

Long-term survival rates and cure modeling with dostarlimab plus chemotherapy in mismatch repair deficient/microsatellite instability-high (dMMR/MSI-H) primary advanced or recurrent endometrial cancer in the ENGOT-EN6-NSGO/GOG-3031/RUBY trial.

Matthew A. Powell, Oleksandr Zub, Nicoline Raashouu-Jensen, Lucy Gilbert, Antoinetta J.M. Beijers, Lyndsay Willmott, Martina Gropp-Meier, Kari Ring, Elisabeth Berge Nilsen, Amy J. Armstrong, Nicole Suzanne Nevadunsky, Sarah Gill, Robert W. Holloway, Eirwen Miller, John Paul Diaz, Michael Teneriello, Katherine Mays, Laura Katherine Austin, Carolyn K. McCourt, Trine Jakobi Noettrup; Washington University School of Medicine, Siteman Cancer Center, St. Louis, MO; Chernihiv Medical Center of Modern Oncology, Chernihiv Regional Council, Chernihiv, Ukraine; NSGO, Copenhagen, and Herlev Hospital, Herlev, Denmark; Division of Gynecologic Oncology, Research Institute, McGill University Health Centre, Gerald Bronfman Department of Oncology, McGill University, Montreal, QC, Canada; Department of Internal Medicine, Division of Medical Oncology, GROW Research Institute for Oncology and Reproduction, Maastricht University Medical Centre+, Maastricht, Netherlands; Arizona Center for Cancer Care, Phoenix, AZ; AGO Study Group, Wiesbaden, and Oberschwabenklinik, St. Elisabethen-Klinikum, Ravensburg, Germany; University of Virginia Health System, Charlottesville, VA; Department of Obstetrics and Gynecology, Stavanger University Hospital, Stavanger, Norway; Division of Gynecologic Oncology, University Hospitals Cleveland Medical Center, Case Comprehensive Cancer Center, Cleveland, OH; Department of Obstetrics, Gynecology, and Women's Health, Montefiore Medical Center, Albert Einstein College of Medicine, Bronx, NY; St. Joseph's/Candler Gynecologic Oncology & Surgical Specialists, Candler Hospital, Savannah, GA; AdventHealth Cancer Institute, Orlando, FL; Division of Gynecologic Oncology, Western Pennsylvania Hospital, Allegheny Health Network, Pittsburgh, PA; Miami Cancer Institute, Baptist Health South Florida, Miami, FL; US Oncology Research, The Woodlands, TX; GSK, Collegeville, PA; Division of Gynecology Oncology, Department of Obstetrics and Gynecology, Washington University School of Medicine, Washington University in St Louis, St Louis, MO; Department of Oncology, Copenhagen University Hospital - Rigshospitalet and NSGO, Copenhagen, Denmark

Background: Dostarlimab + carboplatin-paclitaxel (CP) demonstrated significant progression-free survival (PFS) and clinically meaningful overall survival benefits in patients with dMMR/MSI-H primary advanced or recurrent endometrial cancer (EC) in Part 1 of the phase 3 RUBY trial (NCT03981796). Median PFS was not reached for dostarlimab + CP vs 7.7 months for CP alone in this population. Moreover, plateauing of the PFS Kaplan-Meier (KM) curve suggested that a subset of patients with dMMR/MSI-H EC achieved durable disease control and potential for curative intent with dostarlimab + CP. Mixture cure models (MCMs) complement conventional outcome metrics by quantifying the proportion of patients considered "cured" and by modeling PFS among patients who remain uncured. Here we present an MCM applied to the PFS data from the dMMR/MSI-H population with up to 4.5 years of follow-up treated with dostarlimab + CP. **Methods:** At a median follow-up of 55.6 months (range 49.9–67.7 months), descriptive PFS analyses were conducted in the dMMR/MSI-H population from RUBY Part 1. MCMs were fitted to PFS data to estimate the proportion of patients treated with dostarlimab + CP who had a curative potential. In the MCM, patients with curative potential were assumed to be free of recurrence- and disease-related mortality risks, implying that any additional PFS events would come from death. Mortality risks were assumed to be similar to the background mortality expected in the general population (with matched demographic characteristics). Conversely, the uncured population was considered to be at risk for disease recurrence and death from all causes. **Results:** There was a low rate of progression since PFS was first analyzed, with only 4 new events reported with an additional 2.5 years of follow-up. The 4-year PFS rate was 57.9% (95% CI, 42.3%–70.6%) in the dostarlimab + CP arm vs 15.7% (95% CI, 7.2%–27.0%) in the control arm. The MCM analysis demonstrated that the majority of patients with dMMR/MSI-H EC (54%; 95% CI, 35%–72%) were considered "cured" with dostarlimab + CP. The PFS survival curves estimated from MCMs closely followed the KM curves reported from the RUBY trial data. The model appropriately captured the long-term survival plateau, instilling confidence in the robustness of the model predictions. **Conclusions:** With a minimum of 4 years of follow-up, updated PFS analyses demonstrated that the majority of patients remained alive and progression-free, illustrating durable disease control. Model-based predictions indicated the potential for cure in the dMMR/MSI-H primary advanced or recurrent EC population receiving dostarlimab + CP. These analyses may assist oncologists in understanding long-term survival outcomes and the proportion of patients with a curative potential. Clinical trial information: NCT03981796. Research Sponsor: GSK; N/A.

Updated overall survival analysis and examination of subsequent therapy in endometrial cancer (EC) patients (pts) treated with pembrolizumab plus carboplatin/paclitaxel (CP) as compared to CP plus placebo (PBO) in the NRG-GY018 trial.

Ramez Nassef Eskander, Michael Sill, Lindsey Beffa, Richard G. Moore, Joanie Mayer Hope, Fernanda Musa, Robert S. Mannel, Mark S. Shahin, Guilherme Henrique Cantuaria, Eugenia Girda, Cara Amanda Mathews, Juraj Kavecansky, Charles A. Leath III, Lilian Tran Gien, Emily Hinchcliff, Shashikant B. Lele, Lisa Michelle Landrum, Floor Jenniskens Backes, Matthew A. Powell, Carol Aghajanian; UC San Diego Moores Cancer Center, La Jolla, CA; Gynecologic Oncology Group Statistical and Data Center, Buffalo, NY; CWRU Case Comprehensive Cancer Center, Cleveland, OH; Division of Gynecologic Oncology, Wilmot Cancer Institute, Department of Obstetrics and Gynecology, University of Rochester, Rochester, NY; Alaska Women's Cancer Care, LLC, Anchorage, AK; Providence-Swedish Cancer Institute, Seattle, WA; Stephenson Cancer Center at the University of Oklahoma, Oklahoma City, OK; PennState Health, Hershey; Northside Hospital, Atlanta, GA; Rutgers Cancer Institute of New Jersey, New Brunswick, NJ; Program in Women's Oncology, Department of Obstetrics and Gynecology, Women and Infants Hospital, Brown University, Providence, RI; Kaiser Permanente Northern California, Walnut Creek, CA; O'Neal Comprehensive Cancer Center at The University of Alabama at Birmingham, Birmingham, AL; Sunnybrook Health Sciences Centre, Toronto, ON, Canada; Northwestern University, Chicago, IL; Roswell Park Cancer Institute, Buffalo, NY; IU Health Simon Cancer Center, Indianapolis, IN; Ohio State University James Cancer Hospital Department of Radiation Oncology, Columbus, OH; Washington University in St. Louis, St. Louis, MO; Gynecologic Medical Oncology, Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, NY

