LBA100 **Clinical Science Symposium**

NHS-Galleri: Primary results from a randomised controlled trial to assess the clinical utility of a multi-cancer early detection (MCED) test in population screening.

Robert Charles Swanton, Peter Johnson, Thomas Round, Jane Warwick, Helen Jones, Harpal Kumar, Wei Liang, Rebecca Smittenaar, Richard D. Neal, Peter Sasieni; The Francis Crick Institute and University College London Cancer Institute, London, United Kingdom; School of Cancer Sciences, Southampton, United Kingdom; King's College London, London, United Kingdom; Queen Mary University of London, London, United Kingdom; EMS Healthcare, Cheshire, United Kingdom; GRAIL Bio UK, Ltd., London, United Kingdom; University of Exeter Medical School, Exeter, United Kingdom

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*.

LBA101 **Clinical Science Symposium**

Osimertinib with/without chemotherapy in patients with persistent ctDNA EGFR mutant (EGFRm) NSCLC at 3 weeks after 1L osimertinib: A randomized phase II study (FLAME study).

Zhijie Wang, Jia Zhong, Jianchun Duan, Jie Zhao, Zhehai Wang, Minglei Zhuo, Chengzhi Zhou, Zhenbin Li, Xiangjun Yi, Jianhua Chang, Shi Jin, Di Wu, Qibin Song, Xiaorong Dong, Lixia Ma, Bo Jin, Dongqing Lv, Zhe LIU, Lifeng Wang, Jie Wang; Cancer Hospital Chinese Academy of Medical Sciences (Langfang Section), Langfang, Hebei, China; Cancer Hospital Chinese Academy of Medical Sciences, Beijing, China; Cancer Hospital of Shandong First Medical University, Jinan, China; Department of Thoracic Oncology I, Beijing Cancer Hospital, Beijing, China; The First Affiliated Hospital of Guangzhou Medical University, Guangzhou, China; Jiangxi Provincial Chest Hospital, Nanchang, China; Cancer Hospital Chinese Academy of Medical Sciences, Shenzhen, Shenzhen, China; Cancer Hospital Chinese Academy of Medical Sciences, Shenzhen Center, Shenzhen, Guangdong, China; Shenzhen People's Hospital, Shenzhen, China; Renmin Hospital of Wuhan University, Wuhan, China; Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China; Jilin Cancer Hospital, Changchun, China; The First Hospital of China Medical University, Shenyang, Liaoning, China; Taizhou Hospital of Zhejiang Province, Taizhou, China; Beijing Chest Hospital, Capital Medical University, Beijing, China; Nanjing Drum Tower Hospital, The Affiliated Hospital of Nanjing University Medical School, Nanjing, China; Cancer Hospital, Chinese Academy of Medical Sciences, Beijing, China

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*.

Benefit of adjuvant chemotherapy in resected stage I-IV CRC patients based on ctDNA dynamics across two timepoints: Results from GALAXY study.

Mitsuru Yokota, Hideaki Bando, Yoshiaki Nakamura, Daisuke Kotani, Saori Mishima, Koji Ando, Stephanie A. Sanchez, Kim Magee, Charuta C. Palsuledesai, Robert William Lentz, Adham A. Jurdi, Alexey Aleshin, Hiroya Taniguchi, Jun Watanabe, Takeshi Kato, Yusuke Suwa, Keiji Hirata, Naoya Akazawa, Takayuki Yoshino, Eiji Oki; Department of General Surgery, Kurashiki Central Hospital, Okayama, Japan; Department of Gastroenterology and Gastrointestinal Oncology, National Cancer Center Hospital East, Kashiwa, Japan; Department of Surgery and Science, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan; Natera, Inc., Austin, TX; Department of Clinical Oncology, Aichi Cancer Center Hospital, Nagoya, Japan; Department of Colorectal Surgery, Kansai Medical University, Hirakata, Japan; Department of Surgery, NHO Osaka National Hospital, Osaka, Japan; Department of Surgery, Gastroenterological Center, Yokohama City University Medical Center, Yokohama, Japan; Department of Surgery, School of Medicine, University of Occupational and Environmental Health, Kitakyushu, Japan; Department of Gastroenterological Surgery, Sendai City Medical Center Sendai Open Hospital, Sendai, Japan; Department of Advanced Medicine and Innovative Technology, Kyushu University Hospital, Fukuoka, Japan

