ltd, Jinan, China; Gastric Surgery Department, Zhejiang Cancer Hospital, Hangzhou, China

Background: QLM2010, a novel fixed-dose intravenous antiemetic combination of aprepitant and palonosetron (PALO), can simultaneously antagonize 5-hydroxytryptamine-3 and neurokinin-1 receptors. This study aimed to assess the efficacy and safety of QLM2010 plus dexamethasone (DEX) versus fosaprepitant (FAPR) combined with PALO and DEX for preventing chemotherapy-induced nausea and vomiting (CINV) in patients receiving highly emetogenic chemotherapy (HEC). **Methods:** This was a multicenter, randomized, double-blind, double-dummy, positive-controlled Phase III trial. Chemotherapy-naïve patients with solid tumors were randomly assigned 1:1 to receive QLM2010 (Day 1) or FAPR + PALO (Day 1) prior to cisplatin-based HEC, together with oral DEX (Days 1–4). The primary efficacy endpoint was complete response (CR: no emesis/no rescue medication) during the overall (0–120 hours) phase. **Results:** Baseline demographic and clinical characteristics were well-balanced between the two groups (QLM2010 group: n = 329; FAPR+PALO group: n = 331). The overall CR rate was 82.67% versus 80.97% (risk difference, 1.65%; 95% CI, -4.21–7.50%), confirming the non-inferiority of QLM2010 + DEX to FAPR + PALO + DEX. CR rates in both the acute (0–24 hours) and delayed (24–120 hours) phases were comparable between groups. Across all phases, the QLM2010 group showed similar rates to the FAPR+PALO group for no emesis, no nausea, no significant nausea, no rescue therapy, and complete protection (all $P > 0.05$). Notably, QLM2010 + DEX showed greater proportions of patients reporting no impact on daily life on Day 2 after treatment compared with FAPR + PALO + DEX ($P = 0.0279$). A single injection-site reaction (0.30 %) was confined to the FAPR+PALO group; none was observed in the QLM2010 group. The incidence of hiccups was numerically lower in the QLM2010 group compared with the FAPR+PALO group (8.2% vs. 15.1%). **Conclusions:** QLM2010 + DEX was non-inferior to FAPR + PALO + DEX for preventing CINV in cisplatin-based HEC patients and well tolerated, with the potential to reduce the impact of CINV on daily life. QLM2010 furnishes a novel, more convenient therapeutic alternative for the clinical management of CINV. Clinical trial information: NCT07081256. Research Sponsor: None.

SARM1 inhibition to prevent chemotherapy-induced peripheral neuropathy: Translational and early clinical evaluation of SIR2501.

Linping Yu, Qian Wang, Lianzhu Liu, Yan Ren, Nan Zhang, Xiaoye Ren, Yanping Xu, Yang Shen, Shaohui Wu, Shefali Agarwal, Nasir Mahmood Khan, Weiliang Fan; Sironax, Beijing, China; Sironax, Waltham, MA

Background: Chemotherapy-induced peripheral neuropathy (CIPN) is a common, cumulative, and often irreversible toxicity that limits dose intensity, disrupts cancer treatment, and substantially impairs quality of life. Despite its prevalence, no approved disease-modifying therapies exist. Axonal degeneration is a central pathological driver of CIPN. Sterile alpha and TIR motif-containing protein 1 (SARM1) is a key executioner of programmed axon degeneration across neurotoxic insults. Inhibiting SARM1 offers a mechanism-based strategy to prevent axonal injury without compromising anticancer activity. SIR2501 is a potent, selective, orally bioavailable small-molecule SARM1 inhibitor in clinical development for CIPN prevention.

Methods: SIR2501 was evaluated in rodent models of paclitaxel (PTX)-induced peripheral neuropathy using prophylactic and therapeutic dosing paradigms. Endpoints included sensory neuropathy (mechanical allodynia), axonal injury biomarkers (serum neurofilament light chain [sNfL]), and peripheral nerve integrity (intraepidermal nerve fiber density). The impact of SIR2501 on PTX antitumor efficacy was assessed in rodent tumor models. A randomized, double-blind, placebo-controlled Phase 1 study in healthy volunteers evaluated safety, pharmacokinetics (PK), CNS penetration, and pharmacodynamic evidence of SARM1 target engagement following single and multiple ascending doses. **Results:** SIR2501 robustly attenuated PTX-induced neuropathy in preclinical models, with concordant functional, biomarker, and structural protection, and did not impair PTX-mediated tumor growth inhibition. In Phase 1, 82 volunteers received SIR2501 (up to 600 mg single dose; up to 150 mg once-daily multiple dose). SIR2501 was well tolerated, with no dose-limiting toxicities or clinically meaningful neurologic adverse events. PK supported once-daily dosing with minimal food effect and no CYP3A-mediated drug-drug interaction risk. Dose- and exposure-dependent suppression of circulating cyclic ADP-ribose (cADPR) confirmed SARM1 target engagement at plasma exposures aligned with preclinical efficacy. **Conclusions:** These translational data support SARM1 inhibition as a disease-modifying approach for CIPN. These data have enabled initiation of a global Phase 1b/2 trial of SIR2501 in patients receiving taxane-based chemotherapy in the United States, Australia, and China. Research Sponsor: Sironax Inc.

Baseline telomere length and prediction of cognitive recovery after chemotherapy in patients with breast cancer: An NCORP prospective cohort study.

Jonas M. Ndeke, Kevin Spath, Lindsey Jean Mattick, Song Yao, Judith O. Hopkins, Adedayo A. Onitilo, Steven William Corso, Luke Joseph Peppone, Michelle Christine Janelins; Department of Surgery, Division of Supportive Care in Cancer, University of Rochester Medical Center, Rochester, NY; University of Rochester Medical Center, Rochester, NY; Roswell Park Comprehensive Cancer Center, Buffalo, NY; Southeast Clinical Oncology Research Consortium and NCORP, Winston Salem, NC; Wisconsin NCORP, Marshfield, WI; Upstate Carolina Consortium NCORP, Spartanburg, SC; Department of Surgery, Division of Supportive Care in Cancer and URCC NCORP Research Base, University of Rochester Medical Center, Rochester, NY

Background: Chemotherapy-related cognitive impairment (CRCI) affects up to 70% of breast cancer survivors, yet recovery varies. Telomere length (TL), a marker of biological aging, may reflect biological resilience to CRCI. We evaluated whether baseline TL predicts longitudinal cognitive recovery following chemotherapy. **Methods:** In a nationwide prospective cohort study across 19 NCORP-affiliated community oncology clinics (URCC 10055), 185 women with stage I–IIIC breast cancer were assessed before chemotherapy (T1), post-chemotherapy (T2), and 6 months post-chemotherapy (T3). Baseline TL was measured by qPCR, normalized, and categorized into three groups: Short (S, n = 63, 34.1%), Average (A, n = 75, 40.5%), and Long (L, n = 47, 25.4%). Perceived cognitive function was assessed using the Functional Assessment of Cancer Therapy–Cognitive Function (FACT–Cog; minimum clinically important difference for total ≈7 pts), including total score and subscales for perceived cognitive impairments (PCI), perceived cognitive abilities (PCA), comments from others (OTH), and impact on quality of life (QoL). Changes from T1→T2 and T2→T3 were evaluated using repeated-measures mixed-effects analysis of covariance models adjusted for baseline values. **Results:** Baseline FACT–Cog total scores were similar across TL groups. At T2, all groups experienced comparable acute PCI (FACT–Cog change: S = −13.2, A = −13.3, L = −18.7). By T3, recovery differed by TL. While all groups remained below baseline, patients with long TL demonstrated substantially greater recovery, with a smaller overall decline from T1 (L = −8.6) compared with persistent impairment in Short (S = −14.0) and Average (A = −11.4) groups. This reflected a clinically meaningful improvement in cognitive function from post-chemotherapy to 6-month of +10.0 pts in the Long group (p = .016), whereas changes in the other two groups was not clinically or statistically significant. This recovery pattern was supported by clinically significant improvement in PCI (+7.2) and statistically significant change in OTH (+1.0; p = .003) in the Long group from T2 to T3, while it was attenuated in the Average and Short groups. In contrast, PCA showed minimal change across groups. Impact on quality of life also improved significantly in the Long group over the same period (FACT–Cog QoL T3–T2 change = +2.0; p = .019), reinforcing a coherent cognitive recovery phenotype. **Conclusions:** Baseline TL does not determine susceptibility to acute chemotherapy-related toxicity but strongly predicts cognitive recovery over time. Patients with longer telomeres demonstrate clinically meaningful recovery of cognition, whereas those with shorter telomeres show more persistent perceived cognitive impairment. TL may identify patients at higher risk for long-term impairment who could benefit from early supportive and rehabilitative interventions. Research Sponsor: NIH NCI T32CA102618; NIH NCI R01CA231014; NIH NCI UG1CA189961; NIH NCI UG1CA189858; NIH NCI UG1CA189956; NIH NCI UG1CA239762.

Prophylactic vs reactive PEG tube placement in early-stage head and neck (H&N) cancer treated with curative-intent radiotherapy: Balancing benefit and burden in real-world practice.

Fayaz Aijaz Ahmed Khan, Andrew Chang, Rebecca Calabrese; Roswell Park Comprehensive Cancer Center, Buffalo, NY

Background: Timing of Percutaneous Endoscopic Gastrostomy (PEG) placement during curative-intent radiotherapy for H&N cancer remains controversial. We compared 6-month and 1-year outcomes after prophylactic (pPEG) versus reactive (rPEG) PEG placement in real-world practice. **Methods:** We conducted a retrospective study using the TriNetX Network database. Adults (≥ 18 years) with H&N cancer treated with curative-intent radiotherapy who received PEG were stratified by PEG timing: pPEG (≤ 30 days before or at radiotherapy initiation) versus rPEG (30–90 days after radiotherapy initiation). The index date was PEG insertion. After 1:1 propensity-matching with demographics, comorbidities, nutrition/weight variables, BMI, stage, chemotherapy/surgery, 2,752 patients remained in each cohort. Outcomes at 6 months and 1 year were analyzed using Kaplan–Meier methods with log-rank tests and Cox proportional-hazards models (HR, 95% CI). **Results:** At 6 months, compared with rPEG, pPEG was associated with lower all-cause mortality, but higher hospitalization, sepsis, PEG tube dependence, and PEG tube complications. ICU admission, aspiration pneumonitis, pneumonia, and dehydration were similar between cohorts. At 1 year, all-cause mortality and ICU admission remained similar between groups. However, pPEG was associated with higher hospitalization, aspiration pneumonitis, pneumonia, sepsis, and PEG tube complications, while dehydration and PEG tube dependence were similar (see Table). pPEG was associated with higher risk of dysphagia at 6 months (HR 1.3, 95% CI 1.1–1.6; $p < 0.01$) and 1 year (HR 1.2, 95% CI 1.1–1.5; $p = 0.01$), and malnutrition at 6 months (HR 1.3, 95% CI 1.1–1.6; $p < 0.01$) and 1 year (HR 1.3, 95% CI 1.1–1.6; $p < 0.01$). Unintentional weight loss and PEG tube removal did not differ between groups. **Conclusions:** In this real-world cohort study, pPEG was not associated with improved 1-year survival and was associated with higher acute care utilization, infections, and PEG-related complications compared with rPEG. These findings support selective, risk-stratified pPEG use rather than routine prophylactic placement. Research Sponsor: None.