Background: NRG-GY018, the only phase 3 trial examining dMMR and pMMR EC populations independently, identified a 70% and 46% reduction in the risk of disease progression or death in advanced stage or recurrent dMMR and pMMR EC patients treated with pembrolizumab plus CP. Here we report on updated overall survival and post-study immune checkpoint inhibition (ICI) therapy. **Methods:** 810 pts were randomized 1:1 to pembrolizumab + CP or PBO + CP Q3W for 6 cycles followed by maintenance pembrolizumab or PBO Q6W for up to 24 months. Updated OS analysis data cut off was December 23, 2025, with information fraction of 42% and 78% in the dMMR and pMMR EC cohorts, respectively. Median follow up in the dMMR cohort was 44.6 months (95% CI 42.5 to 46.8) and 40.1 months (95% CI 38.9 to 42.2) in the pMMR cohorts. Study sites were queried to abstract data regarding start and end date of post study ICI use. **Results:** The addition of pembrolizumab resulted in a sustained OS benefit in the dMMR EC cohort. At 48-month landmark assessment, 80% of the pembrolizumab treated dMMR EC patients were alive, versus 60% of those treated with placebo, HR 0.53 (95% CI 0.32 to 0.89). This survival advantage was maintained despite at least 55% (n=62) of dMMR EC patients in the placebo arm receiving post study ICI. In the pMMR EC population, with an information fraction of 78%, the median OS in the pMMR cohort treated with pembrolizumab was 46.9 months versus 35.1 months for those receiving placebo, HR 0.84 (95% CI 0.66 to 1.06). This benefit was maintained despite at least 57% (n=167) pMMR EC patients in the placebo arm receiving post study ICI (most commonly lenvatinib plus pembrolizumab). In the pMMR EC cohort, 70 patients in the pembrolizumab arm and 167 patients in the placebo arm received post study ICI, with the median duration of treatment of 6.2 months in both populations. **Conclusions:** In the NRG GY018 study, with prolonged follow up, the addition of pembrolizumab to CP resulted in a sustained OS benefit despite substantial post study ICI use. In the pMMR population, an 11.8 month OS advantage was observed, despite at least 57% of the placebo patients receiving post study ICI. This data further supports the current US FDA approved indication of this regimen in the treatment of advanced stage or recurrent endometrial cancer irrespective of MMR status. Clinical trial information: NCT03914612. Research Sponsor: National Cancer Institute; U10CA180822; U.S. National Institutes of Health.

Overall survival subgroup analyses for prior taxane use in the phase 3 ROSELLA trial of relacorilant plus nab-paclitaxel versus nab-paclitaxel monotherapy in patients with platinum-resistant ovarian cancer (GOG-3073, ENGOT-ov72, APGOT-Ov10, LACOG-0223, and ANZGOG-2221/2023).

Lucy Gilbert, Benoit You, Alexander Olawaiye, Chel Hun Choi, Mariana Scaranti, Giorgio Valabrega, John K. Chan, Linda R. Mileskin, Toon Van Gorp, Mary E. Gordinier, Cristina Churrua, Carolyn Muller, Laurène Gavaille, Claudia Andreetta, Kofi Agyemang-Prempeh, Andrew R. Clamp, Hristina I. Pashova, Priya Choudhry, Maria Lapresa, Domenica Lorusso; Division of Gynecologic Oncology, Research Institute, McGill University Health Centre, Gerald Bronfman Department of Oncology, McGill University, Montreal, QC, Canada; University Hospital (HCL), and GINECO, Lyon, France; University of Pittsburgh Medical Center and Magee-Women's Hospital of UPMC, Pittsburgh, PA; Department of Obstetrics and Gynecology, Samsung Medical Center, Seoul, South Korea; DASA Oncologia, Hospital 9 de Julho, São Paulo, Brazil; SCU Oncologia Mauriziano Umberto I Hospital of Turin, Turin, Italy; California Pacific Medical Center/Sutter Health, San Francisco, CA; Department of Medical Oncology, Peter MacCallum Cancer Centre, Melbourne, Australia; University Hospital of Leuven, Leuven Cancer Institute, Leuven, Belgium; Norton Cancer Institute, Louisville, KY; Hospital Donostia, Donostia / San Sebastian, Spain; University of New Mexico Health Sciences Center, Albuquerque, NM; Gentilly Oncology Center, Interregional Institute of Oncology, Nancy, France; Azienda Sanitaria Universitaria Integrata di Udine, Udine, Italy; Petz Aladar Cnty Teaching Hospital, Oncologic RAD, Győr, Hungary; The Christie NHS Foundation Trust and University of Manchester, Manchester, United Kingdom; Corcept Therapeutics Inc., Redwood City, CA; IRCCS - Istituto Europeo di Oncologia, Milan, Italy; Department of Biomedical Science, Humanitas University, Pieve Emanuele, Milan and Humanitas San Pio X Hospital, Milan, Italy

Background: Relacorilant is a first-in-class, selective glucocorticoid receptor antagonist that increases tumor sensitivity to chemotherapy-induced apoptosis. The phase 3 ROSELLA trial of relacorilant plus nab-paclitaxel in patients with platinum-resistant ovarian cancer (PROC) recently reported statistically significant results for the dual primary endpoints of progression-free survival (PFS) and overall survival (OS). The relacorilant combination was well tolerated and the safety profile was similar to nab-paclitaxel monotherapy. Here we present final OS subgroup analyses for prior taxane use. **Methods:** Patients (n = 381) were randomized 1:1 to relacorilant (150 mg PO the day before, of, and after nab-paclitaxel) plus nab-paclitaxel (80 mg/m² IV on days 1, 8, and 15 of each 28-day cycle) or nab-paclitaxel alone (100 mg/m² IV on the same schedule). The final OS analysis was performed after 288 deaths had been reported (76% maturity). The hazard ratio (HR) was estimated with a Cox regression model with treatment group as the main effect and stratification factors at randomization as covariates. Kaplan-Meier methods were used to estimate medians and generate survival curves. **Results:** At a median follow-up of 24.8 months, the addition of relacorilant to nab-paclitaxel resulted in a statistically and clinically significant improvement in OS (HR 0.65; 95% confidence interval [CI], 0.51 to 0.83; P = 0.0004). Median OS in the relacorilant combination arm was extended by 4.1 months compared with the nab-paclitaxel monotherapy arm (16.0 vs 11.9 months). Prior taxane use was almost universal (n = 379/381, 99.5%). A consistent OS benefit was observed irrespective of the taxane-free interval: taxane-free interval ≤6 months (n = 55, HR 0.60 [95% CI, 0.31 to 1.15], median difference 5.7 months) and taxane-free interval > 6 months (n = 324, HR 0.66 [95% CI, 0.51 to 0.86], median difference 3.6 months). Moreover, a consistent OS benefit was observed irrespective of whether a taxane was used in the most recent regimen: taxane in the last regimen (n = 73, HR 0.67 [95% CI, 0.38 to 1.19], median difference 3.9 months) and no taxane in the last regimen (n = 308, HR 0.63 [95% CI, 0.48 to 0.82], median difference 4.2 months). Additional safety data will be presented. **Conclusions:** ROSELLA met both dual primary endpoints. Relacorilant plus nab-paclitaxel demonstrated a statistically and clinically significant OS benefit in patients with PROC compared to a weekly taxane, the most efficacious chemotherapy. Subgroup analyses for OS showed a consistent benefit favoring the addition of relacorilant to nab-paclitaxel irrespective of prior taxane use. Clinical trial information: NCT05257408. Research Sponsor: Corcept Therapeutics.

A phase III CHIPRO study of chiauranib plus weekly paclitaxel for platinum-resistant or refractory ovarian cancer.

Xiaohua Wu, Jin Li, Danbo Wang, Jin Wu, Dongling Zou, Wei Duan, Dan Li, Hongying Yang, Jingna Wu, Yuanhuan Xiong, Xiaojian Yan, Xiumin Li, Genhai Zhu, Li Sun, Yuzhi Li, Qing Liu, Yu Kang, Ke Wang, Jieqing Zhang, Li Wang; Fudan University Shanghai Cancer Center, Shanghai, China; Department of Gynecologic Oncology, Fudan University Shanghai Cancer Center, Shanghai, China; Liaoning Cancer Hospital & Institute, Shenyang, Liaoning, China; Harbin Medical University Cancer Hospital, Harbin, China; Gynecological Oncology Center, Chongqing University Cancer Hospital, Chongqing, China; Beijing Obstetrics and Gynecology Hospital, Capital Medical University, Beijing, China; The Affiliated Hospital of Southwest Medical University, Luzhou, China; Yunnan Cancer Hospital, Kunming, Kunming, China; Meizhou People's Hospital, Meizhou, China; Jiangxi Maternal and Child Health Hospital, Nanchang, China; First Affiliated Hospital of Wenzhou Medical University, Wenzhou, China; Linyi Cancer Hospital, Linyi, China; Hainan General Hospital, Haikou, China; Cancer Hospital Chinese Academy of Medical Sciences, Shenzhen Center, Shenzhen, China; The First Affiliated Hospital of Bengbu Medical University, Bengbu, China; Gansu Provincial Maternity and Child-Care Hospital, Lanzhou, China; Obstetrics & Gynecology Hospital of Fudan University, Shanghai, China; Tianjin Medical University Cancer Institute & Hospital, Tianjin, Tianjin, China; Guangxi Medical University Affiliated Cancer Hospital, Nanning, China; Henan Cancer Hospital, Zhengzhou, 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*.