Background: In current clinical practice, ACT for stages IIB-III CRC is administered as soon as the patient is medically able, and within 8 weeks post-surgery. However, initiation >8 weeks may be appropriate in some patients. The interim analysis of the CIRCULATE-Japan GALAXY showed that patients with ctDNA-negativity during 2-10 weeks post-surgery do not derive benefit from ACT, although a small subset of these ctDNA-negative patients recurred. In this study, we analyzed early ctDNA dynamics to assess if turning ctDNA-positive at 12 weeks identifies the subgroup of initially (4-weeks post-surgery) ctDNA-negative patients who will benefit from ACT. **Methods:** This analysis included 1,034 patients with stage I-IV CRC undergoing curative-intent surgery from the GALAXY study who were ctDNA-negative at the first timepoint (TP#1; 4 ± 2 weeks post-surgery) and had subsequent ctDNA results available at the second TP (TP#2; 12 ± 2 weeks post-surgery). ctDNA was assessed using a personalized, tumor-informed assay (Signatera, Natera). DFS was assessed between TP#1-negative patients receiving ACT versus observation, stratified by ctDNA dynamics (turned positive at TP#2 or remained negative at both TPs). Analysis was landmarked at the TP#2 (12 weeks ± 2 weeks post-surgery) and Hazard ratios (HRs) were estimated using Cox proportional hazards models. **Results:** Of the 1,034 patients with ctDNA-negativity at TP#1 included in this analysis, 47.8% were females, and 73.8% had colon cancer, whereas 26.2% had rectal cancer. The pathologic stage distribution included: 11% Stage I / Low Risk Stage II, 72% High Risk Stage II / Stage III, and 17% Stage IV. The median patient age was 69 years (range 25-93) and the median follow-up was 33 months. Median time to ACT initiation was 6.7 weeks (range 3-12) post-surgery. Among patients who became positive at TP#2 (N=36), ACT was associated with significantly improved DFS compared with observation (HR 0.3; p=0.0165). Two-year DFS rates were 45.5% in the ACT group and 9.8% in the observation group, with a median DFS of 22 months and 2.5 months, respectively. In contrast, among patients who remained ctDNA-negative at both TPs (N=998), DFS outcomes were favorable regardless of ACT administration (HR 0.8, p=0.1744), with 2-year DFS rates of 87.1% and 84.1%, respectively, and median DFS was not reached in either group. **Conclusions:** A statistically significant and clinically meaningful benefit of ACT in resected stage I-IV CRC patients who were ctDNA-negative at 4 weeks but converted to positive at 12 weeks post-surgery was observed. These results underscore the critical role of both the 4- and 12-week post-surgery time points for risk stratification and indicate that early ctDNA dynamics can identify a subgroup of initially ctDNA-negative patients who may benefit from delayed ACT. Clinical trial information: UMIN000039205. Research Sponsor: Japan Agency for Medical Research and Development: 19ck0106447h0002, 21ck0106711h0001, 21ck0106710h0001, 22lk0201164h0001 and 22lk0201148h0002 National Cancer Center Research and Development Fund; no. 2021-A-6.

Long-term outcomes of ^{18}F-fluoromisonidazole positron emission tomography (FMISO PET)–guided major radiation dose de-escalation in HPV-associated oropharyngeal cancer: The 30 ROC approach.

Nancy Y. Lee, Eric Jeffrey Sherman, Heiko Schöder, Rick Wray, Edward Christopher Dee, Sean Matthew McBride, Yao Yu, Daphna Y. Gelblum, Achraf Shamseddine, Charles Rutter, Noah Kalman, Winston Wong, Lara Dunn, Ian Ganly, Luc Morris, Jennifer R. Cracchiolo, Alan Loh Ho, Richard J. Wong, Nadeem Riaz; Memorial Sloan Kettering Cancer Center, New York, NY; Department of Radiation Oncology, Memorial Sloan Kettering Cancer Center, New York, NY; Hartford Health Care, Hartford, CT; Miami Cancer Institute, Miami, FL