Outcome	6 Month HR (95% CI, p-value)	1 Year HR (95% CI, p-value)
All-cause mortality	0.8 (0.7-0.9, $p=0.04$)	0.9 (0.8-1.1, $p=0.6$)
Hospitalization	1.3 (1.01-1.6, $p=0.04$)	1.2 (1.1-1.5, $p=0.04$)
ICU admission	1.0 (0.8-1.3, $p=0.6$)	1.1 (0.9-1.3, $p=0.3$)
Aspiration pneumonitis	1.2 (0.9-1.5, $p=0.07$)	1.2 (1.1-1.5, $p=0.03$)
Pneumonia	1.2 (0.9-1.4, $p=0.1$)	1.2 (1.1-1.4, $p=0.04$)
Sepsis	1.3 (1.01-1.5, $p=0.03$)	1.3 (1.1-1.5, $p=0.01$)
Dehydration	1.6 (0.9-2.6, $p=0.08$)	1.5 (0.9-2.3, $p=0.1$)
PEG tube dependence	1.2 (1.01-1.3, $p=0.04$)	1.1 (0.9-1.3, $p=0.07$)
PEG tube complication	1.2 (1.1-1.4, $p < 0.01$)	1.2 (1.1-1.3, $p < 0.01$)

HR > 1 indicates higher hazard in pPEG vs rPEG; HR < 1 indicates lower hazard.

The influence of exercise on the mediational relationship between chemotherapy-induced sensory neuropathy and cancer-related fatigue: A nationwide phase II RCT in 111 patients receiving chemotherapy.

Po-Ju Lin, Hongying Sun, Chin-Shang Li, Umang Gada, Dee Murray, Thushini Manuweera, Lindsey Jean Mattick, Jeffrey L. Berenberg, Jay Carlson, Gregory A. Masters, Jennifer S. Gewandter, Bryan A. Faller, Karen Michelle Mustian, Ian Kleckner; Wilmot Cancer Institute, University of Rochester Medical Center, Rochester, NY; Wilmot Cancer Center, University of Rochester Medical Center, Rochester, NY; University of Maryland Baltimore, Baltimore, MD; Hawai'i MUNCORP, Honolulu, HI; Cancer Research for the Ozarks NCORP, Springfield, MO; Delaware/Christiana Care NCORP, Newark, DE; Heartland Cancer Research NCORP, Saint Louis, MO; James P. Wilmot Cancer Institute, University of Rochester Medical Center, Rochester, NY

Background: Cancer-related fatigue (CRF) and chemotherapy-induced sensory neuropathy (e.g., numbness, tingling, and pain) are common, sometimes debilitating toxicities that often co-occur in patients receiving neurotoxic chemotherapy. Both CRF and sensory neuropathy significantly diminish daily function and quality of life. Exercise is recommended for treating CRF and may also alleviate sensory neuropathy. Whether exercise-induced reductions in CRF are mediated by improvements in sensory neuropathy remains unknown. **Methods:** We conducted a nationwide phase II randomized controlled trial (RCT) through the University of Rochester Cancer Center NCI Community Oncology Research Program (URCC NCORP) Research Base. Patients who received neurotoxic chemotherapy in the past 9 months and developed moderate or severe (rated ≥ 4 on a 0-10 numerical scale) chemotherapy-induced sensory neuropathy (e.g., numbness, tingling, hot/burning or sharp/shooting pain in the hands and feet) in the past 2 weeks were randomized to virtually delivered Exercise for Cancer Patients (vEXCAP) or usual care (UC). vEXCAP is a 6-week, individually tailored, progressive walking and resistance band exercise intervention delivered virtually. CRF severity and sensory neuropathy were assessed via the Brief Fatigue Inventory severity score and the EORTC QLQ-CIPN20 sensory subscale (0-100 scale), respectively, at pre- and post-intervention. Causal mediation analyses were conducted to determine the extent to which exercise-induced improvements in CRF were mediated by changes in sensory neuropathy at post-intervention. **Results:** One hundred eleven patients (mean age 59.5 years; 76% female; 84% white; 37% breast cancer; 36% gastrointestinal cancer) were randomized and completed pre- and post-intervention assessments. vEXCAP participants, compared to UC participants, experienced significantly greater reductions in CRF (-0.95 ± 0.33 , $p = 0.014$) and clinically meaningful improvements in sensory neuropathy at post-intervention (-5.38 ± 2.77 [MCID = 4.2], $p = 0.055$). Causal mediation analyses indicated that reductions in sensory neuropathy significantly mediate exercise-induced improvements in CRF severity (-0.18 ± 0.13 , $p = 0.056$), accounting for 19% (95% CI: 0% - 64%) of the exercise effect on CRF severity at post-intervention. **Conclusions:** vEXCAP reduces CRF severity and chemotherapy-induced sensory neuropathy among patients receiving neurotoxic chemotherapy. Approximately 19% of the exercise-induced improvements in CRF severity are mediated by reductions in chemotherapy-induced sensory neuropathy. Future Phase III RCTs are needed to confirm these findings and further explore the mediational role of chemotherapy-induced sensory neuropathy on CRF to help optimize the treatment of CRF using exercise. Clinical trial information: NCT04888988. Research Sponsor: National Cancer Institute; R21CA256154, K07CA221931, UG1CA189961, UG1CA189804, UG1CA189822, UG1CA189819, UG1CA189830, T32CA102618.

Trilaciclib for myeloprotection in adjuvant and first-line chemotherapy for advanced gastric/gastroesophageal junction adenocarcinoma: A multicohort study.

Wenhui Yang; Department of Gastroenterology, Shanxi Province Cancer Hospital/Shanxi Hospital Affiliated to Cancer Hospital, Chinese Academy of Medical Sciences/Cancer Hospital Affiliated to Shanxi Medical University, Taiyuan, China

Background: Chemotherapy-induced myelosuppression (CIM) has become one of the important limiting factors in the treatment of gastric cancer, which significantly impairs patients' prognosis. Trilaciclib, a highly selective reversible CDK4/6 inhibitor, reduces chemotherapy-induced hematopoietic stem/progenitor cell (HSPC) damage via transient G1 arrest when administered intravenously pre-chemotherapy, while its transient T-cell suppression may modulate the tumor immune microenvironment. This study evaluates trilaciclib's myeloprotective efficacy in adjuvant and first-line metastatic gastric/gastroesophageal junction adenocarcinoma (GA/GEJA) and explores immunomodulatory effects. **Methods:** This prospective multicohort study (ChiCTR2500097520) enrolled Cohort 1 (resectable GA/GEJA, T1-4bN0-3Mo post-D2/R0 resection; n = 75) and Cohort 2 (first-line metastatic GA/GEJA, including recurrence > 6 months post-adjuvant; n = 40). Regimens included SOX/XELOX/FOLFOX ± immune checkpoint inhibitors (ICIs) ± trastuzumab. Trilaciclib (240 mg/m²) was given on days 1 and 3 every 21 days for 6–8 cycles. Primary endpoints: incidence of grade ≥3 neutropenia and febrile neutropenia (FN); exploratory analyses included immune biomarkers and antitumor efficacy. **Results:** As of January 2026, 204 patients were enrolled (male: 158; female: 46; median age: 63 years [range: 31–82]). Cohort 1: 118 patients (primary prophylaxis [PP]: 98; secondary prophylaxis [SP]: 20). Cohort 2: 86 patients (PP: 48; SP: 38). Grade ≥3 CIM incidence: Cohort 1 vs. Cohort 2: 4.46% vs. 2.96%; grade ≥3 neutropenia: 3.24% vs. 1.73%; thrombocytopenia: 1.54% vs. 0.74%; anemia: 0.77% vs. 1.97%. Prophylaxis-stratified analysis showed superior myeloprotection with PP: overall grade ≥3 CIM (PP: 3.35% vs. SP: 4.56%), neutropenia (PP: 2.75% vs. SP: 1.83%), thrombocytopenia (PP: 0.6% vs. SP: 2.29%), and anemia (PP: 1.32% vs. SP: 0.91%). Furthermore, the collection and detection of immune cells from 97 patients before and after treatment revealed that: the total number of T cells in patients showed an increasing trend after prophylactic medication. The number of CD4+ T cells showed an increasing trend; the number of CD8+ T cells began to decline after more than 3 cycles of chemotherapy; the number of Treg T cells increased and returned to the pre-chemotherapy level after more than 4 cycles. **Conclusions:** Trilaciclib demonstrated effective myeloprotection and immunoregulation in GA/GEJA, with PP showing a favorable trend. Grade ≥3 CIM rates were ≤5.88% (adjuvant) and ≤3.49% (metastatic), with no new safety signals. The studies will continue to analyze the correlation between immune-related indicators and anti-tumor efficacy. Clinical trial information: ChiCTR2500097520. Research Sponsor: None.

Machine learning approach for prediction of immune-related pneumonitis.

Barlitz Waissengrin, Yasaman Fatapour, Jose Acitores, Rama Chandra Das, Hongyu Liu, Nadine Friedrich, Kamya Sankar, Nicholas Tatonetti, Jane Figueiredo, Karen L. Reckamp; Medicine, Cedars Sinai Cancer Center, Los Angeles, CA; Department of Computational Biomedicine, Cedars Sinai Medical Center, Los Angeles, CA

Background: Immune-related adverse events (irAE) associated with immune checkpoint inhibitors (ICI) substantially contribute to treatment-related morbidity, yet reliable pretreatment predictors remain unavailable. Immune-related pneumonitis (irP) is among the most serious irAE and is associated with a significant risk for mortality. Machine learning (ML) offers an opportunity to analyze complex clinical data to improve risk stratification. We aimed to develop a personalized ML-based model to identify and predict irP from electronic health records (EHR) using patient characteristics prior to ICI initiation. **Methods:** We extracted data from the EHR of patients with solid malignancies, in various disease stages, who were treated with ICI at Cedars-Sinai Medical Center between 2015 and 2024. For each patient, we collected comprehensive treatment data, including demographics and clinical variables from structured fields and clinical notes. Variables not reliably captured in structured fields, such as smoking or family history, were extracted using our pipeline. Using a large language model (LLM)-based pipeline, we identified irAE cases, enabling precise extraction and classification of irAE subtypes, and validated results against physician annotations for irP (excluding pneumonitis due to other causes). Chi-square analyses assessed associations between features and irAE. We used TPOT, an automated machine learning tool, to develop predictive models and explore sampling strategies for class imbalance. The model was trained on a balanced dataset, evaluated on an unbalanced test set (80/20 split), and hyperparameter-optimized using five-fold cross-validation. **Results:** Our study included 4,302 cancer patients treated with ICI, of whom 910 were identified by our pipeline as having an irAE and 276 cases of irP. The model achieved a sensitivity of 0.964 on a physician-annotated irP dataset. The best-performing predictive model was a tree-based classifier with an AUC of 0.68. Chi-square analysis identified significant associations ($p < 0.05$) between irP and multiple clinical features, including prior lung disease, radiotherapy, age at immunotherapy, comorbidity burden, and inflammatory markers. Odds ratio analysis based on model-derived risk score quartiles, showing that patients in the highest-risk quartile exhibited an average 10.3-fold increase in the odds of developing pneumonitis compared to those in the lowest-risk quartile. **Conclusions:** This study establishes a strong baseline for ML algorithms to identify and predict irP specifically in patients treated with ICI, using EHR-derived data. Our results demonstrate that pre-treatment clinical and laboratory variables can be effectively used to stratify irP risk. Future research should aim to refine these predictive models and incorporate a broader range of EHR-based features to further improve predictive performance and clinical applicability. Research Sponsor: None.