CHRONO: A randomized phase II trial of the chronology of surgery after neoadjuvant chemotherapy for ovarian cancer.

Gwenael Ferron, Pierre-Francois Dupre, Constantin Georgeac, Claire Cropet, Pierre Meeus, Christophe Pomel, Claire Bonneau, Lobna Ouldamer, Sheik Emambux, Hélène Costaz, Sandrine Martin, Sebastien Gouy, Pierre-Emmanuel Colombo, Anne-Sophie Bats, Johanna Wassermann, Vincent Villefranque, Isabelle Cumin, Cyriac Blonz, Tristan Gauthier, Jean-Marc Classe; Institut Claudius Regaud, IUCT-Oncopole and GINECO, Toulouse, France; CHU de Brest- Hôpital Cavale Blanche, Brest, France; Institut inter-régional de Cancérologie - Centre Jean Bernard, Le Mans, France; Department of Biostatistics, Centre Léon Bérard, Lyon, France; Centre Léon Bérard and GINECO, Lyon, France; Centre Jean Perrin and GINECO, Clermont Ferrand, France; Department of Surgical Oncology, Institut Curie - Saint-Cloud, University of Versailles Saint-Quentin en Yvelines, INSERM U1331, Institut des Cancers de la Femme, Saint-Cloud, France and GINECO, Paris and St Cloud, France; Department of Medical Oncology, Centre Hospitalo-Universitaire Bretonneau, Tours, France; Centre Hospitalier Universitaire de Poitiers, Poitiers, France; Georges François Leclerc Comprehensive Cancer Care Centre, Dijon, France; Centre François Baclesse and GINECO, Caen, France; Gustave Roussy Cancer Center and GINECO, Villejuif, France; Department of Surgical Oncology, Montpellier Cancer Institute (ICM), Montpellier, France; Inserm U1194, Montpellier Cancer Research Institute (IRCM), University of Montpellier and GINECO, Montpellier, France; Hôpital Européen Georges Pompidou, Paris, France; Hôpital Pitié-Salpêtrière, Paris, France; Departments of Obstetrics and Gynecology, Hôpital Simone Veil, Eaubonne, France; Groupe Hospitalier Bretagne Sud - Hôpital du Scorff, Lorient, France; Hôpital Privé du Confluent and GINECO, Nantes, France; CHU Limoges, Hopital de la Femme, de la mère et de l'Enfant, Limoges, France; Institut de Cancérologie de l'Ouest and GINECO, Saint-Herblain, France

Background: In patients treated for advanced ovarian cancer not suitable for complete primary surgery, interval surgery after three courses of neoadjuvant chemotherapy (NAC) has been considered standard management since the EORTC randomized trial published in 2010 (NCT00003636, DOI: 10.1056/NEJMoa090880). Delaying surgery after six courses of NAC in highly chemosensitive patients amenable to complete surgery after 3 cycles remains controversial. CHRONO is a multicenter, randomized phase II trial addressing this question (NCT03579394). **Methods:** Patients treated for a stage IIIB-IVA high grade epithelial ovarian cancer by NAC and amenable to complete surgery after 3 cycles were randomized (1:1) to either complete surgery followed by 5 cycles of chemotherapy (control arm: C) or an additional 3 cycles of NAC followed by complete surgery then 2 cycles of chemotherapy (experimental arm: E). Maintenance treatment was administered according to standard of care. Primary endpoint was disease free survival (DFS) defined as the time from randomization until the date of disease progression or second cancer or death from any cause. The study was designed to detect an improvement in median (m) DFS from 10 months to 17 months (HR=0.59) with a 85% power and 2-sided $\alpha=0.05$. Main secondary endpoints were Pathological complete response (CCo) rate, post operative morbidity and mortality, quality of life (QoL) and overall survival (OS). **Results:** Between 18/10/2018 and 23/04/2024, 209 patients (median age: 69 years) were randomized to arm C (n=103) or E (n=106). Median total number of cycles of NAC was 7 (5-9) and 8 (3-9) in arm C and E. CCo rate was 83.2% vs 90%. After a median follow up of 40.4 months, mDFS was 20.2 months (95%CI: 18.2-23.6) in arm C vs 23.4 (19.0-30.4) in arm E (Log-rank test $p=0.48$, HR: 0.88 (95%CI: 0.63-1.24)). The longitudinal analysis of QoL found no significant differences between the two arms, however, social functioning, insomnia, and sexuality showed a trend toward further improvement (≥ 5 points) in arm E. Major postoperative complication rates within 30 days were 5% and 11% in arm C and E, ($p=0.11$), with no death within 30 days after surgery. **Conclusions:** CHRONO is the first randomized trial addressing the clinical impact of delayed surgery after 6 courses of NAC in first line treatment of advanced ovarian cancer. No statistically significant difference was shown between the two arms of the study considering DFS, severe morbidity, mortality or QoL. New trials are needed for a better understanding of this alternative to interval surgery in highly chemosensitive advanced ovarian cancer patients. Clinical trial information: NCT03579394. Research Sponsor: This study was fully funded by ARCAGY-GINECO.

A randomized phase II trial of mirvetuximab soravtansine in folate receptor alpha (FR α)-high recurrent ovarian cancer eligible for platinum-based chemotherapy (MIROVA/AGO-OVAR 2.34).

Philipp Harter, Florian Heitz, Frederik Marmé, Joern Rau, Bastian Czogalla, Jalid Sehouli, Fabienne Schochter, Pauline Wimberger, Holger Bronger, Oliver Tome, Tjong-Won Park-Simon, Maximilian Rost, Ralf Witteler, Barbara Schmalfeldt, Martin Poelcher, Marina Wirtz, Christina Balser, Sabrina Kaiser, Anja Krueger, Fabian Trillsch; Ev. Kliniken Essen-Mitte, Essen, Germany; Medical Faculty Mannheim, Heidelberg University, University Hospital Mannheim, Mannheim, Germany; Coordinating Center for Clinical Trials, Philipps-University, Marburg, Germany; LMU University Hospital, LMU Munich, Munich, Germany; Charité-Universitätsmedizin Berlin, Campus Virchow Klinikum, Berlin, Germany; University Hospital Ulm, Ulm, Germany; University Hospital Carl Gustav Carus, TU Dresden and National Center for Tumor Diseases (NCT), Dresden, Germany; TUM Klinikum Rechts der Isar, Technical University of Munich, Munich, Germany; ViDia Christliche Kliniken Karlsruhe, Karlsruhe, Germany; Hannover Medical School, Hannover, Germany; University Hospital Frankfurt/M., Frankfurt, Germany; University Hospital Münster, Münster, Germany; University Medical Center Hamburg-Eppendorf, Hamburg, Germany; Red Cross Hospital Munich, Munich, Germany; Helios Klinikum Krefeld, Krefeld, Germany; OnkoNet Marburg GmbH, Marburg, Germany; AGO Study Group, Wiesbaden, Germany