Background: We previously demonstrated favorable short-term outcomes in patients with human papillomavirus–associated oropharyngeal carcinoma (HPV+ OPC) treated with biologically selected major radiation dose de-escalation, guided by functional hypoxia imaging. We now report mature long-term outcomes from a substantially larger prospective cohort to evaluate the durability and long-term safety of this approach. **Methods:** We conducted a prespecified integrated analysis of a series of three consecutive phase II trials, each trial representing a progressive refinement with the same therapeutic strategy, enrolling patients with T0–3/N1–2c HPV+ OPC from 10/1/2015 to 11/30/2023. ^{18}F-fluoromisonidazole positron emission tomography (FMISO PET) assessed intratumoral hypoxia to stratify treatment: patients without hypoxia received de-escalated chemoradiotherapy (CRT) to 30Gy, while those with intra-treatment hypoxia received standard CRT to 70Gy. The primary endpoint was 5-year overall survival (OS); secondary endpoints included local, regional, and distant failure, progression-free survival (PFS), treatment-related toxicities, and patient-reported outcomes (PROs). Time-to-event outcomes were analyzed using Kaplan-Meier method and cumulative incidence function. **Results:** A total of 430 patients were enrolled and received treatment. T, N stages were: T0/TX(51), T1(198), T2(173), T3(8); N1 (62), N2a (48), N2b (252), and N2c (68). 96 patients (22.3%) had >10 pack-years of smoking history. There were 323 patients (75%) who had no hypoxia on FMISO PET and received 30Gy while 107 patients (25%) had evidence of intra-treatment tumor hypoxia and received 70Gy. With a median follow-up of 4.05 years (range 1.27–10.03 years), the 5-year OS was 97% in both the 30Gy and 70Gy cohorts. All oncologic endpoints were equivalent in the 30Gy vs 70Gy cohorts: 5-year local failure (2.2% vs 1.9%, p=0.7), regional failure (6.2% vs 3.9%, p=0.4), and PFS (91% vs 89%, p=0.5). Notably, patients with intra-treatment hypoxia, who received 70Gy had higher distant failure rates versus those without intra-treatment hypoxia and received 30Gy (7.5% vs 1.3%, p=0.004). Detailed acute/late toxicities and PROs will be presented at the meeting. **Conclusions:** FMISO PET–guided biological and personalized major radiation dose de-escalation results in durable long-term outcomes, benefiting ~75% of the patients. These findings establish a precision-based paradigm for definitive CRT in HPV+ OPC, currently being validated in an on-going randomized phase III trial (NCT06563479, >1/3 randomized). Patients with intra-treatment hypoxia had a higher rate of distant metastasis where additional therapy can be considered in future trials. Clinical trial information: NCT03323463, NCT05491512. Research Sponsor: U.S. National Institutes of Health.

Phase 3, multicenter, randomized, controlled open-label study: Efficacy and safety of M701 (EpCAM×CD3 bispecific antibody) intraperitoneal infusion in advanced epithelial solid tumor with malignant ascites vs paracentesis.

Jianming Xu, Yanqiao Zhang, Rong-Bo Lin, Xinyu Qian, Weijie Zhang, Caigang Liu, Xizhi Zhang, Jun Zhang, Huiqing Zhang, Bihui Li, Shengmian Li, Haiyan Liu, Jun Zhao, Jiayi Li, Linzhi Lu, Meili Sun, Jun Cai, Hanxiang An, Pengfei Zhou, Shaoyi Huang; The First Medical Center, Chinese PLA General Hospital, Beijing, China; Harbin Medical University Cancer Hospital, Harbin, China; Department of Gastrointestinal Oncology, Fujian Cancer Hospital, Fuzhou, China; Department of Medical Oncology, Hangzhou Cancer Hospital, Hangzhou, China; Department of Medical Oncology, The First Affiliated Hospital of Zhengzhou University, Zhengzhou, China; Department of Oncology, Shengjing Hospital of China Medical University, Shenyang, China; Northern Jiangsu People's Hospital, Yangzhou, China; Department of Oncology, The Third People's Hospital of Chengdu, Chengdu, China; Jiangxi Provincial Cancer Hospital, Nanchang, China; The Second Affiliated Hospital of Guilin Medical University, Guilin, China; Department of Gastroenterology, The Fourth Hospital of Hebei Medical University, Shijiazhuang, China; The Second Affiliated Hospital of Shandong First Medical University, Shandong, China; Department of Oncology, Changzhi People's Hospital, The Affiliated Hospital of Changzhi Medical College, Changzhi, China; Department of Oncology, The First Affiliated Hospital of Xiamen University, Xiamen, China; Department of Gastroenterology , Gansu Wuwei Cancer Hospital, Wuwei, China; Department of Oncology, Jinan Central Hospital affiliated to Shandong University, Jinan, China; Department of Oncology, The First Affiliated Hospital of Yangtze University, Jingzhou, China; Shanxi Bethune Hospital, Taiyuan, China; Wuhan YZY Biopharma Co, Ltd., Wuhan, China