Efficacy and safety of a temperature-controlled oral cryotherapy device in preventing oral mucositis among patients receiving high-risk anticancer regimens.

Xiaojia Wang, Xiyang Shao, Jia Wang, Huanhuan Zhou, Guangliang Li, Junyao Xu, Wei-Wu Ye, Zhanhong Chen, Xiabo Shen; Department of Breast Oncology, Zhejiang Cancer Hospital, Hangzhou, China; Zhejiang Cancer Hospital, Hangzhou, China; Department of Breast Medicine, Zhejiang Cancer Hospital, Hangzhou, China; Department of Breast Medical Oncology, Zhejiang Cancer Hospital, Hangzhou, China

Background: Oral mucositis (OM) is a severe dose-limiting toxicity in cancer patients receiving intensive chemotherapy or novel antibody-drug conjugates (ADCs). Recent clinical data indicate that the incidence of OM with Sacituzumab Tirumotecan (sac-TMT) is as high as 54.1%, with approximately 11.1% of patients experiencing severe (Grade $\geq$ 3) events. For Liposomal Doxorubicin, reported OM incidence is approximately 22%. Established therapies such as Docetaxel, Paclitaxel plus Carboplatin, and Sacituzumab Govitecan exhibit OM rates ranging from 10% to 30%. Severe OM frequently leads to excruciating pain, nutritional compromise, and treatment delays. This study evaluated the efficacy of a specialized oral cryotherapy (OC) device in preventing treatment-induced OM across these high-risk regimens. **Methods:** In this prospective trial, patients scheduled for high-risk regimens including Sacituzumab Tirumotecan, Sacituzumab Govitecan, Liposomal Doxorubicin, Docetaxel, or Taxane plus Carboplatin were enrolled. The intervention group received continuous OC using 8°C purified water, delivered via safe, non-toxic intraoral molds regulated by a temperature-controlled device. The protocol was administered 15 minutes prior to, throughout, and 30 minutes post-infusion. Primary endpoints included time to first OM onset, OM incidence, and WHO severity grading. **Results:** From September, 2025 to January, 2026, 116 patients were enrolled, with the most frequent user completing 13 OC sessions. The overall incidence of OM was only 6.9% (8/116), and all cases were Grade 1, with no interference with oral intake. In the Sacituzumab Tirumotecan (sac-TMT) subgroup (n = 26), the OM incidence was 11.5% (3/26) occurring at C2D1 (n = 2) and C4D8 (n = 1). Other subgroup incidences were as follows: Sacituzumab Govitecan, 50.0% (1/2) occurring at C2D1; Liposomal Doxorubicin, 4.2% (1/24) occurring at C2D1; Taxanes, 7.1% (2/28) both occurring at C2D8; and Epirubicin, 5.6% (1/18) occurring in C3D1. Notably, zero Grade $\geq$ 2 OM events were observed across all cohorts. No serious adverse events related to the temperature-controlled device were reported, and patient compliance with the OC protocol was high. **Conclusions:** Regulated oral cryotherapy using a temperature-controlled device and intraoral molds is a simple, cost-effective, and well-tolerated intervention that significantly reduces the incidence and severity of treatment-induced oral mucositis. Particularly for patients receiving high-risk ADCs such as Sacituzumab Tirumotecan, this standardized OC protocol should be considered a standard prophylactic measure to improve clinical outcomes and treatment adherence. Research Sponsor: None.

Cardiovascular toxicity across epidermal growth factor receptor (EGFR) tyrosine kinase inhibitors in *EGFR*-mutated non–small cell lung cancer: A population-based retrospective cohort study.

Yun-Gyoo Lee, Dayeon Seo, Jungwon Choi; Department of Internal Medicine, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, Seoul, South Korea; Sungkyunkwan University School of Medicine, Suwon, South Korea; Division of Hematology & Medical Oncology, Department of Internal Medicine, Samsung Kangbuk Hospital,, Seoul, South Korea

Background: Epidermal growth factor receptor (EGFR) tyrosine kinase inhibitors (TKIs) are the therapeutic backbone for *EGFR*-mutated non–small cell lung cancer (NSCLC) and often requiring prolonged exposure. Adverse cardiovascular events limit a long-term treatment and remain a major concern for cancer survivors. Osimertinib, the 3rd generation EGFR TKI, was associated with cardiac dysfunction. Although Osimertinib is a preferred first-line option, many countries still use first- or second-generation EGFR TKIs upfront; therefore, robust studies are needed to define cardiotoxicity across these earlier-generation EGFR TKIs.

Methods: In this retrospective cohort study using a nationwide Health Insurance Claim Database in Korea, patients newly diagnosed with NSCLC between 2010 and 2023 were identified. Patients were classified into three groups: first-generation (1G) EGFR TKIs (gefitinib or erlotinib), second-generation (2G) TKIs (afatinib or dacomitinib), and third-generation (3G) TKI sequence (initial first- or second-generation TKI followed by a switched to osimertinib). The incidence of cardiovascular disease (CVD) during treatment period was compared between groups. CVD included ischemic heart disease, heart failure, atrial tachyarrhythmias, and stroke. For patients with pre-existing CVD, only new-onset CVD were counted as events. Follow-up was completed December 31, 2024. **Results:** Among the 51,218 patients (58,317 [51%] female; mean [SD] age, 65.5 [10.8] years), 36,335 (70.9%), 8173 (16.0%), 6710 (13.1%) were treated with 1G, 2G and 3G EGFR TKI respectively. Among all patients, 16.7% were receiving medication for diabetes, 52.7% for hypertension, and 19.8% for dyslipidemia. Before lung cancer diagnosis, 1.1% had coronary artery disease and 2.7% had heart failure. In patients treated with 1G EGFR TKIs, the cumulative incidence of CVD at 1, 2, 3, and 5 years was 4.8%, 8.1%, 11.2%, and 16.2%, respectively. In those treated with 2G EGFR TKIs, the corresponding cumulative incidence was 4.2%, 7.0%, 9.4%, and 12.3%. In the group of 3G TKI sequence, the cumulative incidence of CVD at 1, 2, 3, and 5 years was 2.9%, 6.1%, 8.9%, and 14.8%, respectively. There was no statistically significant long-term difference in CVD incidence between the 1G TKI and the 3G TKI group ($p = .245$). **Conclusions:** The long-term risk of CVD associated with sustained treatment with 1G EGFR TKIs appears comparable to the risk observed among patients who started with 1G or 2G and switched to 3G EGFR TKI sequence. As long-term survivors with EGFR mutant NSCLC increases in number, ongoing surveillance for cardiotoxicity and proactive risk mitigation are essential. Research Sponsor: None.

Oncologic outcomes following biologic therapy for immune-related cutaneous adverse events.

Tara Maier, Alina Markova, Stephen W. Dusz, Elena Goleva, Donald YM Leung, Jeffrey Kern, Allison Gordon, Fazilat Khwaja, Michael A. Postow, Jonathan E. Rosenberg, Mario E. Lacouture, Neil J. Shah; Stony Brook University, Stony Brook, NY; Department of Medicine, Dermatology Service, Memorial Sloan Kettering Cancer Center, New York, NY; Department of Dermatology, Memorial Sloan Kettering Cancer Center, New York, NY; National Jewish Health, Denver, CO; Memorial Sloan Kettering Cancer Center, New York, NY; Memorial Sloan Kettering Cancer Center; Weill Cornell Medical College, New York, NY; New York University, New York, NY; Genitourinary Oncology, Memorial Sloan Kettering Cancer Center; Weill Cornell Medical College, New York, NY

Background: Biologic agents are increasingly used to treat immune-related cutaneous adverse events (irCAEs). However, limited data exist regarding immune checkpoint inhibitor (ICI) rechallenge and ICI efficacy following biologic therapy for irCAE management. **Methods:** We conducted a retrospective cohort study of patients enrolled under U01AR077511-01 (PIs Leung, Kern, Lacouture) treated with ICIs who developed dermatologist-confirmed grade ≥ 2 irCAEs. Demographics, irCAE treatments, and dermatologic and oncologic outcomes were collected via chart review and compared using t-tests and chi-square tests. **Results:** We identified 159 patients who developed grade ≥ 2 irCAEs, including 80 treated with biologic agents. Mean age was 66.8 years; 40% were female, 79% White, and 78% had stage IV disease. The most common tumor types were kidney (20%), lung (16%), and melanoma (12%). Common ICI regimens included ICI monotherapy (46%), ICI-ICI combination (21%), and ICI+chemotherapy (19%). Pruritus (23%), maculopapular rash (21%), and eczema (19%) were the most common irCAEs. Most patients received topical steroids (88%), while systemic steroids were used sparsely (13%). Biologics were used in ~50% of patients; the most common agents were dupilumab (43%), omalizumab (33%), and ustekinumab (11%). Median biologic duration was 16 weeks, with 25% receiving therapy for >40 weeks. ICI rechallenge occurred in 60% of biologic-treated versus 67% of non-biologic patients ($p=0.35$). Rechallenge rates were 67% vs 65% for grade 2 ($p=0.85$) and 44% vs 74% for grade 3 irCAEs ($p=0.05$) (biologic vs non-biologic, respectively). Antitumor outcomes were similar between biologics and non-biologic groups: 31% vs 28% achieved partial/complete response, 43% had stable disease, and 26% vs 29% had progressive disease, respectively. **Conclusions:** In this oncodermatology-managed cohort, irCAEs were primarily treated with topical corticosteroids and targeted biologics, with infrequent systemic steroid use. Biologic therapy enabled ICI rechallenge in most patients, and oncologic outcomes were comparable to those not receiving biologics. Overall, these findings support biologics as a steroid-sparing option for moderate-to-severe irCAEs that may allow continued immunotherapy without apparent loss of antitumor efficacy, warranting prospective validation. Research Sponsor: None.

Clinical characteristics.