Background: Mirvetuximab soravtansine (MIRV) has demonstrated single agent activity in patients with platinum-resistant ovarian cancer with FR α high expression. However, its activity and safety in combination with carboplatin has not been defined in platinum eligible patients so far. **Methods:** Randomized phase II trial comparing 6 cycles of carboplatin AUC5+-MIRV 6 mg/kg AIBW every 3 weeks followed by MIRV versus 6 cycles of carboplatin combined with either paclitaxel, gemcitabine or pegylated liposomal doxorubicin followed by maintenance PARP inhibitor (PARPi) if applicable. All histologic subtypes were eligible with a platinum-free interval >3 months and FR α high expression ($\geq 75\%$ with PS2+ scoring) confirmed by central laboratory. Prior PARPi therapy in BRCAmut patients was mandatory. Strata were BRCA-Status, TFIp and number of prior lines of chemotherapy. The primary endpoint was PFS. **Results:** In total, 145 patients were randomized. Of them, 112/145 (77.2%) patients had received prior bevacizumab and 97/145 (66.9%) had prior PARPi, 15.2% were BRCAmut. In the standard arm, 39.15% received PARPi as maintenance. Median PFS in the standard arm was 9.79 months versus 9.53 months in the experimental arm ($p=0.996$; HR=1.00; 95% CI: 0.68; 1.46). **Conclusions:** MIROVA/AGO-OVAR 2.34 is the first randomized trial evaluating the activity and safety of the combination of carboplatin with an antibody-drug conjugate in the setting of platinum-eligible relapsed ovarian cancer. The primary endpoint regarding improvement of PFS was not met. Further analysis will be presented. Clinical trial information: NCT04274426. Research Sponsor: ImmunoGen/AbbVie.

Updated efficacy results from the phase I cervical cancer cohort of BAT8008, a TROP-2-directed antibody-drug conjugate, in patients with advanced cervical cancer.

Jianli Zhao, Wenjuan Chen, Mingjun Zhang, Yongsheng Li, Yanhong Zhuo, Zhengbo Song, Qing Wen, Meili Sun, Hongrui Niu, Jinfeng Ma, Xiumin Li, Hong Wang, Jin Yang, Tianan Yi, Zhiguo Luo, Hao Wang, Shengfeng Li, Erwei Song; Sun Yat-sen Memorial Hospital, Sun Yat-sen University, Guangzhou, China; Fujian Medical University Cancer Hospital, Fuzhou, China; The Second Affiliated Hospital of Anhui Medical University, Hefei, China; Chongqing University Cancer Hospital, Chongqing, China; Zhangzhou Hospital, Teaching Hospital of Fujian Medical University, Zhangzhou, China; Department of Thoracic Oncology, Zhejiang Cancer Hospital, Hangzhou, China; Jinan Central Hospital, Jinan, China; Department of Oncology, Central Hospital affiliated to Shandong First Medical University, Jinan, Shandong, China; Department of Oncology, The First Affiliated Hospital of Xinxiang Medical University, Xinxiang, China; Shanxi Cancer Hospital, Taiyuan, China; Linyi Cancer Hospital, Linyi, China; The Nanchang Third Hospital, Nanchang, China; The First Affiliated Hospital of Xi'an Jiao Tong University, Xi'an, China; Oncology Department, Xiangyang Central Hospital, Xiangyang, China; Department of Clinical Oncology, Taihe Hospital, Hubei University of Medicine, Shiyan, China; Bio-Thera Solutions, Ltd, Guangzhou, China

Background: BAT8008 is a novel antibody-drug conjugate comprising a TROP-2 antibody and an exatecan payload. Patients with recurrent or metastatic cervical cancer (r/m CC) who have progressed on platinum-based chemotherapy have limited treatment options and poor prognosis. This study reports the safety and efficacy of BAT8008 in a cohort of r/m CC patients from a phase 1 trial. **Methods:** This analysis is part of BAT-8008-001-CR, a multi-center, open-label phase 1 study with dose escalation and expansion cohorts. Patients with r/m CC who had failed prior systemic treatments were enrolled. BAT8008 was administered 2.4 mg/kg or 2.1mg/kg intravenously every two weeks (Q2W) 2.4 mg/kg. **Results:** As of Jan 5, 2026, 68 evaluable patients with r/m CC were enrolled (27 at 2.1 mg/kg, 41 at the 2.4 mg/kg). Patients were heavily pre-treated, with 55.9% having received ≥ 2 prior lines of therapy. 64.7% had prior anti-angiogenic therapy and 38.2% had prior immunotherapy. At the 2.4 mg/kg dose (n=44), the most common TRAEs (any grade/ $\geq G3$) were anemia (63.6%/15.9%), WBC decreased (68.2%/25.0%), stomatitis (54.5%/6.8%), and neutrophil count decreased (45.5%/20.5%). No treatment-related deaths occurred. For the RP2D cohort (n=41), the confirmed objective response rate (cORR) was 29.3% and disease control rate (DCR) was 78.0%. The median progression-free survival (mPFS) was 6.7 months (95% CI: 3.5-12.1) and median duration of response (mDoR) was 9.0 months (95% CI: 4.2-12.3). Efficacy was observed across subgroups and was independent of TROP-2 expression level. **Conclusions:** BAT8008 demonstrated promising and durable anti-tumor activity with a manageable safety profile in heavily pre-treated patients with r/m cervical cancer. These findings support the continued development of BAT8008 in this patient population. Clinical trial information: NCT05620017. Research Sponsor: None.

Efficacy Endpoint	2.1 mg/kg (n=27)	2.4 mg/kg (n=41)	Overall (n=68)
cORR, % (95% CI)	22.2 (10.6-40.8)	29.3 (17.6-44.5)	26.5 (17.4-38.0)
DCR, % (95% CI)	81.5 (63.3-91.8)	78.0 (63.3-88.0)	79.4 (68.4-87.3)
mPFS, months (95% CI)	5.3 (3.3-8.3)	6.7 (3.5-12.1)	6.5 (3.5-8.3)
mDoR, months (95% CI)	Not Reached	9.0 (4.2-12.3)	9.0 (5.3-12.3)

A phase 1/2 study of the next-generation nectin-4–targeting antibody-drug conjugate CRB-701 (SYS6002) in patients with recurrent or metastatic cervical cancer.

Tudor-Eliade Ciuleanu, Dominique Berton, Gennaro Daniele, Laurentia N. Gales, Diego Tosi, Giuseppe Curigliano, M. Julia Lostes-Bardaji, Lorenzo Antonuzzo, Bernard Gaston Doger de Spéville, Constantin D. Volovat, Debra Josephs, Guillermo Suay Montagud, David James Pinato, Sarah A. Ackroyd, Ivan Barrera, Kurt Preugschat, Paola M. Grant, Ian Hodgson, Dominic Smethurst, Yohann Lorient, Arensia Research Clinic, Cluj-Napoca, Romania; Institut de Cancerologie de l'Ouest, Saint-Herblain, France; Phase 1 Unit, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Italy; Arensia Research Clinic, Bucharest, Romania; Institut régional du Cancer de Montpellier-Val d'Aurelle, Montpellier, France; European Institute of Oncology, IRCCS, University of Milano, Milano, Italy; Vall d'Hebron University Hospital and Vall d'Hebron Institute of Oncology, Barcelona, Spain; Azienda Ospedaliero Universitaria Careggi, Florence, Italy; START Madrid Fundación Jiménez Díaz, Madrid, Spain; Centrul de Oncologie Euroclinic, Iasi, Romania; Guys' and St Thomas' NHS Foundation Trust, London, United Kingdom; Hospital Universitario y Politécnico La Fe de Valencia, Valencia, Spain; Imperial College London, London, United Kingdom; University of Chicago, Chicago, IL; Precision for Medicine, Flemington, NJ; Corbus Pharmaceuticals, Inc., Norwood, MA; Institut Gustave Roussy, Université Paris-Saclay, Villejuif, France