Background: Malignant ascites (MA) is a severe complication of advanced epithelial cancers, imposing a heavy symptom burden, compromising systemic therapy efficacy, and correlating with poor survival and impaired quality of life. While only one pharmacologic therapy is approved; guideline-recommended paracentesis provides merely transient symptomatic relief. Consequently, a significant unmet medical need persists for effective therapies that durably control MA. **Methods:** Patients with malignant ascites (MA) secondary to advanced gastric, colorectal, or ovarian cancer after failure of standard anticancer therapy were enrolled. Patients were randomized to Arm T, receiving therapeutic paracentesis plus intraperitoneal M701, or Arm C, receiving paracentesis alone. All patients continued background systemic treatment. The primary endpoint was puncture-free survival (PuFS), defined as the time from Day 18 to the subsequent paracentesis or death. Secondary endpoints included overall survival (OS), time to next paracentesis (TTNP), patient-reported outcomes (PROs) evaluated using the EORTC QLQ-C30 questionnaire and a Likert scale, and safety profiles between the two arms. **Results:** As of January 15, 2026, 312 pts were enrolled (Arm T, n = 206; Arm C, n = 106). Median PuFS was significantly longer in Arm T than in Arm C (87.59 vs 49.96 days; HR = 0.57, 95% CI: 0.42–0.78; p = 0.0003). TTNP was also markedly improved with M701 (186.7 vs 55.1 days; HR = 0.42, 95% CI: 0.29–0.60, p < 0.0001). Overall survival was comparable between arms (p = 0.8407, HR = 0.97, 95% CI: 0.74–1.28). Patient-reported outcomes showed a longer median time to global health status deterioration in Arm T (72.0 vs 39.0 days; HR = 0.73, p = 0.049). A statistically significant between-group difference was observed in the change from baseline in total Likert score at Day 116 (Visit 12) (mean difference −2.45; p = 0.0130), indicating sustained symptom relief with M701. Grade ≥3 treatment-emergent adverse events (TEAEs) occurred in 70.39% of patients in Arm T and 51.89% in Arm C. Serious adverse events (SAEs) occurred in 48.54% and 33.02% of patients in the two arms, respectively. Only one grade 1 cytokine release syndrome (CRS) event was reported in Arm T, and the incidence of CRS-like symptoms (e.g., pyrexia and dyspnea) was very low. **Conclusions:** Intraperitoneal M701 was well tolerated when combined with systemic therapy. In patients with epithelial cancer-associated MA, M701 significantly prolonged puncture-free survival with comparable overall survival. These encouraging findings further support the clinical development of M701 and its potential therapeutic role in the management of malignant ascites. Clinical trial information: NCT06432296. Research Sponsor: Wuhan YZY Biopharma Co. Ltd.

Patient reported outcomes (PRO) during and after multimodal treatment for resectable esophageal adenocarcinoma in the prospective, randomized, controlled, multicenter phase III ESOPEC trial.

Jens Hoeppner, Claudia Schmoor, Florian Lordick, Thomas B. Brunner, Zsolt Madarasz, Julia Michel, Stephan Voegele, Fabian Nimczewski; University of Bielefeld, University Medical Center OWL, Campus Hospital Lippe, Bielefeld, Germany; Clinical Trials Unit, Faculty of Medicine and Medical Center, University of Freiburg, Freiburg, Germany; University of Leipzig Medical Center, Comprehensive Cancer Center Central Germany, Department of Medicine, Leipzig, Germany; Medical University of Graz, Graz, Austria; Bielefeld University, University Medical Center OWL, Campus Hospital Lippe, Detmold, Germany; University of Bielefeld, University Medical Center OWL, Campus Hospital Lippe, Bielefeld, Detmold, Germany

Background: The ESOPEC trial showed that perioperative chemotherapy improved survival compared with preoperative chemoradiotherapy in pts with esophageal adenocarcinoma (EAC). Here we report on PRO which was a key secondary endpoint. **Methods:** Pts with cT1 cN+ cM0 or cT2-4a cNany cM0 EAC were randomized between perioperative chemotherapy with FLOT (5-FU/leucovorin/oxaliplatin/docetaxel) or preoperative chemoradiotherapy with CROSS (41.4Gy/carboplatin/paclitaxel) both plus tumor resection. PRO was measured using the EORTC Quality of Life Questionnaire Core 30 (C30), Oesophageal Cancer Module (OES18) and Chemotherapy-Induced Peripheral Neuropathy Module (CIPN20) at baseline and during treatment and follow-up. The global health status / QOL (GH; C30), physical functioning (PF; C30), fatigue (FA; C30), dyspnoea (DY; C30), eating problems (EP; OES18), and sensory scale (SS; CIPN20) were chosen as primary outcomes. Predefined time points for comparison of PRO between treatment groups were directly before surgery, after discharge from surgery, and 6, 12, 24, and 36 months after start of treatment. Analyses were performed with mixed linear models for repeated measurements. **Results:** Of 438 randomized patients, 401 (197 FLOT, 204 CROSS) were included in the PRO analysis. Differences between The FLOT and CROSS groups are shown in the table. Before, surgery, GH and PF were higher in the FLOT group, while FA, DY, and EP were less pronounced in the FLOT as compared to CROSS group. At discharge from surgery and at follow-up, no significant differences in GH, PF, FA, DY, and EP were measured. Results in SS were worse in FLOT as compared to CROSS at all timepoints. **Conclusions:** Patients treated with FLOT as compared to CROSS reported better PRO results following neoadjuvant therapy and before surgery. In contrast, sensory problems were higher in FLOT versus CROSS over the whole treatment trajectory and follow-up. Clinical trial information: NCT02509286. Research Sponsor: Deutsche Forschungsgemeinschaft.