Variable	Overall n=159	No Biologics n=79	Biologics n=80
Age at ICI (mean)	66.8	64.3	69.4
Tumor Types Kidney/Lung/Melanoma (%)	20/16/12	22/17/9	18/15/15
Line of treatment 1L/2L/2+L (%)	52/25/23	49/27/24	54/24/22
irCAEs: Pruritus/MPR/Eczema/Others (%)	23/21/19/37	22/33/17/28	25/9/21/45
irCAE Grade 2/Grade 3 (%)	74/26	76/24	71/29
Dupilumab/Omalizumab/Ustekinumab/Others (%)	33/33/11/23	N/A	33/33/11/23
Systemic Steroids - Yes (%)	13	8	18
ICI Rechallenge - Yes (%)	64	67	60
Response CR-PR/SD/PD (%)	30/43/27	31/43/26	28/43/29

Major adverse cardiovascular events among prostate cancer patients in the VA, stratified by HIV status and androgen deprivation therapy.

Debanjan Pain, Yongquan Dong, Christine Hartman, Rulin Hechter, Michael Silverberg, Jennifer Kramer, Elizabeth Y. Chiao; Department of Health Services Research, The University of Texas MD Anderson Cancer Center, Houston, TX; Baylor College of Medicine, Houston, TX; Kaiser Permanente Southern California, Pasadena, CA; Kaiser Permanente Northern California, Oakland, CA; Baylor College of Medicine Division of Diabetes Endocrinology and Metabolism, Houston, TX; Department of Epidemiology, Division of Cancer Prevention and Population Sciences, The University of Texas MD Anderson Cancer Center, Houston, TX

Background: Despite the rapidly increasing trend in incidence of prostate cancer among persons with HIV (PWH), comprehensive data outlining outcomes and treatment toxicities of prostate cancer in this population remain sparse. Notably, both HIV infection and prostate cancer treatment independently increase the risk of cardiovascular disease. We sought to quantify the risk of major cardiovascular adverse events (MACE) among a large Veterans Affairs (VA) cohort of PWH and people without HIV (PWoH). **Methods:** We used patient data from the VA Corporate Data Warehouse and the VA Central Cancer Registry, including demographics, laboratory data, medications administered in inpatient/outpatient pharmacies, International Classification of Diseases 9th Edition and 10th edition diagnoses and procedure codes. Patients were included if they had diagnosis of prostate adenocarcinoma between 1/1/2008 and 12/31/2020. Patients were excluded if they had a diagnosis with any prior invasive cancer on or prior to prostate cancer diagnosis, diagnosis with prostate cancer prior to HIV positive diagnosis, or MACE within 6 months prior to prostate cancer diagnosis. MACE was defined as having a diagnosis code of myocardial infarction, stroke, or arrhythmia, within five years of start of treatment approach for prostate cancer (defined as androgen deprivation therapy (ADT) or active surveillance). We conducted a time-to-event analysis using the Cox proportional hazards model to examine the time to first occurrence of MACE, accounting for censoring and varying follow-up times. **Results:** A total of 87,144 prostate cancer patients were included (654 PWH and 86,490 PWoH). About 37.5% of PWH were < 60-years-old at time of prostate cancer diagnosis (compared with 19.6% of PWoH). Among 62,259 patients with low-risk or intermediate-risk localized prostate cancer, the risk of MACE was 24% greater among PWH compared with PWoH (HR 1.24, 95% CI 1.02–1.51, $p = 0.03$) after controlling for age, race, and cardiovascular risk factors at time of cancer diagnosis. Among PWH with prostate cancer, receiving ADT was associated with a 3.5 fold increased risk of developing MACE vs. those not receiving ADT (HR 3.51, 95% CI 2.25–5.49, $p < 0.01$). Among PWoH with prostate cancer, receiving ADT had a 2.7-fold increased risk of developing MACE vs. those not receiving ADT (HR 2.72, 95% CI 2.61–2.84). **Conclusions:** Both HIV infection and ADT increase the risk of MACE among prostate cancer patients. Future studies are warranted to explore the mechanistic links between HIV infection, ADT, and cardiovascular health. Research Sponsor: None.

Identification of nutritional risk in chimeric antigen receptor T-cell (CAR-T) therapy: Protein-energy malnutrition and its impact on patient outcomes.

Anu Priyamvadha Ramakrishnan, Daniel Cruceta Reynoso, Shruthi Sridhar, Swapnil Surpur; Nassau Health Care Corporation, East Meadow, NY; Nassau University Medical Center, East Meadow, NY; The Wright Center for GME, Scranton, PA

Background: Protein-energy malnutrition (PEM), an imbalance between protein and energy intake and the body's requirements, is highly prevalent in cancer, affecting 20–70% of patients, with an overall prevalence of approximately 41%. PEM and cachexia impair therapeutic efficacy, increase treatment-related toxicities, and worsen survival outcomes. Although CAR T-cell therapy has revolutionized oncology, its associated complications—such as cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS) further affects nutritional status, creating a complex bidirectional relationship between PEM and CAR-T complications. This study utilizes the National Inpatient Sample (NIS) to assess nutritional status in CAR T-cell therapy recipients and potential impact on outcomes and treatment-related complications. **Methods:** A retrospective cohort study was conducted using the 2021–2023 National Inpatient Sample (NIS) database. Adult patients (aged ≥ 18 years) who were hospitalized and received CAR-T therapy were identified using ICD-10 codes and stratified according to the presence of PEM. The primary outcome was the inpatient mortality rate, while secondary outcomes included length of hospital stay, total hospital charges, incidence of CRS, ICANS, and other medical complications. **Results:** Among 10,690 hospitalized adult CAR-T recipients, 2,190 (20%) had PEM. In-hospital mortality in this group was 190 (9%). The PEM cohort was predominantly male (79%) and White (74%), with a mean age of 61.5 years. Compared to patients without PEM, those with PEM experienced higher in-hospital mortality (8% vs 1.2%; OR 7.2; $P < 0.001$), longer hospital stays (LHS) (24 vs 15 days; Coefficient 9.2; $P < 0.001$), and higher costs (\$1,428,895 vs \$1,106,642; Coefficient 322,253; $P < 0.001$) and more CAR-T-related complications, including CRS (44% vs 39%; OR 1.3; $P < 0.05$), ICANS (12% vs 7%; OR 1.7; $P < 0.05$), sepsis (OR 3.13; $P < 0.001$), stroke (OR 4; $P < 0.001$), and cardiovascular events (OR 1.6; $P < 0.001$). **Conclusions:** This analysis identifies PEM as a significant predictor of mortality, prolonged hospitalization, higher costs and increased complications among CAR-T recipients. This highlights baseline nutritional status as a critical outcome determinant. This emphasizes the need for pre-treatment nutritional screening and early, targeted interventions to break the vicious cycle of malnutrition, improve treatment tolerance, reduce adverse events, and optimize outcomes. Further studies should evaluate tailored nutritional strategies and supportive care to enhance CAR-T safety and efficacy. Research Sponsor: None.

Impact of corticosteroid exposure on long-term immune checkpoint inhibitor responses in solid tumors.

Theresa Medina; University of Colorado, Aurora, CO

Background: Multiple analyses offer conflicting evidence regarding the implications of immune related adverse events (irAE) on survival of patients with solid tumors treated with immune checkpoint inhibitor(s) (ICIs). Furthermore, the treatments used to manage irAEs also have an unclear impact on progression free survival (PFS) and overall survival (OS) on patients with solid tumors treated with ICIs. We present the PFS, OS and tumor specific survival (TSS) for pts with metastatic solid tumors treated with ICIs at an academic cancer center. **Methods:** 848 pts with metastatic solid tumors diagnosed between 2014 through January 2026 were identified via retrospective chart review. PFS was defined as the time from starting ICIs to progression or death, OS was defined as the time from starting ICIs to death and TSS was defined as the time from starting ICIs to death from malignancy (when available). The corticosteroid (CS) exposure was defined as low if prednisone (or equivalent) $< 1\text{mg/kg/day}$ and/or length of exposure $< / = 21$ days. The CS exposure was defined as high if prednisone (or equivalent) was $> / = 1\text{mg/kg/day}$ and/or length of exposure $> / = 22$ days. The CS exposure was defined as very high if prednisone (or equivalent) $> 20\text{mg/day}$ and length of exposure was > 42 days. Steroid sparing agents were considered low impact if given once and within 14 days of starting CS. Steroid sparing agents were considered high impact if given more than once. Steroid sparing agents were considered very high impact if given more than once and/or given after 14 days of starting CS. Acute irAE was defined if symptom and immunosuppression resolved within 42 days. Chronic irAE was defined if symptom and/or immunosuppression continued beyond 42 days. The effects of CS, steroid sparing agent exposure on PFS, OS, TSS were evaluated using multivariable Cox proportional hazards models. The effect of acute irAE versus chronic irAE on PFS, OS, TSS were evaluated using multivariable Cox proportional hazards models. **Results:** 64.8% of patients experienced an irAE and 44.7% of patients developed G3-4 irAE requiring corticosteroids +/- steroid sparing agent. The low impact corticosteroid exposure did not affect PFS, OS or tumor specific survival. The very high impact CS exposure was associated with decrease in PFS ($p = 0.02$) but not with OS or TSS ($p = 0.3$). The high impact steroid sparing agent was associated with decrease in PFS (not significant) but the very high impact steroid sparing agent was associated with decrease in PFS. The chronic irAE was associated with slight improvement in PFS (not significant). **Conclusions:** The presence of an irAE was not significantly associated with PFS, OS or tumor specific survival treated with ICIs. There was a negative impact on the length of corticosteroid exposure and steroid sparing agents on PFS, TSS. The delay or interruption in treatment due to irAE did not affect survival. Research Sponsor: None.

Supporting treatment resilience with optimized nutrition and guided exercise (STRONGER) in head and neck cancer patients undergoing chemoradiation.

Anton Jose Agana, Madeline R. Hardacre, Katharine Thomas; University of Nevada, Reno School of Medicine, Reno, NV; Renown Health, Reno, NV; Renown Regional Medical Center, Reno, NV

Background: Patients with head and neck cancer (HNC) undergoing concurrent chemoradiation (chemoRT) frequently experience debilitating toxicities, including mucositis, dysphagia, fatigue, and anorexia. These treatment-related effects are associated with weight loss, sarcopenia, and functional decline, which may adversely impact treatment adherence and quality of life. Although patients commonly seek lifestyle-based supportive interventions, evidence-based, structured multimodal programs integrated during active chemoradiation remain limited. The STRONGER pilot study was designed to evaluate the feasibility and acceptability of an integrated nutrition, guided exercise, and wellness education intervention aimed at supporting treatment resilience and characterizing functional and body composition changes in this population. **Methods:** STRONGER is a single-arm pilot study enrolling up to 30 adult patients with biopsy-confirmed squamous cell carcinoma of the head and neck undergoing definitive or adjuvant chemoRT at Renown Health and the William N. Pennington Institute for Cancer. Eligible participants have an ECOG performance status of 0 to 2 and are able to participate in light-to-moderate physical activity. Patients with severe malnutrition, defined by Global Leadership Initiative on Malnutrition criteria and greater than 90% caloric intake via enteral feeding, or with comorbidities precluding safe exercise participation, are excluded. The 20-week multimodal intervention begins at pre-treatment baseline and continues through three months post-chemoRT, incorporating individualized nutrition counseling with calorie and protein targets informed by indirect calorimetry, twice-weekly virtual home-based resistance and mobility training with prescribed daily walking goals, and structured wellness programming, including facilitated group sessions focused on stress and fatigue management and a speech-language pathology education series. The primary objective is to assess feasibility and acceptability, defined by prespecified thresholds for recruitment, retention, and intervention adherence, as well as participant-reported acceptability measured using Likert-scaled surveys. Secondary exploratory outcomes include measures of body composition, physical function, and patient-reported quality of life and symptom burden assessed using validated instruments. Descriptive statistics and exploratory paired analyses will be used to characterize within-participant changes over time. Enrollment is ongoing. As of January 24, 2026, 2 of 30 planned participants have been enrolled. Clinical trial information: NCT07160296. Research Sponsor: Renown Health Foundation.