Background: CRB-701 is a next-generation Nectin-4–targeted monomethyl auristatin E (MMAE)–based antibody–drug conjugate with differentiated safety, efficacy and pharmacokinetics compared with other agents in the same class. As previously reported, CRB-701 demonstrated antitumor responses independent of Nectin-4 expression levels in solid tumors, notably in patients with heavily pretreated head and neck squamous cell carcinoma (HNSCC) and cervical cancer, as well as those with urothelial carcinoma. Here, we provide data from this phase 1/2 trial in patients with cervical cancer enrolled in dose escalation (part A) and dose optimization (part B) (NCT06265727). **Methods:** Patients with recurrent or metastatic (R/M) cervical cancer who had received ≥ 1 line of therapy were enrolled. Part A employed a Bayesian Optimal Interval design with four doses (1.8, 2.7, 3.6 and 4.5 mg/kg; each every 3 weeks [Q3W]) to determine the maximum tolerated dose. In part B, the pharmacologically active dose range identified in part A was evaluated using a time-to-event Bayesian optimal phase 2 design. Patients were randomized 1:1 to receive CRB-701 at 2.7 or 3.6 mg/kg Q3W. The primary endpoints for parts A and B were dose-limiting toxicities and objective response rate (ORR), respectively. Safety, tolerability and pharmacokinetics were also assessed. Nectin-4 expression was evaluated retrospectively. **Results:** As of September 2025, 54 patients with cervical cancer had enrolled across parts A and B. At the time of data cut, most patients were awaiting a confirmatory scan. The unconfirmed ORR was 22.2% (4/18 evaluable patients) at the 2.7 mg/kg dose and 37.5% (6/16 evaluable patients) at the 3.6 mg/kg dose. Confirmed partial responses were observed in 1/18 participants at the 2.7 mg/kg dose and 3/16 patients at the 3.6 mg/kg dose. One patient had a confirmed complete response at the 2.7 mg/kg dose. The safety profile of CRB-701 was broadly consistent with earlier findings: keratitis, anemia, alopecia, fatigue and dysgeusia were the most frequently reported treatment-emergent adverse events ($\geq 15\%$ of overall solid tumor population [N = 167]). An expanded efficacy analysis reporting an additional 6 months of follow-up, including ORR, duration of response and progression-free survival, will be presented at the congress. Subgroup analyses by treatment history and disease extent will also be presented. **Conclusions:** CRB-701 has shown promising efficacy in patients with R/M cervical cancer, as well as a favorable safety profile compared with other MMAE-based therapies. Ongoing evaluation of CRB-701 will determine its potential as a new treatment option for this patient population. Clinical trial information: NCT06265727. Research Sponsor: None.

Phase 1a study results for IMA203CD8, a PRAME-directed T-cell receptor (TCR) T-cell therapy, in ovarian cancer.

Antonia Busse, Winfried Alsdorf, Oladapo O. Yeku, Sarah E. Taylor, Deika M. Araujo, Dirk Jaeger, Katrin Wetzko, Amir A. Jazaeri, Samer Ali Srou, Martin Wermke, Alexander Mustea, Friedrich Vollmer, Norbert Hilf, Natalia Chorna, Cedrik Michael Britten, Tobias Albert Wilhelm Holderried; Charite Medical University Hospital, Berlin, Germany; Department of Hematology and Oncology University Hospital Hamburg Eppendorf, Hamburg, Germany; Massachusetts General Hospital, Harvard Medical School, Boston, MA; Department of Obstetrics, Gynecology and Reproductive Services, University of Pittsburgh Medical Center, Pittsburgh, PA; The University of Texas MD Anderson Cancer Center, Houston, TX; Department of Medical Oncology, National Center for Tumor Diseases (NCT), Heidelberg University Hospital, Heidelberg, Germany; University Hospital Dresden, Dresden, Germany; TU Dresden University of Technology, NCT/UCC Early Clinical Trial Unit, Dresden, Germany; Department of Gynecology and Gynecological Oncology, Bonn University Hospital, Bonn, Germany; Immatics Biotechnologies GmbH, Tübingen, Germany; Immatics Biotechnologies, Tübingen, Germany; Immatics Biotechnologies GmbH, Munich, Germany; University of Bonn, University Hospital Bonn, Medical Clinic and Polyclinic III Internal Medicine with a focus on Oncology, Hematology, and Rheumatology, Bonn, Germany

Background: Pts with advanced ovarian cancer (OC) that progresses after platinum-based chemotherapy and subsequent treatment are lacking therapeutic options for durable clinical benefit. TCR T-cell therapies enable immune recognition of intracellular tumor antigens presented by HLA, expanding the therapeutic landscape beyond targets accessible to conventional immunotherapies. PRAME is a cancer-associated antigen expressed across >50 cancers, including OC. IMA203CD8 is a TCR T-cell therapy that engineers CD8⁺ and CD4⁺ T cells to detect and destroy PRAME-expressing tumor cells that evade conventional therapeutic approaches. Results from a phase 1a basket trial (NCT03686124) indicated the potential to target several PRAME⁺ tumors. Here we present updated dose-escalation results for the subset of pts with OC. **Methods:** Pts were ≥ 18 y, HLA-A*02:01⁺, had R/R solid tumors, measurable disease (RECIST 1.1), ECOG PS 0-1, and had exhausted SOC options, including platinum therapy. Following leukapheresis and IMA203CD8 manufacture, pts underwent lymphodepletion (LD) with Cy (500 mg/m² $\times$ 4 d) and Flu (30 mg/m² $\times$ 4 d), followed by IMA203CD8 infusion +/- low-dose SUBQ IL-2. Dose escalation is ongoing. **Results:** As of Oct 27, 2025, 16 heavily pretreated pts with OC were infused with IMA203CD8. Most common TEAEs were LD-related cytopenias (100%). Cytokine release syndrome occurred in 100% of pts and was mostly mild to moderate (G1: 44%, G2: 50%, G3: 6%). Immune effector cell-associated neurotoxicity syndrome occurred in 1 pt (G1: 6%). Tolerability in pts with OC was generally consistent with the known IMA203CD8 safety profile. Eleven pts were efficacy evaluable with ≥ 1 post-baseline scan (median 4 prior lines of therapy) after treatment with IMA203CD8 across escalating dose levels (median: 2.26×10^9 total TCR T cells; range: 1.4 – 7.1×10^9 TCR T cells). Tumor reduction was observed in 7 pts with maximum reduction of 74%; 3 responses were >6 mo and durable disease control occurred for up to 12 mo. A dose-dependent signal of activity was observed in pts treated at higher doses (n=5; range: 2.3 – 7.1×10^9 TCR T cells), including 2 confirmed partial responses (PRs) with 1 ongoing metabolic complete response (CRs) at 6 mo, and 1 unconfirmed PR. All responses were observed in pts without post-infusion low-dose IL-2. Updated results from ≥ 20 efficacy-evaluable pts (including several unconfirmed PRs and CRs after data cutoff) with longer follow-up will be presented. **Conclusions:** In pts with metastatic and/or relapsed OC, IMA203CD8 demonstrated a tolerability profile consistent with prior experience in other solid tumors and encouraging dose-dependent antitumor activity, including durable objective responses according to RECIST. Dose escalation with and without IL-2 at higher doses is currently ongoing to determine RP2D and unlock the full potential of IMA203CD8 in OC. Clinical trial information: NCT03686124. Research Sponsor: Immatics US.

The neo-epitope-based vaccine OSE2101 with or without pembrolizumab versus best supportive care as maintenance in platinum-sensitive recurrent ovarian cancer patients with controlled disease after platinum-based chemotherapy: The academic randomized TEDOVA/GINECO-OV244b/ENGOT-ov58 trial.