	Adjusted mean difference in points (FLOT minus CROSS) with 95%-CI and two-sided p-value			
	Preoperatively	**Discharge**	**6 months**	**36 months**
Global health status / QOL*	6.3 (1.1,11.5) p=0.019	0.6 (-4.9,6.1) p=0.83	-4.3 (-9.6,1.0) p=0.11	2.7 (-3.4,8.8) p=0.38
Physical functioning*	7.7 (3.1,12.4) p=0.001	5.3 (-0.6,11.1) p=0.076	-3.1 (-9.0,2.7) p=0.29	2.8 (-3.5,9.1) p=0.39
Fatigue**	-8.6 (-14.2,-3.0) p=0.003	-2.7 (-9.1,3.7) p=0.41	5.2 (-1.5,11.8) p=0.13	-4.8 (-12.3,2.6) p=0.20
Dyspnoea**	-10.9 (-17.1,-4.7) p<0.001	-1.8 (-10.5,6.8) p=0.68	1.5 (-7.5,10.4) p=0.75	0.7 (-8.9,10.2) p=0.89
Eating problems**	-12.7 (-18.9,-6.4) p<0.001	-2.9 (-10.1,4.3) p=0.43	-0.0 (-7.3,7.3) p=1.00	-5.3 (-13.5,3.0) p=0.21
Sensory scale**	14.8 (11.6,18.0) p<0.001	4.8 (1.7,8.0) p=0.003	14.6 (10.7,18.5) p<0.001	7.1 (1.1,13.0) p=0.020

*Higher scores indicate better QOL/function.
**Higher scores indicate more symptoms.

An actionable machine learning–driven clinicogenomic model as a predictor of brain metastasis risk in breast cancer.

Luke Roy George Pike, Anton Safonov, Subhiksha Nandakumar, Deborah Ruth Smith, Lillian A. Boe, Emanuela Ferraro, Tatiana Erazo, Luca Bielo, Kamran A. Ahmed, Kathryn Chen Tsai, Ishaani S. Khatri, Julia Ah-Reum An, Justin Jee, Mark Robson, Adrienne Boire, Nikolaus Schultz, Nelson S. Moss, Walid Khaled Chatila, Pedram Razavi; Memorial Sloan Kettering Cancer Center, New York, NY; Montefiore Einstein Center for Cancer Care, New York, NY; H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL; Carle Illinois College of Medicine, Urbana, IL; New York University Langone, New York City, NY; Breast Medicine Service, Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, NY; Department of Epidemiology and Biostatistics, Memorial Sloan Kettering Cancer Center, New York, NY; Memorial Sloan Kettering Cancer Center, New York City, NY

Background: Brain metastasis (BM) is a frequent site of disease progression for patients living with metastatic breast cancer (MBC). Guidelines do not recommend routine MRI brain surveillance in asymptomatic patients. Consequently, patients with MBC who develop BM often present with extensive disease, leading to lasting neurological damage or death. **Methods:** This study included MBC patients without known BM at presentation who underwent genomic sequencing of a non-BM specimen with MSK-IMPACT, a custom tumor-normal next-generation sequencing assay, within one year of M1 diagnosis. We developed an ensemble time-dependent LASSO machine learning (ML) model with BM-free survival (BMFS) as the primary endpoint, integrating baseline clinical, pathologic, and genomic features for risk stratification, using a cross-validation framework. Benchmarking was conducted using a time-dependent neural network designed to model competing risks (DeepHit), and further validation was performed using an independent clinical trial dataset. **Results:** 1594 MBC patients were divided into a training set (n=1118) and a test set (n=476), with 320 events over a median follow-up of 39.7 months. The ensemble ML model identified distinct clinicogenomic features associated with shorter BMFS, including receptor subtype, ER/PR percent positivity, menopausal status, metastatic burden, metastatic site distribution, disease-free interval, and alterations in *TP53*, *ERBB2*, and *RB1*. The model stratified patients into low-, intermediate-, and high-risk groups (training C-index: 0.690; test C-index: 0.696). In the test cohort, 24-month BMFS was 68%, 89%, and 98% in high, intermediate, and low risk groups (HR 19.2, $p<0.001$ high vs. low risk; HR 6.5, $p<0.001$ intermediate vs. low risk), with model predictions retaining robust predictive ability beyond 24 months (time-dependent AUC at 10 years of 0.79). These results were confirmed using DeepHit, a competing-risk-specific neural network (training C-index 0.71; test C-index 0.61). The model similarly identified high-risk patients within a single-arm phase II clinical trial dataset utilizing MRI screening in patients with MBC. **Conclusions:** We developed an actionable ML-driven clinicogenomic model that accurately identifies MBC patients at high risk of developing BM. Biologically plausible and readily available features defined a high-risk patient category with a >30% risk of developing BM within 2 years and would likely benefit from MRI screening. The results will be prospectively validated in BRAINSTORM (Breast Cancer Radiologic Assessment and Intervention for Neurological Surveillance, Tracking, and Optimized Risk Management), a phase II randomized clinical trial of intensified MRI surveillance versus standard symptom-based screening in high-risk MBC patients. Research Sponsor: National Cancer Institute; (P30-CA008748).