Hetrombopag in patients with chemotherapy-induced thrombocytopenia: A global phase 3, randomized, double-blind study.

Jodi Victoria Mones, Florian Scotté, Philip Choi, Liwei Wang, Bo H. Chao, Junye Xiong, Hanny Al-Samkari; Department of Medicine, Hematology Service, Memorial Sloan Kettering Cancer Center, New York, NY; Département Interdisciplinaire d'Organisation des Parcours Patients (DIOPP), Institut Gustave-Roussy, Villejuif, France; Haematology Department, Canberra Hospital, Canberra, Australia; State Key Laboratory of Oncogenes and Related Genes, Shanghai Cancer Institute, Department of Oncology, Renji Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai, China; Jiangsu Hengrui Pharmaceuticals Co., Ltd., New York, NY; Jiangsu Hengrui Pharmaceuticals Co., Ltd., Shanghai, China; Division of Hematology Oncology, Massachusetts General Hospital, Boston, MA

Background: Chemotherapy-induced thrombocytopenia (CIT) is a common complication of cancer therapy, frequently resulting in chemotherapy modifications including dose reduction, delay, or discontinuation. Thrombopoietin receptor agonists (TPO-RAs) represent a therapeutic approach aimed at stimulating platelet production. Given there are limited society-sanctioned therapies, contemporary management converges on platelet transfusions which are limited in global supply or parenteral TPO-RAs which are inconvenient. Hetrombopag is an oral TPO-RA that supports platelet counts and facilitates chemotherapy delivery, as evidenced by a prior positive randomized, controlled study conducted in China (ASH 2025; NCT05864014). This global phase 3 study is designed to evaluate the efficacy and safety of hetrombopag in patients with CIT (NCT07286032). **Methods:** This study comprises two sequential parts: an open-label, single-arm, pharmacokinetic (PK) lead-in part (A) and a randomized, double-blind, placebo-controlled part (B). In Part A, approximately 8–12 non-Asian patients with CIT are planned to be enrolled to receive oral hetrombopag (15.0 mg once daily, fasted) to evaluate the PK profile. Part B will enroll approximately 138 patients with solid tumors who have experienced a ≥ 7 -day chemotherapy delay due to CIT during platinum- and/or gemcitabine-based therapy at schedule of 21-day cycles. Eligible patients will be randomized in 2:1 to hetrombopag or placebo, stratified by baseline platelet count (PC; $\geq 50 \times 10^9/L$ vs. $< 50 \times 10^9/L$) and enrollment region (Asia vs. rest of world). Hetrombopag will be initiated at 7.5- or 15 mg (dose will be finalized after considering results from Part A) once daily, with dose adjustments based on platelet counts. All enrolled patients are expected, per investigator assessment, to be eligible to complete two consecutive cycles of on-study chemotherapy (C1 and C2) of the same regimen administered prior to enrollment. Initiation of each chemotherapy cycle requires a PC $\geq 100 \times 10^9/L$; if the PC remains $< 100 \times 10^9/L$ on day 14 after hetrombopag initiation (for C1) or at the C1D21 visit (for C2), the investigator may exercise discretion to proceed with the respective chemotherapy cycle and/or implement rescue therapy (platelet transfusions and/or approved TPO-RAs). The primary endpoint of Part A is the PK profile of hetrombopag in non-Asian patients with CIT; the primary endpoint of Part B is the proportion of treatment responders, defined as patients who achieve a PC $\geq 100 \times 10^9/L$ within 14 days of hetrombopag initiation and who complete two consecutive chemotherapy cycles without either thrombocytopenia-related modifications, or thrombocytopenia rescue therapy through C2D21. Clinical trial information: NCT07286032. Research Sponsor: Jiangsu Hengrui Pharmaceuticals.

A randomized, double-blind, placebo-controlled trial of antiviral prophylaxis and oral *Herpesviridae* dynamics during radiotherapy for head and neck cancer.

Renata Ferrari, Wanessa Miranda Silva, Daniele Araujo, Lourenço Siqueira, Clara Lopes, Leticia Araujo, Luana Abreu, Tauana Fernandes, Ana Carolina Guimaraes, Pedro Marinho, Aline Lauda Chaves, Marcus Castilho, Stella Sala, Bruna Bonaccorsi, Rodrigo Dienstmann, Vanessa Salete de Paula, Carlos Gil Moreira Ferreira, Bruno Lemos Ferrari, Cristiane Decat Bergerot, Eduardo Fregnani; Hospital Sirio Libanes, Sao Paulo, Brazil; Hospital Sirio Libanes, São Paulo, Brazil; Oncoclinicas&Co - Medica Scientia Innovation Research (MEDSIR), São Paulo, Brazil; Oncoclinicas & Co - Medica Scientia Innovation Research (MEDSIR), São Paulo, Brazil; Fundação Oswaldo Cruz, Rio De Janeiro, Brazil; Fundação Oswaldo Cruz, Rio De Janeiro, Brazil; Oc Precision Medicine, São Paulo, Brazil; Oncobio, Nova Lima, Brazil; Oncoclinicas & Co.-Medica Scientia Innovation Research (MedSir), São Paulo, Brazil; Oncoclinicas&Co/MedSir, Rio De Janeiro, RJ, Brazil; Oncoclinicas&Co - Medica Scientia Innovation Research (MEDSIR), Sao Paulo, Brazil

Background: Oral mucositis (OM) is a frequent and debilitating toxicity of radiotherapy (RT) for head and neck cancer (HNC), often leading to pain, nutritional compromise, and treatment interruptions. Reactivation of viruses from the *Herpesviridae* family has been proposed as a potential contributor to the pathogenesis and severity of OM, but prospective, controlled data remain limited. Antiviral prophylaxis is not standard of care in this setting, and its role in preventing viral reactivation and modulating OM severity during RT has not been systematically evaluated. This randomized trial investigates the association between oral *Herpesviridae* detection, antiviral prophylaxis, and OM development in patients undergoing RT for HNC. **Methods:** This is a prospective, randomized, double-blind, placebo-controlled phase II trial conducted across four oncology centers in Brazil. Adult patients (≥ 18 years) with HNC undergoing intensity-modulated radiotherapy (IMRT), with or without concurrent systemic therapy, are randomized 1:1 to receive antiviral prophylaxis or placebo. Randomization is stratified by age (< 60 vs ≥ 60 years) and anatomic tumor site (oral cavity/salivary glands; oropharynx/pharynx; nasopharynx/paranasal sinuses). The investigational intervention consists of oral antiviral prophylaxis administered once weekly throughout the course of RT; the control arm receives a matching placebo. Comprehensive dental evaluation and oral care optimization are performed prior to RT initiation in all patients. Serial oral mucosal and saliva samples are collected weekly during RT and after treatment completion. Quantitative real-time PCR is used to detect and quantify viruses from the *Herpesviridae* family, including HSV-1, HSV-2, VZV, EBV, CMV, HHV-6A/B, HHV-7, and HHV-8. Clinical assessments include OM incidence, severity graded by CTCAE criteria, pain intensity, and timing of OM onset and resolution. Correlative analyses will explore temporal associations between viral detection, viral load, antiviral prophylaxis, and OM outcomes. The planned sample size is 84 patients (42 per arm), providing adequate power to detect differences in viral manifestation and OM-related outcomes. Clinical trial information: NCT07363031. Research Sponsor: None.

Symptom monitoring program linked to electronic referrals (SyMPLER): A single-arm pilot feasibility study of remote symptom monitoring with palliative care self-referral.

Julia L. Agne, Jason Benedict, Madison Grogan, Jessica Merlin, Ann Scheck McAlearney, Carolyn J. Presley; The Ohio State University Comprehensive Cancer Center – Arthur G. James Cancer Hospital and Richard J. Solove Research Institute, Columbus, OH; The Ohio State University Center for Biostatistics, Columbus, OH; The Arthur G. James Cancer Hospital and Richard J. Solove Research Institute, The Ohio State University, Columbus, OH; The Ohio State University James Cancer Hospital & Solove Research Institute, Columbus, OH; The Ohio State University College of Medicine, The Center for the Advancement of Team Science, Analytics, and Systems Thinking (CATALYST), Columbus, OH

Background: Symptoms often fluctuate during an individual's cancer trajectory, and this can impact patients' health-related quality of life (HRQOL). Two evidence-based approaches—symptom monitoring programs (SMPs) and specialty palliative care (PC)—have independently been shown to improve HRQOL through identification and treatment of cancer-related symptoms, especially among patients with thoracic cancers (i.e. lung cancer). However, PC remains underutilized when patients report uncontrolled symptoms via SMPs. Therefore, we developed SyMPLER, a digital SMP with an integrated option for PC self-referral. The primary aim of this phase 1 clinical trial is to determine the feasibility of SyMPLER among patients newly diagnosed with a thoracic cancer. If feasible for remote symptom reporting, SyMPLER may overcome logistical and attitudinal barriers towards provider-driven PC referral processes for cancer symptom management. **Methods:** SyMPLER is a prospective single-arm feasibility study of a novel digital health intervention for remote symptom reporting with an optional PC self-referral for cancer symptom management (NCT06396598). SyMPLER includes 5 main components: (1) a brief education about PC, (2) weekly text reminders to encourage symptom logging, (3) on-demand symptom reporting using the Edmonton Symptom Assessment System on a mobile health application interface, (4) an active choice option for PC self-referral, and (5) the ability to request a callback from oncology clinicians to discuss symptom concerns. Per the IRB-approved protocol, adults (> 18 years) with any stage thoracic malignancy, without a prior PC referral, are consented within the first 12 weeks of outpatient oncology care. The primary outcome is frequency of symptom reporting with a feasibility benchmark set at 50% of participants logging symptoms at least monthly over a 6-month intervention period. PC referrals (secondary outcome) and exploratory outcomes, including telephone encounters with the oncology team, HRQOL (Function Assessment of Cancer Therapy – Lung; FACT-L), and patient satisfaction with medical care (FAMCARE-P13) are measured every 3 months for up to 12 months post-enrollment. Study enrollment commenced in February 2024. The target enrollment of 94 evaluable participants was achieved in August 2025. Data collection is ongoing for 23 patients still active on study. Clinical trial information: NCT06396598. Research Sponsor: None.