Alexandra Leary, Toon Van Gorp, Frederik Marmé, Xavier Paoletti, Lauriane Eberst, Antoine Angelergues, Coriolan Lebreton, Stanislas Quesada, Thibault de La Motte Rouge, Benoit You, Renaud Sabatier, Laura Mansi, Emilie Kaczmarek, Jerome Alexandre, Thomas Grellety, Pierre Combe, Anne-Claire Hardy-Bessard, Laurence Gladieff, Jean-Sebastien Frenel, Isabelle Laure Ray-Coquard; Gustave-Roussy Cancer Campus, Villejuif, and GINECO, Paris, France; University Hospital Leuven, Leuven Cancer Institute and BGOG, Leuven, Belgium; AGO Study Group & Medical Faculty Mannheim, Heidelberg University, Mannheim, Germany; Inserm U1331, STAMPM, Institut Curie, Université de Versailles St Quentin/Paris-Saclay and GINECO, St-Cloud, France; Hopitaux Universitaires de Strasbourg and GINECO, Strasbourg, France; Department of Medical Oncology, Groupe Hospitalier Diaconesses-Croix Saint Simon and GINECO, Paris, France; GINECO and Institut Bergonié, Bordeaux, France; Department of Medical Oncology, Montpellier Cancer Institute (ICM), GINEGEPS and GINECO, Montpellier, France; Department of Oncology, Eugene Marquis Cancer Center and GINECO, Rennes, France; Centre Hospitalier Lyon Sud, Pierre-Benite and GINECO, Paris, France; Institut Paoli Calmettes, Marseille, and GINECO, Paris, France; CHU de Besançon, Service d'Oncologie Médicale and GINECO, Besançon, France; Centre Oscar Lambret, Lille, and GINECO, Paris, France; Université de Paris Cité, AP-HP, Hôpital Cochin, Paris, and GINECO, Paris, France; Department of Medical Oncology, Centre Hospitalier de la côte basque and GINECO, Bayonne, France; Pôle santé Léonard de Vinci, Centre d'Oncologie et Radiothérapie, and GINECO, Paris, France; Centre CARIO – HPCA, Plérin Sur Mer, and GINECO, Paris, France; Institut Claudius Regaud, IUCT-OncoPole, Toulouse, and GINECO, Paris, France; Institut de Cancérologie de l'Ouest, Saint Herblain, France; Centre Léon Bérard, Centre Régional de Lutte Contre Le Cancer de Lyon, Lyon, France

Background: OSE2101 is a neo-epitope vaccine targeting 5 tumor-associated antigens (TP53, MAGE2, MAGE3, CEA and HER2) modified to increase both HLA-A2 and TCR affinity, designed to turn immunogenic 'cold' ovarian cancer (OC) to 'hot' tumors. Patients with platinum sensitive OC (PSOC) relapsing post-PARP inhibitor (PARPi) and bevacizumab (BEV) represent an area of unmet medical need. **Methods:** This international multicenter GINECO-sponsored phase II study randomized PSOC patients in CR, PR, or SD after platinum therapy to best supportive care (BSC, arm A), or maintenance treatment with OSE2101 ((SC, q3w until week 18, then q6w to week 48, then q12w, arm B) or OSE2101+pembrolizumab (IV q6w, Arm C) (1:1:2) for up to 2 years. Eligible pts were HLA-A2 positive and previously treated with, or ineligible for, BEV and a PARPi. Primary endpoint was PFS and randomization was stratified for best response to platinum (CR/PR vs SD). Sample size was calculated to provide 90% power to detect an improved PFS in arm C vs A with HR=0.57. Subsequent hierarchical testing then compared arms C vs B, and arms B vs A. **Results:** 185 pts were randomized to BSC (N=48), OSE2101 (N=46) or OSE+PEMBRO (N=91). Histology was mainly high grade (93%) and serous (93%), 20% harbored a BRCA1/2 mutation, 51% of pts were in CR/PR and 49% in SD at randomization, 85% and 83% of pts were PARPi and BEV-exposed, respectively. Baseline characteristics were balanced between arms. With a median follow up of 22 months, PFS was significantly improved with OSE2101+Pembro vs BSC (4.1 vs 2.8mo in arms C vs A; HR=0.53, 95%CI, 0.36-0.78; $p<0.001$), especially among pts in CR/PR to platinum (HR=0.31, 95% CI, 0.17-0.53; $p<0.01$; test for interaction $p=0.02$). For OSE2101+Pembro vs OSE2101, HR was 0.72 ($p=0.074$) and for OSE2101 vs BSC, HR was 0.70 ($p=0.099$). Treatment emergent AEs were increased in arm C vs B with most common being injection site reaction (57% vs 35%), cytokine release syndrome (CRS, mainly G1/2: 28% vs 9%), arthralgia (21% vs 17%) and >G2 immune related events (18% vs 4%). **Conclusions:** This is the 1st trial demonstrating a significant improvement in PFS with a combination of a neo-epitope vaccine and an anti-PD1 as maintenance after platinum for patients with platinum sensitive relapsed OC progressing post-PARPi and bevacizumab. Clinical trial information: 2024-516096-32-00. Research Sponsor: OSE Immunotherapeutics, SA; ARCAGY-GINECO organization; MSD France.

Overall survival for patients with pre-treated platinum-resistant ovarian cancer receiving gotistobart in combination with pembrolizumab.

Joyce N. Barlin, Peter C. Lim, Jessica Thomes Pepin, Elizabeth Hopp, Noelle Cloven, Helen Dinkelspiel Eshed, Destin Black, Hope M. Cottrill, Lauren Hand, David M. O'Malley, Linus T. Chuang, Christine M. Lee, Lyndsay Willmott, Michael Jon Chisamore, Joan Durbin, Pan Zheng, Yang Liu, Andre Overesch, Svetlana Shpyro, Bradley J. Monk; Womens Cancer Care Associates, Albany, NY; Gynecologic Oncology, Center of Hope, Reno, NV; Minnesota Oncology, Minneapolis, MN; Medical College of Wisconsin, Milwaukee, WI; Texas Oncology, Fort Worth, Fort Worth, TX; Texas Oncology, Austin, TX; Willis-Knighton Cancer Center, Shreveport, LA; Baptist Health Lexington, Lexington, KY; Baptist MD Anderson Cancer Center, Jacksonville, FL; The Ohio State University and the James Comprehensive Cancer Center, Columbus, OH; Zucker School of Medicine at Hofstra/Northwell, Hempstead, Long Island, NY; Texas Oncology - The Woodlands, The Woodlands, TX; Honor Health Cancer Care - Biltmore, Phoenix, AZ; Merck & Co., Inc., Rahway, NJ; OncoC4, Inc., Rockville, MD; BioNTech SE, Mainz, Germany; Florida Cancer Specialists & Research Institute, West Palm Beach, FL

Background: Gotistobart, an investigational tumor microenvironment-selective Treg depletion antibody targeting CTLA-4 with a novel mechanism of action, demonstrated anti-tumor activity when combined with pembrolizumab in the PRESERVE-004/GOG-3081 trial in patients (pts) with platinum-resistant ovarian cancer (PROC; Barlin et al., ESMO 2024). Here, we present overall survival (OS) and updated safety data from the Phase 2 trial (NCT05446298). **Methods:** Pts with PROC, tubal, or peritoneal cancer who previously received 1 line of platinum-based therapy and progressed between 3–6 months or received ≥1 line and progressed within 6 months of last dose, were treated with gotistobart (1, 2, 3, or 6 mg/kg, Q3W) and pembrolizumab (200 mg, Q3W). Here we present data from patients that received 1 or 2 mg/kg gotistobart Q3W and pembrolizumab. Primary endpoints included objective response rate (ORR) based on RECIST 1.1 and safety. Secondary endpoints included duration of response (DoR), progression-free survival (PFS) and OS. **Results:** As of November 12, 2025, 83 pts were treated with ≥1 dose of gotistobart in combination with pembrolizumab. Among them, 62 pts (85.5% White with a median age of 65 years and 83.9% with high grade serous OC) had received 1 or 2 mg/kg gotistobart, and 75.8% had received ≥3 lines of prior therapy (median 4, range: 1–10). The median time from randomization to database cutoff was 22.3 months (range 17.8, 27.2). Median OS was 18.9 m (95% CI 3.9, NE) and 8.3 m (95% CI 3.9 – 17.1) with the OS rates at 18 months at 54.3% (95% CI 35.1, 70.0) and 26.9% (95% CI 11.7 – 44.7) in pts that received 1 or 2 mg/kg gotistobart, respectively. Efficacy data are summarized in the table below. Grade ≥3 treatment-related (gotistobart or pembrolizumab) adverse events (TRAEs) were observed in 51.5% and 55.2% pts treated with 1 mg/kg or 2 mg/kg, respectively. Common (≥5%) grade ≥3 TRAEs were colitis (1 mg/kg: 12.1%, 2 mg/kg: 10.3%), hyponatremia (1 mg/kg: 12.1%, 2 mg/kg: 3.4%), increased ALT (1 mg/kg: 9.1%, 2 mg/kg: 3.4%), increased AST (1mg/kg: 9.1%, 2 mg/kg: 3.4%), adrenal insufficiency (1 mg/kg: 9.1%, 2 mg/kg: 3.4%), diarrhea (1 mg/kg: 9.1%, 2 mg/kg: 3.4%), and hypokalemia (1 mg/kg: 0%, 2 mg/kg: 6.9%). **Conclusions:** The chemotherapy-free combination of gotistobart and pembrolizumab demonstrated clinically meaningful ORR, OS and a manageable safety profile in pts with PROC, where the majority were heavily pretreated with no further standard-of-care treatment options. Clinical trial information: NCT05446298. Research Sponsor: Onco C4 Inc.