External validation of a MMAI model for prognosis and chemotherapy benefit prediction in postmenopausal, node-positive, hormone receptor–positive breast cancer patients: Analysis of SWOG S8814.

Corey Wayne Speers, Alexander Piehler, Allison Meisner, Jingbin Zhang, William E. Barlow, Wouter Zwerink, Lajos Pusztai, Priyanka Sharma, Calvin Y. Chao, Alastair Mark Thompson, Andrew K. Godwin, Kathy S. Albain, Jacqueline R. Griffin, James M. Rae; Comprehensive Cancer Center, University of Alabama at Birmingham, Birmingham, AL; Artera, Menlo Park, CA; Public Health Sciences Division, Fred Hutchinson Cancer Center, Seattle, WA; Artera, Mountain View, CA; Cancer Research and Biostatistics (CRAB), Seattle, WA; Artera AI, Los Altos, CA; Yale Cancer Center, New Haven, CT; University of Kansas Medical Center, Westwood, KS; Artera, Los Altos, CA; Baylor College of Medicine, Houston, TX; Department of Pathology and Laboratory Medicine, University of Kansas Medical Center, Kansas City, KS; Loyola University Chicago Stritch School of Medicine, Cardinal Bernardin Cancer Center, Maywood, Chicago, IL; University of Michigan, Ann Arbor, MI

Background: Despite effective endocrine therapy, the absolute benefit of adjuvant chemotherapy varies widely in node-positive HR+ disease, particularly among patients with 1-3 positive nodes. Prognostic tools for these patients often rely on genomic assays, which are costly, timely, or inaccessible in many clinical settings. We present a multimodal artificial intelligence (MMAI) model that integrates clinical and histopathological data to quickly stratify risk of distant metastasis and inform therapeutic decisions. Developed in six phase III randomized clinical and validated for chemotherapy benefit in N0 patients, MMAI offers an accessible alternative to genomic tools. Here, we validated MMAI for prognosis and prediction of chemotherapy benefit in SWOG S8814 – a randomized phase III trial of tamoxifen ± chemotherapy (CT) in postmenopausal women with node-positive (N+) HR+ breast cancer. **Methods:** Patients with digitized baseline H&E- stained diagnostic slides and clinical data (age, tumor size, nodal status) were analyzed (N = 413). The locked MMAI generated a continuous risk score and categorical risk groups (low, high). Associations with disease-free survival (DFS; 168 events) and overall survival (OS; 125 events) were assessed using univariable and multivariable Cox Proportional Hazard models. Hazard ratios (HRs) and 95% confidence intervals (CI) were estimated. Differential CT benefit was evaluated by estimating relative risk reduction by MMAI risk groups. **Results:** MMAI was prognostic for DFS (HR per SD 1.73, 95% CI 1.48–2.03; $p < 0.001$) and OS (HR per SD 1.93, 95% CI 1.60–2.32; $p < 0.001$), remaining significant after adjustment for age, tumor size, and nodal burden. In the subset of patients with 1–3 positive nodes (n = 253), MMAI identified differential CT benefit: high-risk patients (56% of the patients) demonstrated a 26.3% relative reduction in 10-year DFS risk with CAF-T+TAM versus TAM alone, while low-risk patients (44% of the patients) derived minimal benefit (1.8% relative reduction in 10-year DFS risk). Additionally, the addition of CT resulted in DFS HRs of 1.21 (95% CI: 0.51-2.83) and 0.85 (95% CI: 0.55-1.23) in low- and high-risk patients, respectively. **Conclusions:** In SWOG S8814, a locked MMAI model using routinely available pathology and clinical data independently stratified prognosis and identified node-positive HR+ patients most likely to benefit from adjuvant CT, with minimal benefit among MMAI low-risk patients with 1–3 nodes. These findings support the use of MMAI as a fast (hours instead of weeks), scalable, cost-effective, and non-tissue consumptive alternative to genomic testing to inform adjuvant decisions in HR+ N+ EBC patients. Research Sponsor: None.