Structured interventional strategies to prevent and reduce burnout in medical oncologists: The Resilience–Spanish Society of Medical Oncology (SEOM) multi-center project.

Yago Garitaonandia, Sonia Martínez Morante, Luis Leon, Beatriz García Paredes, María Matilde Sánchez del Corral, Berta Obispo, Pilar Lianes, Laura Punti, Alexandra Cortegoso, Eduardo Ceballos, Susana de la Cruz, Esther García Asencio, Ana Isabel Martín Quesada, Rodrigo Sánchez-Bayona, Arturo Lecumberri, Domingo Antonio Sánchez Martínez Sr., CESAR Augusto Rodríguez Sánchez, Javier De Castro, Elena Elez, Vilma Pacheco-Barcia; National Center for Cancer Immune Therapy, Department of Oncology, Copenhagen University Hospital, Herlev, Denmark; Instituto de Neurociencias del Hospital Blua Sanitas Valdebebas, Madrid, Spain; Hospital Clínico Universitario de Santiago Health Research Institute of Santiago de Compostela (IDIS), Santiago, Spain; Hospital Clínico San Carlos, Madrid, Spain; Hospital Universitario de Álava - Txagorritxu, Vitoria, Spain; Department of Medical Oncology, Infanta Leonor University Hospital, Madrid, Spain; Hospital Universitario de Mataró, Barcelona, Spain; Hospital Clínico Universitario de Santiago de Compostela, Madrid, Spain; Hospital San Pedro Alcantara, Cáceres, Spain; Hospital Universitario de Navarra (HUN), Madrid, Spain; Hosp. Universitari i Politecnic La Fe de Valencia, Valencia, Spain; Immuno-oncology Service, Department of Oncology, University Hospital of Lausanne, Lausanne, Switzerland; SOLTI Cancer Research Group, Hospital 12 de Octubre, Madrid, Spain; Hospital Universitario de Navarra (HUN), Navarra, Spain; Hospital Universitario Virgen de la Arrixaca, Murcia, Spain; Hospital Universitario de Salamanca-IBSAL, Salamanca, Spain; Hospital La Paz, Madrid, Spain; Gastrointestinal Cancer Unit, Vall d'Hebron University Hospital, Barcelona, Spain; Head of Medical Oncology, Assistant Professor Universidad Francisco de Vitoria, Hospital Universitario La Luz, Quirónsalud, Madrid, Spain

Background: Burnout is highly prevalent among young medical oncologists, with an estimated incidence exceeding 70% in Europe, and poses a growing threat to physician well-being and quality of care. Early-career oncologists are particularly vulnerable due to high clinical workload, emotional burden, and limited access to structured psychological support. Evidence-based interventions integrated into routine professional activity remain scarce. The Spanish Resilience–SEOM project previously demonstrated that communication skills workshops improved personal achievement and group psychotherapy was feasible to address emotional distress. Building on these findings, this study evaluates a structured, hospital-based structured intervention combining communication skills training and psychotherapy to prevent and mitigate burnout in early-career medical oncologists. **Methods:** This is a prospective, post-authorization, multicenter cohort study including residents and medical oncologists across 7 hospitals in Spain, with a planned follow-up of 6 months. Baseline assessments include demographic data, the Maslach Burnout Inventory (MBI), and the Clance Impostor Phenomenon Scale (CIPS). The intervention consists of eight modules: 1) individual interviews, 2) biopsychosocial model workshop, 3) coregulation workshop, 4) communication skills workshop, 5) individual sessions, 6) vulnerability workshop, and 7–8) emotional regulation workshops. The program combines individualized sessions to activate personal coping resources with six progressive group workshops addressing systemic contributors to burnout, holistic patient perception, professional vulnerability, and practical emotional regulation strategies. Follow-up MBI and CIPS assessments are conducted at program completion and at 6- and 12-month intervals. Current enrollment includes 62 participants across 7 hospitals. Research Sponsor: Fundación SEOM.

Enhancing communication about cancer management and cancer care delivery for older adults with dementia and their care partners.

Molly Wilgucki, Anna Job, Davida Rogers, Emilyn Nguyen, Sofiia Hryniv, Oscar Franco-Rocha, Nancy Dukelow, Kathi Heffner, Jessica Bauer, Jessica Mortimer, Michelle Christine Janelins, Supriya Gupta Mohile, Allison Magnuson; Wilmot Cancer Center, University of Rochester Medical Center, Rochester, NY; University of Rochester, Rochester, NY; University of Rochester, Wilmot Cancer Institute, Rochester, NY; James P. Wilmot Cancer Center, University of Rochester Medical Center, Rochester, NY

Background: Dementia affects 7–10% of older adults with cancer and is associated with worse cancer outcomes. Many patients (pts) have reduced decisional capacity, leading care partners (CPs) to play a major role in cancer management decision-making, which can increase CP burden and negatively affect their well-being. Cancer communication in this population is complex, requiring clinicians to balance pt preferences, CP input, and dementia-related considerations. Despite this, no standard approach exists to support triadic communication in this setting. COACH-Cog is a triadic communication intervention that promotes shared decision-making by integrating CP involvement while centering pt values in cancer care. **Methods:** *Eligibility:* Pts are age ≥ 65 with a diagnosis of dementia and cancer (any type or stage), have an identified CP, and receive oncology care from a participating clinician. CPs are age ≥ 18 and identified by the pt. Oncology clinicians (physicians or advanced practice providers) must practice at the Wilmot Cancer Institute. *Study Design:* This is a pilot cluster-randomized trial (clinician-level randomization). The COACH-Cog intervention includes: 1) a brief clinician training video on dementia and its relevance to cancer care; 2) distribution of pt geriatric assessment results with care recommendations to clinicians, pts, and CPs; and (3) CP communication coaching to elicit dementia-related concerns and develop questions for the next oncology visit. Baseline measures include pt geriatric assessment and dementia severity, CP well-being (burden, quality of life, depression, anxiety), and pt/CP communication and decision-making preferences. Pts and CPs receive either COACH-Cog or usual care based on clinician randomization. The subsequent clinical encounter is audio-recorded. *Outcome Measures:* The primary outcome is CP autonomy support, which evaluates how supported CPs feel in the decision-making process. Secondary outcomes include healthcare communication and CP well-being. Tertiary outcomes assess goal-concordant care and decisional regret. Exploratory outcomes evaluate communication impact by integrating qualitative clinical encounter data with quantitative measures. Current enrollment includes 36 clinicians and 36 pt/CP dyads (target 40 clinicians, 130 dyads). Accrual initiated April 2025. Data collection will conclude May 2027 (NCT06313853; NIA R01 AG077053). *Novel/Innovative aspects:* (1) This is the first study to prospectively enroll patients with dementia in an oncology intervention trial; (2) We are evaluation of a novel triadic communication intervention targeting clinicians, pts, and CPs; and (3) We have incorporated standard procedures for assessing consent capacity and engaging Legally Authorized Representatives for pts lacking capacity given enrollment of pts with dementia. Clinical trial information: NCT06313853. Research Sponsor: National Institute of Health/National Institute on Aging; R01 AG077053.

RISE trial: A novel virtually delivered supervised exercise intervention targeting cognitive impairment and gut microbiome in adolescent and young adult (AYA) brain tumor survivors.

Elizabeth Pan, Maria Chang Swartz, Keri L. Schadler, Tricia Z. King, Avery Giffen, Ashley Rajan, Caitlin I. Webster, Theresa Honey, Alison Vargo, Jenny E. Blevins, Emma Chow, Emily LaVoy, Nathan Parker, Shiao-Pei S. Weathers, Lindsay Smegal, Tobey J. MacDonald, Jinbing Bai; Duke University, School of Medicine, Durham, NC; The University of Texas Medical Branch, Nutrition Sciences & Health Behavior Department, Galveston, TX; The University of Texas MD Anderson Cancer Center, Houston, TX; Emory University School of Nursing, Atlanta, GA; Emory University, School of Nursing, Atlanta, GA; Department of Pediatrics Research, The University of Texas MD Anderson Cancer Center, Houston, TX; Emory University, Atlanta, GA; The University of Texas Medical Branch, School of Physical Therapy, Galveston, TX; The University of Texas Medical Branch, Department of Physical Therapy and Rehabilitation Sciences, Galveston, TX; University of Houston, Houston, TX; H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL; Department of Neuro-Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX; Georgia State University, Department of Clinical Neuropsychology, Atlanta, GA; Nell Hodgson Woodruff School of Nursing, Emory University, Atlanta, GA

Background: Up to 45% of AYA brain tumor survivors experience cancer-related cognitive impairment (CRCI) affecting processing speed, attention, working memory, and executive function—domains critically impacting quality of life (QOL). Moderate-intensity exercise can improve cognitive function by enhancing gut microbiome composition and function. However, only 50% of AYA cancer survivors receive any exercise information from medical providers, with 42% actually meeting physical activity recommendations. Considering developmental milestones and the unique needs of AYA brain tumor survivors, tailoring virtually delivered exercise interventions paired with behavioral coaching and supportive care navigation to promote the adoption of a physically active lifestyle may be a promising approach to reducing CRCI through modulation of gut microbiome health. Few randomized controlled trials (RCTs) have examined this type of exercise intervention for AYA brain tumor survivors. Additionally, the influence of the gut microbiome on the relationship between exercise and cognitive function in AYA brain tumor survivors has not yet been studied. To address these gaps, we developed the Remote Implementation of Supervised Exercise (RISE) intervention, a 12-week personalized aerobic and strength training exercise intervention with behavior coaching and supportive care navigation. The RISE trial aims to evaluate feasibility (primary), cognitive and physical activity (secondary), and gut microbial composition changes (exploratory). **Methods:** RISE is a two-arm 1:1 pilot RCT (NCT06799481) of 40 AYA brain tumor survivors (aged 18–39) with CRCI enrolled at Emory University and MD Anderson Cancer Center. Controls receive an activity tracker and 18 wellness calls from a trainer inquiring about adverse events and survivorship topics. Intervention participants participate in 18 virtual exercise sessions with an exercise coach, consisting of progressive aerobic and strength training exercises with active lifestyle behavior coaching. Intervention participants also receive an activity tracker and participate in self-led exercise sessions via the Physitrack telehealth app for 12 weeks. Assessments at baseline, 6, 12, and 18 weeks measure cognitive function, physical activity levels, gut microbiome, physical function, diet, and QOL. Descriptive analysis will be used to assess feasibility, defined as enrollment of 50% eligible AYAs, 75% adherence to intervention, and 80% retention at the end of the 12-week intervention. As of January 2026, 17 of 40 patients have been enrolled, and accrual is expected to be complete within 1 year. Clinical trial information: NCT06799481. Research Sponsor: NRG Oncology Foundation.

Targeting cellular senescence to enhance skeletal muscle recovery in survivors of breast cancer: An ancillary study of the phase II randomized PROFFi clinical trial.