	1 mg/kg gotistobart + pembrolizumab (n=33)	2 mg/kg gotistobart + pembrolizumab (n=29)
Confirmed ORR, % (95% CI)	21.2 (9.0, 38.9)	20.7 (8.0, 39.7)
Median DoR, m (95% CI)	10.8 (3.3, NE)	11.6 (4.0, NE)
Median PFS, m (95% CI)	2.2 (2.0, 4.2)	2.5 (1.9, 6.0)
Median OS, m (95% CI)	18.9 (3.9, NE)	8.3 (3.9, 17.1)
OS rate at 18 months, % (95% CI)	54.3 (35.1, 70.0)	26.9 (11.7, 44.7)

Safety and efficacy of BAT8006 in combination with BAT1308 in patients with advanced endometrial cancer.

Xingtao Long, Yi Gong, Yibiao Chen, Jiandong Tong, Funan Liu, Liang Chen, Juan Li, Hongwei Zhao, Xin Wang, Guiling Li, Dan Bo Wang, Keqiang Zhang, Hui Zhang, Hui Qiu, Tianmin Xu, Qi Zhou; Chongqing University Cancer Hospital, Chongqing, China; Department of Phase I Clinical Trial Ward, Chongqing University Cancer Hospital, Chongqing, China; Meizhou People's Hospital, Meizhou, China; Affiliated Hospital of Yangzhou University, Yangzhou, China; The First Hospital of China Medical University, Shenyang, China; Department of Gynecologic Oncology, Shandong Cancer Hospital and Institute, Shandong First Medical University and Shandong Academy of Medical Sciences, Jinan, Shandong, China; Cancer Hospital of Shandong First Medical University (Shandong Cancer Institute, Shandong Cancer Hospital), Jinan, China; Shanxi Cancer Hospital, Taiyuan, China; Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China; Liaoning Cancer Hospital, Shenyang, China; Hunan Cancer Hospital, Changsha, China; The Fourth Hospital of Hebei Medical University, Shijiazhuang, HeBei, China; Zhongnan Hospital of Wuhan University, Wuhan, China; Department of Gynecology and Obstetrics, The Second Hospital of Jilin University, Jilin, China

Background: BAT8006 is a folate receptor α (FR α)-targeting antibody-drug conjugate (ADC), while BAT1308 is a recombinant humanized anti-PD-1 monoclonal antibody. Both agents have individually demonstrated acceptable tolerability and promising antitumor activity in solid tumors. Herein, we report a phase Ib/II trial designed to evaluate the safety and efficacy of BAT8006 in combination with BAT1308 for patients with advanced endometrial cancer. **Methods:** Eligible patients included those with pathologically confirmed endometrial cancer who had experienced disease recurrence or progression following at least 1 line of platinum-based chemotherapy or immunotherapy-based regimen, with no more than 3 prior lines of systemic therapy. Enrolled patients received BAT8006 (76 mg/m² or 84 mg/m²) in combination with BAT1308 (fixed dose of 300 mg) every 3 weeks until disease progression, intolerable toxicity, or other protocol-specified reasons. The primary endpoints were safety and ORR as assessed by investigators per RECIST v1.1. **Results:** As of December 25, 2025, a total of 45 patients with advanced endometrial cancer were enrolled in this study. The median age of the cohort was 62 years (range, 27–75 years). Among these patients, 80.0% had ECOG PS of 0, and 80.0% presented with metastatic disease at baseline. All patients had received prior platinum-based chemotherapy; additionally, 48.9% had undergone prior immunotherapy, and 15.6% had received two or more prior lines of systemic therapy. The proportion of patients with FR α positivity (defined as FR α expression $\geq 1\%$) was 62.2%. TRAEs were reported in 41 patients (91.1%). Grade ≥ 3 (G3) TRAEs occurred in 24 patients (53.3%), and SAEs were observed in 17 patients (37.8%). The most common TRAEs (incidence $\geq 20\%$) included leukopenia (77.8%), anemia (77.8%), neutropenia (62.2%), nausea (55.6%), thrombocytopenia (53.3%), vomiting (48.9%), lymphopenia (35.6%), pyrexia (26.7%), decreased appetite (26.7%), increased alanine aminotransferase (22.2%), and asthenia (22.2%). No cases of interstitial lung disease were reported. IrAEs occurred in 3 patients (6.7%). TRAEs resulted in dose reduction in 10 patients (22.2%) and treatment discontinuation in 2 patients (4.4%). No treatment-related deaths were recorded. Efficacy was evaluable in 34 patients. The overall ORR was 38.2% (95% CI: 22.2–56.4), and DCR was 70.6% (95% CI: 52.5–84.9). In the BAT8006 (76 mg/m²) + BAT1308 cohort, ORR was 44.4% (95% CI: 21.5–69.2) and DCR was 72.2% (95% CI: 46.5–90.3). In the BAT8006 (84 mg/m²) + BAT1308 cohort, ORR was 31.3% (95% CI: 11.0–58.7) and DCR was 68.8% (95% CI: 41.3–89.0). **Conclusions:** These findings suggest that BAT8006 in combination with BAT1308 may represent an effective therapeutic strategy for advanced endometrial cancer, with a manageable safety profile. Further prospective studies are warranted to validate the efficacy and safety of this combination regimen. Clinical trial information: CTR20242449. Research Sponsor: None.

NAPISTAR 1-01: Results of phase 1 dose escalation of monotherapy with TUB-040, a novel NaPi2b-targeting exatecan ADC, in patients (pts) with platinum-resistant ovarian cancer (PROC).

Toon Van Gorp, Jalid Sehoul, Debra L. Richardson, Rebecca Kristeleit, Shiraj Sen, Juergen Wolf, Valentina Boni, Alex Spira, Alexander Starodub, Bjorn M. Hock, Charles S. Fuchs, Yariv Houvras, Ines Isabel Monteiro Vasconcelos, Antonio Gonzalez Martin; BGOG and University Hospital Leuven, Leuven Cancer Institute, Leuven, Belgium; Department of Gynecology with Center for Oncological Surgery, Charité - Universitätsmedizin Berlin, and North-Eastern German Society of Gynaecologic Oncology (NOGGO) and AGO Study Group, Berlin, Germany; Gynecologic Oncology Department, Stephenson Cancer Center, University of Oklahoma Health Science Center/ SCRI, Oklahoma City, OK; Guy's Cancer Department of Oncology, Guy's and St Thomas' NHS Foundation Trust and Department of Precision and Population Oncology, King's College London, London, United Kingdom; NEXT Oncology Dallas, Dallas, TX; Department I of Internal Medicine, Center for Integrated Oncology, University Hospital Cologne, Cologne, Germany; Phase 1 Clinical Trial Unit, NEXT Oncology, Hospital Universitario Quirón Salud, Madrid, Spain; NEXT Oncology Virginia, Fairfax, VA; The Christ Hospital Cancer Center, Cincinnati, OH; Tubulis, Planegg, Germany; Tubulis Inc., Cambridge, MA; Tubulis, Berlin, Germany; GEICO and Cancer Center Clinica Universidad de Navarra, Madrid, Spain