An AI-based pathology classifier to predict benefit from enzalutamide in metastatic hormone-sensitive prostate cancer (mHSPC) from ENZAMET (ANZUP 1304).

Sebastian R. Medina, Naoto Tokuyama, Vaishnavi Putcha, Tilak Pathak, Pingfu Fu, Hayley Thomas, Vinod Subhash, Sonia Yip, Hui-Ming Lin, Lisa Horvath, James G. Kench, Alison Yan Zhang, Martin R. Stockler, Anthony M. Joshua, Arun Azad, Samantha Richelle Oakes, Ian D. Davis, Christopher Sweeney, Anant Madabhushi; Wallace H. Coulter Department of Biomedical Engineering at Georgia Tech and Emory University, Atlanta, GA; Wallace H. Coulter Department of Biomedical Engineering, Georgia Tech and Emory University, Atlanta, GA; Department of Biomedical Engineering, Emory University, Atlanta, GA; Department of Population and Quantitative Health Sciences, Case Western Reserve University, Cleveland, OH; NHMRC Clinical Trials Centre, University of Sydney, Sydney, Australia; ANZUP Cancer Clinical Trials Group, Sydney, Australia; NHMRC Clinical Trials Centre, The University of Sydney, Sydney, NSW, Australia; Garvan Institute of Medical Research, Sydney, NSW, Australia; Chris O'Brien Lifehouse, Camperdown, NSW, Australia; NSW Health Pathology and University of Sydney, Sydney, Australia; NHMRC Clinical Trials Centre, University of Sydney, Sydney, NSW, Australia; The University of Sydney, Camperdown, Australia; Kinghorn Cancer Centre, St Vincent's Hospital, Sydney, NSW, Australia; Peter MacCallum Cancer Center, Melbourne, Australia; Australian & New Zealand Urogenital and Prostate (ANZUP) Cancer Trials Group, Camperdown, Australia; Monash University and Eastern Health, Box Hill, Australia; South Australian Immunogenomics Cancer Institute, Adelaide University, Adelaide, SA, Australia

Background: The ENZAMET trial established that adding enzalutamide (ENZ) to androgen deprivation therapy (ADT) improves overall survival (OS) in mHSPC. However, heterogeneity in treatment response and toxicity complicate clinical decision-making. We evaluated a previously developed Artificial Intelligence Pathology Image Classifier (APIC) to determine whether it could identify ENZAMET participants (pts) more likely to benefit from adding ENZ rather than NSAA to ADT. **Methods:** This AI biomarker study analyzed digitized H&E tumor specimens from ENZAMET (ANZUP 1304, NCT02446405), a phase 3 trial randomizing pts with mHSPC to ADT plus ENZ or a non-steroidal antiandrogen (NSAA), with early docetaxel (EDx) permitted. APIC, a model quantifying nuclear morphology and tumor-immune architecture validated in CHAARTED (Medina et al, Clin Can Res 2025), was applied without modification. The primary multivariable analysis evaluated the treatment-APIC interaction for OS using Cox models adjusted for disease volume (CHAARTED criteria), EDx, and age. Sensitivity analyses excluded pts receiving EDx. APIC associations with 18 circulating immune markers were explored. All tests were two-sided with $p<0.05$ considered significant. **Results:** Among 393 evaluable pts (median follow-up 70 months), 248 (63%) were APIC-negative and 145 (37%) APIC-positive. APIC significantly modified ENZ benefit (interaction p=0.010). APIC-negative was associated with improved OS with ENZ versus NSAA (HR 0.42, $p<0.001$; 5-year OS 82% vs 59%), while APIC-positive showed no benefit (HR 0.98, p=0.92; 5-year OS 57% vs 57%). APIC-treatment interaction was significant (p=0.02) in the multivariable model adjusted for clinical covariates. In low-volume disease, ENZ improved OS in APIC-negative (HR 0.19, p=0.0001) but not APIC-positive (HR 1.12, p=0.8; interaction p=0.002). Excluding EDx use (n=227), APIC-negative was associated with ENZ benefit (HR 0.29, $p<0.001$; 5-year OS 88% vs 60%, interaction p=0.043), while no significant benefit was observed for APIC-positive (HR 0.75, p=0.39; 5-year OS 61% vs 54%) (Table). Analysis of circulating immune markers identified elevated plasma myeloid progenitor inhibitory factor 1 (MPIF1) in APIC-positive pts (1.32-fold, 95% CI 1.11–1.58, p=0.002). **Conclusions:** APIC status was associated with benefit of ENZ for pts with mHSPC. APIC might help guide treatment selection for pts with mHSPC considered for androgen receptor pathway inhibitors and/or docetaxel. Clinical trial information: NCT02446405. Research Sponsor: National Cancer Institute/U.S. National Institutes of Health; R01CA268287A1, R01CA26828703, U01CA269181, R01CA26820701A1, R01CA249992-01A1,R01CA202752-01A1,R01CA208236-01A1,R01CA216579-01A1,R01CA220581-01A1, R01CA257612- 01A1, 1U01CA239055-01, 1U01CA248226-01, 1U54CA254566-01; Astellas.