Jingran Ji, Yuliya Zektser, Marla Lipsyc-Sharf, Alexis Ann LeVee, Rena Desai Callahan, Aashini Master, Kelly Elizabeth McCann, Juan M. Alcantar, Maurice J. Berkowitz, Karo K. Arzoo, Julie Huynh, Lauren Eisenbud, Aditya Bardia, Nicolaos Jay Palaskas, Nicholas Patrick McAndrew, Nikita V. Baclig, Samuel Jacob Margolis, Arman Niknafs, Miriam Silliman, Mina S. Sedrak; UCLA Health Jonsson Comprehensive Cancer Center, Los Angeles, CA; UCLA Jonsson Comprehensive Cancer Center, Los Angeles, CA; UCLA Department of Medicine, Los Angeles, CA

Background: Postmenopausal survivors of breast cancer frequently experience persistent physical function decline after chemotherapy. A key contributor is skeletal muscle dysfunction, leading to weakness, fatigue, and reduced physical activity. One potentially targetable mechanism of chemotherapy-induced skeletal muscle dysfunction is cellular senescence. Senescence is a state of terminal growth arrest that leads to a senescence-associated secretory phenotype marked by the secretion of pro-inflammatory cytokines. These cytokines worsen muscle dysfunction by impairing calcium handling and muscle fiber contractility. Emerging evidence suggests senolytics and exercise may reduce senescent cell (SnC) burden. Senolytics are agents that selectively eliminate SnCs and can improve physical function in non-cancer populations. Exercise not only enhances physical function but also reduces blood markers of senescence. Preclinical studies demonstrate a synergistic effect of senolytics and exercise on SnC reduction. However, no human studies have examined the independent or combined effects of senolytics and exercise on skeletal muscle function and senescence in cancer survivors. We hypothesize that fisetin plus exercise will produce independent and synergistic effects that enhance skeletal muscle recovery in survivors of breast cancer. **Methods:** This site-specific ancillary mechanistic study at UCLA is embedded within PROFFi (Prevention of Frailty with Fisetin), an ongoing phase II multicenter, randomized, placebo-controlled clinical trial evaluating fisetin and exercise in postmenopausal survivors of breast cancer. Eligible participants are within 12 months of completing neo/adjuvant chemotherapy and have reduced physical function as measured by a 6-minute walk distance of 400–480 meters. PROFFi uses a 2x2 factorial design, randomizing 200 participants 1:1:1:1 to exercise plus fisetin, exercise alone, fisetin alone, or placebo for 16 weeks. Fisetin is administered orally at 20mg/kg/day on days 1–3 every 14 days. Exercise is individually tailored and remotely supervised by an exercise physiologist and includes aerobic and resistance exercises. The ancillary study will enroll 84 of the 200 participants (21 per arm) to undergo additional muscle-specific assessments including Biodex strength testing, thigh magnetic resonance imaging (MRI), and vastus lateralis muscle biopsies. The primary objectives of the ancillary study are to evaluate the effects of fisetin and/or exercise on muscle strength (Biodex peak torque), muscle volume (on MRI), and muscle mitochondrial function (oxidative phosphorylation capacity). Secondary objectives include assessing changes in blood and muscle-specific markers of senescence from baseline to end of study. Enrollment to this study began July 2024 and is ongoing (NCT06113016). Clinical trial information: NCT06113016. Research Sponsor: U.S. National Institutes of Health; R01 CA280088; The Breast Cancer Research Foundation; Rising Tide Foundation for Clinical Cancer Research.

Exercise therapy in survivors of gastroesophageal cancer: A phase I, randomized dose-finding study of an individually tailored, remotely supervised exercise intervention.

Jingran Ji, Lee Jones, Sabina Lee, Chaiyaporn Charles Vatanatham, Yuliya Zektser, Nikita V. Baclig, Arman Niknafs, Samuel Jacob Margolis, Sunha Park, Claire Smith, Miriam Silliman, Catherine Lee, Saiya Smith, Karo K. Arzoo, Maurice J. Berkowitz, Mina S. Sedrak; UCLA Health Jonsson Comprehensive Cancer Center, Los Angeles, CA; City of Hope Beckman Research Institute, Duarte, CA; UCLA Department of Medicine, Los Angeles, CA

Background: Advances in perioperative systemic therapy and surgery have extended survival for patients with locoregional gastroesophageal cancer (GEC). However, intensive multimodality treatment often causes substantial physical function decline, leading to loss of independence and poor quality of life. No evidence-based interventions are currently approved to prevent or reverse this decline. Although exercise can improve fatigue, quality of life, and functional outcomes in other malignancies, it remains poorly studied in survivors of GEC. In patients with colon cancer, exercise after treatment is feasible, improves quality of life, and alleviates anxiety and depression. More recently, the CHALLENGE randomized trial demonstrated that a structured, in-person, supervised exercise intervention after chemotherapy for early-stage colon cancer can improve physical function, decrease cancer recurrence, and increase survival versus health education alone. However, the in-person exercise intervention was limited by low adherence and lack of exercise dose optimization, with only one target dose tested. These findings may not generalize to survivors of GEC, where treatment is more intensive and surgery more morbid. In this patient population, we hypothesize that aerobic exercise up to 225 minutes per week will be feasible, but higher doses will lead to lower levels of relative exercise dose intensity (REDI), defined as the ratio of completed to prescribed exercise dose over the course of the intervention. **Methods:** This phase I, randomized dose-finding study will enroll 24 adults (age ≥ 18 years) with stage I-III GEC who completed perioperative systemic therapy within 12 months and are sedentary (< 30 minutes/week of moderate-to-vigorous physical activity). Participants will be randomized 1:1:1 to one of three individually tailored, remotely supervised aerobic programs led by an exercise physiologist. Each 16-week program will target either 75 minutes (25 minutes, 3x/week), 140 minutes (35 minutes, 4x/week), or 225 minutes (45 minutes, 5x/week) of moderate-intensity exercise. Demographic and disease/treatment data will be collected at enrollment. Assessments at baseline and post-intervention include measures of cardiorespiratory fitness (submaximal exercise test), other measures of physical, cognitive, and psychological function, and quality of life. Heart rate, body weight/composition, and step count will be measured throughout using remote monitoring devices. The primary outcome is feasibility, as measured by the REDI. An exercise dose will be considered feasible if $> 60\%$ of the participants ($\geq 5/8$ per arm) achieve a REDI of $> 75\%$. Secondary outcomes include changes in cardiorespiratory fitness and other functional and quality of life measures. This study has been IRB approved and is ongoing (NCI202600630). Clinical trial information: NCI202600630. Research Sponsor: U.S. National Institutes of Health; R03 AG095803; Jonsson Comprehensive Cancer Center Seed Grant.

MPOWER: A pilot trial among men with prostate cancer—Optimizing wellness by enhanced relief from hot flashes with acupuncture.

Jeanny B. Aragon-Ching, Mustafa Abugideiri, Joshua Allen, Rahul Bashyal, Stephanie Calvert, Sabrina Frazier, Daniel Kim, Grace Lee, Karen Lopez-Jovel, Laura Meili Linville, Elahe Mollapour, Tuyetson Nguyen, Natasha Raja, Inger Rosner, Karen Sachse, Reid W. Saunders, Natasha Toussaint, Helina Williams, Eun-mi Yu, Melissa Farmer Miller; Inova Schar Cancer Institute, Fairfax, VA; Inova Schar Cancer, Fairfax, VA; Inova Health System, Fairfax, VA; Inova Alexandria Hospital, Alexandria, VA; Inova Schar Cancer, Peterson Life with Cancer, Fairfax, VA

Background: Prostate cancer is the most commonly diagnosed cancer among men, and advanced disease often requires androgen deprivation therapy (ADT). ADT is associated with distressing side-effects, including hot flashes, sleep disturbance, fatigue, and cognitive symptoms. Acupuncture is a nonpharmacologic intervention shown to reduce hot flashes in other hormone-treated cancers, such as breast cancer; however, standardized acupuncture protocols for men receiving ADT are lacking. The primary objective of the MPOWER trial (NCT07335224) is to evaluate the feasibility and acceptability of study procedures, recruitment strategies, and delivery of a standardized acupuncture protocol to reduce hot flashes in men with prostate cancer. Feasibility will be assessed through enrollment and intervention engagement, and acceptability through satisfaction ratings and post-intervention qualitative feedback. Secondary objectives include patient-reported hot flash frequency and severity, hot flash interference, endocrine symptoms, sleep disturbance, and health-related quality of life. **Methods:** This randomized study compares Immediate Start Acupuncture (IA) with an Active Comparator: Delayed-Start Acupuncture (DA), allowing all participants eventual access to the intervention, among 24 men treated with ADT and/or androgen receptor pathway inhibitors. The intervention consists of a standardized 10-week protocol with weekly 30-minute manual acupuncture sessions delivered by a certified acupuncturist with oncology expertise. All participants receive lifestyle education from a nurse navigator as part of usual care. Participants randomized to the IA arm receive the acupuncture protocol during the initial 10-week intervention period, followed by 12 weeks of follow-up without acupuncture. Participants randomized to the active comparator DA arm will receive lifestyle education per usual care without acupuncture during the initial 10-week comparison period, with bi-weekly check-ins serving as an attention control, and then initiate the acupuncture protocol after the delay period. Study assessments integrate real-time patient-reported hot flash diaries collected via a secure mobile application for remote symptom monitoring (Locus Health), validated patient-reported outcome measures, and continuous Fitbit monitoring to capture physiologic and sleep metrics, including heart rate variability, sleep duration, and nighttime awakenings. Feasibility outcomes include enrollment rates and intervention engagement. Acceptability is assessed quantitatively at multiple time points and qualitatively through semi-structured interviews. The primary patient outcome is the Hot Flash Severity Score, calculated as weekly mean hot flash frequency multiplied by severity. Enrollment began in January 2026, with accrual expected within 12 months. Clinical trial information: NCT07335224. Research Sponsor: Inova Seed Grant.

SWIVEL: A randomized phase II trial of switching medications versus guideline-directed interventions for adjuvant aromatase inhibitor side effects in breast cancer patients.

Elaine Patricia Kuhn, Isabella Marchal, Tonya MacLean, Rebecca E. Dabrowski, Mary D. Chamberlin, Linda T. Vahdat; Dartmouth-Hitchcock Medical Center, Lebanon, NH; Dartmouth-Geisel School of Medicine, Hanover, NH; Dartmouth Hitchcock Medical Center, Lebanon, NH; Dartmouth Cancer Center, Lebanon, NH

Background: Approximately half of breast cancer patients do not complete the standard 5-year course of adjuvant hormone therapy due to side effects, a finding associated with increased recurrence rates and breast cancer-specific mortality. In clinical practice, side effects are commonly addressed by switching to an alternative hormone therapy; however, this strategy has not been prospectively evaluated. In prior retrospective work, adherence was significantly lower among patients who switched therapies compared with those who remained on the same therapy and received treatment for side effects (62% vs 91%, $p=0.013$); however, interpretation is limited by the retrospective design. Therefore, a prospective randomized clinical trial was initiated to address this evidence gap by directly comparing medication switching with guideline-directed symptom management. **Methods:** SWIVEL is an ongoing phase II randomized trial comparing medication switching with guideline-directed interventions for the management of aromatase inhibitor side effects. Eligible patients are postmenopausal women or men with stage I–III ER-positive/HER2-negative breast cancer who are planning to initiate aromatase inhibitor monotherapy in the adjuvant setting. Upon enrollment, participants will be screened every 4 weeks with a validated single-item questionnaire (FACIT/GP5). Those who respond that they are ‘quite a bit’ or ‘very much’ bothered by side effects of treatment will be randomized to either (1) switch to a different hormone therapy, which may include an alternative aromatase inhibitor or tamoxifen, or (2) initiate an evidence-based intervention for side effects in accordance with NCCN guidelines and patient-provider preference. Participants may crossover between strategies at any time. The primary outcome is change in patient-reported symptom burden at 3 months following randomization or at crossover, whichever occurs first, measured by the FACT-ES survey. Secondary outcomes include patient-reported symptom burden at 6 months assessed in an intention-to-treat analysis using FACT-ES and PROMIS measures, and medication adherence assessed at 3, 6, 12, and 24 months using a multi-modal approach incorporating validated patient-reported measures (VOILS), pharmacy records, and urine testing for drug metabolites. Additional outcomes include patient-reported quality of life (FACT-G) and sexual function (FSFI), factors associated with adherence including access to care among rural communities, and evaluation of a novel screening tool to identify patients at higher risk for non-adherence. The study is open at Dartmouth Health and has enrolled 7 of 200 planned participants (NCT# 07071038). Clinical trial information: RCT07071038. Research Sponsor: Dartmouth Cancer Center.

A late-phase randomized open-label multi-cohort trial to evaluate immune-related adverse events with different standard-of-care dosing strategies of standard-of-care immunotherapies: ImmuRAD trial.

Anup Kasi, Anusha Chidharla, Raed Moh'd Taiseer Al-Rajabi, Shannon Bradbury, Milind A. Phadnis, Lauren Clark, Chao Hui Huang, Gary C. Doolittle, Prakash C. Neupane, Nina S. Mathew, Elizabeth Wulff, Haoran Li, Saqib Abbasi, Joaquina Celebre Baranda, Weijing Sun, Rahul Atul Parikh; University of Kansas Cancer Center, Kansas City, KS; University of Kansas Cancer Center, Westwood, KS; Department of Biostatistics & Data Science, University of Kansas Medical Center, Kansas City, KS; University of Kansas Medical Center (KUMC), Kansas City, KS; University of Kansas Medical Center, Westwood, KS; The University of Kansas Cancer Center, Shawnee Mission, KS; University of Kansas Medical Center, Department of Internal Medicine, Kansas City, KS; Department of Medical Oncology, University of Kansas Cancer Center, Westwood, KS

Background: Programmed cell death-1 (PD-1) inhibitors, such as nivolumab and pembrolizumab, are widely used in treating solid tumors. These inhibitors have multiple FDA-approved dosing schedules. Extended-interval, higher-dose regimens offer patient convenience and health-system efficiencies. However, there is limited comparative prospective data evaluating immune-related adverse events (irAEs) across different dosing strategies. Our study aims to evaluate this important safety question in routine clinical practice. **Methods:** ImmuRAD is an investigator-initiated, open-label, randomized late phase trial. Adults (≥ 18 years) with histologically or cytologically confirmed solid tumor malignancies who are scheduled to receive standard-of-care PD-1 inhibitor-based therapy in any disease setting or line of therapy are eligible for the study. Participants are randomly assigned to one of two pre-defined standard dosing strategies based on their physician-selected PD-1 inhibitor cohort. In the nivolumab cohort, patients are randomized 1:1 to receive nivolumab 240 mg every 2 weeks or nivolumab 480 mg every 4 weeks. In the pembrolizumab cohort, patients are randomized 1:1 to receive pembrolizumab 200 mg every 3 weeks or pembrolizumab 400 mg every 6 weeks. Route of administration is at the discretion of the investigator and can be given intravenous or subcutaneous. After completing 12 weeks of therapy, patients meeting predefined treatment-tolerance criteria may transition to extended-interval dosing at the discretion of the treating investigator. The primary objective is to determine the proportion of patients experiencing grade ≥ 3 immune-related adverse events (CTCAE v5.0) in each dosing arm within each cohort. Secondary endpoints include the incidence of all-grade immune-related adverse events, the time to resolution of these adverse events, treatment discontinuation due to immune-related adverse events, the overall response rate (for patients with measurable disease), progression-free or disease-free survival, and overall survival. Exploratory analyses will investigate the associations between immune-related adverse events and factors such as tumor type, treatment setting, microsatellite instability status, tumor mutational burden, and NGS biomarker profiles. The planned sample size is 192 evaluable patients (96 per cohort and 48 per arm). The study will enroll patients over a period of 24 months and will have a follow-up period of up to 2 years. In this IRB approved clinical trial, safety oversight will be provided by the institutional Data Safety Monitoring Committee. Trial Status: The study is actively enrolling at The University of Kansas Cancer Center and affiliated network sites. Clinical trial information: NCT07174453. Research Sponsor: Kansas University IIT Steering Committee.

Interrupting sedentary time to improve cardiometabolic health and toxicity in patients with lymphoma receiving chemotherapy: The iSTAND trial.

Rebekah Wilson, Samantha Sterghos, James Cannon, Noah Chigier, Mary Norris, Indy Robles, Oreofe Olukemi Odejide, Britni Belcher, Christina Marie Dieli-Conwright, Dana-Farber Cancer Institute, Boston, MA; University of Southern California, Los Angeles, CA

Background: Among lymphoma patients treated with steroids, hyperglycemia is a common side effect. Episodes of hyperglycemia increase the likelihood of chemotherapy alterations, infection risk, and decreased overall survival. Interrupting sedentary time (IST) helps manage glycemic control in the diabetic population but is understudied among lymphoma patients. Additionally, there is preliminary evidence that IST during a chemotherapy infusion may reduce chemotherapy-related adverse effects. Therefore, we designed the iSTAND study to assess the feasibility of a 12-week IST intervention at home and during chemotherapy infusion appointments, and the preliminary efficacy on said intervention on a) cardiometabolic biomarkers and b) chemotherapy completion and toxicities among lymphoma patients. **Methods:** The iSTAND study is a prospective study aiming to recruit 24 patients diagnosed with lymphoma receiving either R-CHOP or POLA-R-CHP chemotherapy regimens. The first 3 enrolled patients will automatically be assigned to the intervention group to pilot the intervention (pre-pilot group). The remaining 21 patients will be randomly assigned IST intervention (n = 14) or control (n = 7). Five patients have been enrolled thus far (January 2026). The 12-week intervention will include a supervised component completed during chemotherapy infusion appointments and a self-directed home-based component. The in-clinic component will involve 2-minutes of walking every 30-minutes at 65-70% age predicted heart rate maximum, and two lower body resistance exercises every hour (1 set, 5-12 repetitions, 6-7 RPE) repeated for up to 4 hours of the infusion appointment. The home-based component will involve walking 250 steps per hour and alternating two lower and two upper body resistance exercises every hour (6 days/week for 6-12 hours/day). Patients will receive a Fitbit and resistance bands. Additionally, patients will receive daily movement prompts via Fitbit and text messages to encourage and assess adherence. Outcomes will be assessed at baseline prior to the second infusion and post-intervention after the 12-week intervention period. The primary outcome will be feasibility assessed via completion of $\geq 70\%$ of prescribed activities, $\leq 50\%$ rate of refusal, $\geq 70\%$ retention rate, and $\geq 70\%$ acceptance rate via acceptability of intervention questionnaire. Secondary outcomes include glucose levels and insulin assessed via continuous glucose monitor and fasting blood. Exploratory outcomes include quality of life, sleep quality, chemotherapy completion rate, and chemotoxicities assessed via questionnaires and medical records. Clinical trial information: NCT06923397. Research Sponsor: Helen B Gurley Foundation.

WINSHIP 4468-18: Phase II evaluation of the effect of 2- versus 6-hour oxaliplatin infusions on neuropathy and pharmacokinetics in patients with gastrointestinal cancers.

Olumide B. Gbolahan, Amber Draper, Deborah Watkins Bruner, Lindsay Marie Hannan, Sujata Kane, Oluwadunni Eunice Emiloju, Udhayvir Singh Grewal, Jesse Stone Handler, Gideon T. Dosunmu, Olatunji B. Alese, Donald Harvey; Emory University School of Medicine and Winship Cancer Institute, Atlanta, GA; Winship Cancer Institute of Emory University, Atlanta, GA; Emory University Winship Cancer Institute, Atlanta, GA; Emory Clinic, Roswell, GA; Department of Hematology and Oncology, Winship Cancer Institute of Emory University, Atlanta, GA; Emory University School of Medicine, Atlanta, GA; Emory University, Atlanta, GA

Background: Oxaliplatin, a third-generation platinum agent, improves outcomes in gastrointestinal (GI) cancers when combined with fluoropyrimidines. However, it is also associated with clinically significant acute and chronic neurotoxicity. Approximately 33% of patients develop grade 3–4 sensory neuropathy, and up to 11% discontinue therapy due to neuropathy. Acute neurotoxicity is linked to the maximum plasma concentration (C_{max}) of platinum ultrafiltrate, and greater acute sensory neuropathic symptoms predict later chronic neuropathy. Prior data suggest that extending infusion duration from 2 hours to 4–6 hours lowers C_{max} by ~32–50% and reduces recurrence of acute neuropathic symptoms. We hypothesize that a 6-hour oxaliplatin infusion will reduce platinum ultrafiltrate C_{max} and decrease the incidence and severity of chronic sensory neuropathy. **Methods:** WINSHIP 4468-18 is a randomized, open-label phase II trial enrolling a real-world population of patients with gastrointestinal (GI) cancers for whom oxaliplatin-containing combination therapy is indicated. All participants receive IV infusion of oxaliplatin 85 mg/m² every 2 weeks as part of a standard combination regimen. Sixty patients will be randomized 2:1 to 6-hour (n = 40) versus 2-hour (n = 20) oxaliplatin infusion duration. Eligibility includes confirmed GI malignancy, ECOG 0–2, and adequate organ function. Key exclusion criteria are baseline grade ≥2 neuropathy and prior hypersensitivity/intolerance to oxaliplatin. The primary endpoint is the between-arm difference in EORTC Chemotherapy Induced Peripheral Neuropathy (CIPN)₂₀ sensory scores from baseline to cycle 4. Secondary endpoints include comparison of pharmacokinetic parameters, particularly C_{max} of platinum ultrafiltrate. With an assumed 10-point between-group difference in CIPN₂₀ sensory score at cycle 4, 60 patients provide 80% power (two-sided $\alpha = 0.05$). The study is open and accruing (NCT03800693). Clinical trial information: NCT03800693. Research Sponsor: None.