	APIC Status	HR (95% CI)	P Value	Interaction P
Biomarker cohort (n=393)	Negative	0.42 (0.27–0.64)	<0.001	0.01
	Positive	0.98 (0.61–1.56)	0.9	
Low-Volume Disease Subgroup (n=209)	Negative	0.19 (0.08–0.44)	0.0001	0.002
	Positive	1.12 (0.55–2.29)	0.8	
No docetaxel cohort (n=227)	Negative	0.29 (0.15–0.56)	<0.001	0.04
	Positive	0.75 (0.40–1.44)	0.4	

Implementing a centralized navigator-led and AI-assisted platform to improve lung cancer screening rates and early detection: A 6-year health system analysis.

Jun Zhang, Tenille Oderwald, Thomas Cox, Ashley Chitwood, Shannon Foiles, Caelin LaFary, Brandi Clark, Mark Morris, Syed R. Zaidi, Brian S. Curtis, Ryan S. Luginbuhl, James Louis McGee; OSF HealthCare Cancer Institute, Peoria, IL; OSF Oncall, Peoria, IL; OSF Medical Group, Peoria, IL

Background: Despite the known mortality benefits of low-dose computed tomography (LDCT) for lung cancer screening (LCS), national uptake remains stagnant (~15-20%). Significant barriers include primary care burden and geographic disparities in rural areas. This study evaluates the impact of a centralized navigation model combined with AI-assisted electronic health record (EHR) alerts on LCS rates and stage distribution within a large integrated health system. **Methods:** We conducted a retrospective analysis of LCS performance across a 16-hospital system (OSF HealthCare) from 2019 to 2025. The intervention included: 1) centralization of LCS navigators to manage registries and scheduling, and 2) implementation of AI-assisted EHR alerts to identify eligible high-risk patients. Outcome measures included absolute LDCT volume, system-wide screening rates, and AJCC staging at diagnosis. Benchmarks were derived from American Lung Association (ALA) national and state (Illinois) data. **Results:** The system-wide LCS screening rate increased from 18.2% in 2020 to 42.8% in 2025, significantly outperforming the projected 2025 US national average (19.5%) and the Illinois state average (20.8%). Absolute screening volume nearly doubled, rising from 2,257 scans in 2019 to 4,108 in 2025. Notably, the program demonstrated high resilience during the 2020 COVID-19 pandemic, maintaining 98.5% of prior-year volume compared to a 5% national decline. Early-stage detection (Stage I) showed the greatest improvement in rural facilities, with some centers seeing a +21% increase in Stage I diagnoses over the study period. **Conclusions:** A centralized, technology-enabled navigation model effectively doubles the national benchmark for lung cancer screening uptake. By removing administrative burdens from primary care and utilizing AI-assisted EHR alert system to close the "eligibility gap", this model provides a scalable blueprint for improving early cancer detection and addressing rural health inequities. Research Sponsor: None.

OSF HealthCare lung cancer screening performance vs. national benchmarks (2020–2025).

Year	OSF Annual LDCT Volume	OSF Screening Rate (%)	National Screening Rate (%)*	Performance Gap (Percentage Points)
2020	2,223	18.2%	14.5%	+3.7%
2021	2,647	21.4%	14.8%	+6.6%
2022	3,280	27.8%	15.5%	+12.3%
2023	3,406	33.6%	16.0%	+17.6%
2024	3,522	38.2%	18.2%	+20.0%
2025	4,108	42.8%	19.5%	**+23.3%**

*National benchmarks based on American Lung Association "State of Lung Cancer" annual reports and CDC/ACS prevalence estimates.