Background: NaPi2b is overexpressed in high-grade serous ovarian cancer and non-small cell lung cancer (NSCLC). TUB-040 is a DAR8 ADC targeting NaPi2b, comprising a humanized Fc-silenced IgG1 mAb conjugated to exatecan via a cleavable, cysteine-selective, stable, solubility-mediating P5 linker providing excellent stability and biophysical ADC properties. In preclinical studies, TUB-040 induces potent antigen-specific cytotoxicity and demonstrates strong by-stander activity. **Methods:** NAPISTAR 1-01 is a phase 1/2a study in biomarker-unselected pts with PROC and NSCLC. TUB-040 was administered Q3W in dose escalation (range 0.5–5.3 mg/kg) to pts with PROC until progression or unacceptable toxicity. **Results:** As of Dec 1, 2025, 67 PROC pts received TUB-040 for a median of 10 cycles (1–25), median duration of exposure was 213 days (21–546), and 42 (63%) pts were ongoing. Median age: 62 years (34–81), ECOG PS 0–1, median prior lines: 4 (1–7), prior treatment included bevacizumab (84%), PARPi (76%), and mirvetuximab soravtansine (13%). Between dose levels 1.67–3.3mg/kg (N=46), the most common all-grade TEAEs were nausea (78%), fatigue (54%), neutropenia (43.5%), anemia (37%), constipation (34%), diarrhea (33%), vomiting (28%), alopecia (28%), and decreased appetite (26%). Gr $\geq$ 3 heme TEAEs by dose are in Table 1. There were no fatal TEAEs or treatment discontinuations due to TEAEs. Three pts (6.5%) experienced Gr1 pneumonitis, which resolved. Between dose levels 1.67–3.3 mg/kg, 46 pts were evaluated for efficacy. The uORR was 63% [95% CI, 47.5–77.2] and cORR was 60.9% [95% CI, 45.3–75.1] (RECIST; v1.1), including two cCRs. Responses by dose are in Table 1. The majority of responses, 90% (26/29), were ongoing. Disease control rate was 96% [95% CI, 85.2–99.5]. Among CA-125 evaluable pts (N=42), CA-125 response occurred in 81% (34/42) [95% CI, 65.6–91.5]. cORRs were similar across subgroups, including: $\geq$ 4 prior lines of therapy (cORR=71%), prior exposures to bevacizumab (62%), mirvetuximab soravtansine (63%) or PARPi (67%). Five pts with stable disease remain on treatment and eligible for response. **Conclusions:** TUB-040 was well tolerated with promising clinical activity at low doses, offering a potential new treatment option with a differentiated, favorable benefit–risk profile and a wide therapeutic window in PROC pts. Dose optimization is currently ongoing. Clinical trial information: NCT06303505. Research Sponsor: Tubulis GmbH.

	1.67 mg/kg (N=10), n (%)	2.1 mg/kg (N=12), n (%)	2.50 mg/kg (N=12), n (%)	3.3 mg/kg (N=12), n (%)	Total (N=46), n (%)
Complete response	1 (10)	0	1 (8)	0	2 (4)
Partial response	6 (60)	7 (58)	7 (58)	6 (50)	26 (57)
Stable disease	2 (20)	5 (42)	3 (25)	6 (50)	16 (35)
Progressive disease	1 (10)	0	1 (8)	0	2 (4)
Overall responses (PR + CR)	7 (70)	7 (58)	8 (67)	6 (50)	28 (60.9)
Gr $\geq$ 3 neutropenia	0	2 (17)	4 (33)	6 (50)	12 (26)
Gr $\geq$ 3 anemia	0	0	1 (8)	5 (42)	6 (13)
Gr $\geq$ 3 thrombocytopenia	0	0	1 (8)	1 (8)	2 (4)

Phase 1 basket study of telisotuzumab adizutecan (Temab-A, ABBV-400), a c-Met protein–targeting antibody-drug conjugate: Results from patients with platinum-resistant ovarian/primary peritoneal/fallopian tube cancer (PROC).

Gini F. Fleming, Katherine Kurnit, Meredith Pelster, Pamela N. Munster, Raymond Couric Wadlow, Shigehiro Koganemaru, Chiyo Kitagawa, Takako Eguchi Nakajima, Yuta Maruki, Ruth Perets, Akosua Badu-Nkansah, Martha Elizabeth Blaney, Manal Mehibel, Pin Li, Marjilla Seddiq, Anna Shurshalina, Omar N. Al Yacoub, Michael Charles Burns, Shigehisa Kitano; University of Chicago Medicine, Chicago, IL; Sarah Cannon Research Institute, Nashville, TN; Division of Hematology and Oncology, University of California San Francisco, San Francisco, CA; Inova Schar Cancer Institute, Fairfax, VA; Department of Experimental Therapeutics, National Cancer Center Hospital East, Kashiwa, Japan; National Hospital Organization Nagoya Medical Center, Nagoya, Japan; Department of Early Clinical Development, Kyoto University Graduate School of Medicine, Kyoto, Japan; National Cancer Center Hospital, Tokyo, Japan; Rambam Health Care Campus, Technion - Israel Institute of Technology, Haifa, Israel; AbbVie, Inc., North Chicago, IL; Cancer Institute Hospital of JFCR, Tokyo, Japan

Background: c-Met protein is expressed in several tumor types, including PROC, and is linked with poor clinical outcomes. Temab-A comprises a c-Met protein–targeting antibody conjugated to a topoisomerase 1 inhibitor. Phase 1 studies evaluating Temab-A monotherapy in solid tumors showed antitumor activity and a manageable safety profile (NCT05029882, NCT06084481). Here, we report on the efficacy and safety of Temab-A in PROC. **Methods:** This phase 1, open-label basket study (NCT06084481) enrolled patients (pts) ≥ 18 years with histologically/cytologically confirmed recurrent PROC, with Eastern Cooperative Oncology Group performance score ≤ 1 . Pts must have had measurable disease per investigator-assessed RECIST v1.1 criteria, have had platinum-resistant disease, and have received ≥ 1 but ≤ 5 prior lines of systemic therapy, with ≤ 2 prior therapies since the development of platinum resistance. Pts received Temab-A at 2.4 mg/kg every 3 weeks. Primary endpoints were safety and efficacy. **Results:** As of Sept. 11, 2025, 41 pts with PROC received Temab-A. Tumor histology included serous carcinoma (n=26), clear cell carcinoma (n=7), and other rare histologies (n=8). The median age was 64 years (range 43–89), and the median number of prior lines of systemic therapy was 3 (range 1–6). Median follow-up was 5.1 months. Objective response rate (ORR) was 37%. Duration of response, progression-free survival, and overall survival were immature at data cutoff. Efficacy data are shown in the Table. The most common treatment-related adverse events (TRAEs) of any Grade (G) included anemia (59%), nausea (59%), and fatigue (39%); G ≥ 3 TRAEs occurring in $\geq 10\%$ of pts were anemia (34%), neutrophil count decreased (17%), and white blood cell count decreased (15%). The adjudicated interstitial lung disease/pneumonitis rate was 5% (G1, n=2). TRAEs led to treatment discontinuation in 5%, dose interruption in 39%, and dose reduction in 37% of pts. There were no TRAEs that led to death. Temab-A pharmacokinetics in pts with PROC were consistent with those in other tumor types. Exploratory biomarker analyses are ongoing. **Conclusions:** Temab-A had a manageable safety profile and showed antitumor activity in pts with PROC. Clinical trial information: NCT06084481. Research Sponsor: AbbVie Inc.

Efficacy of Temab-A.^a

Outcome	Pts with PROC (N=41)
Best overall response, n (%)	
Complete response	0
Partial response	19 (46)
Stable disease	16 (39)
Progressive disease	5 (12)
Not assessed ^b	1 (2)
Objective response rate ^c , n (%)	15 (37)
95% CI	22, 53
Clinical benefit rate ^c , n (%)	35 (85)
95% CI	71, 94

^aResponses were assessed by investigators per RECIST v 1.1 criteria.

^bPts without postbaseline scan.

^cConfirmed.

CI, confidence interval.

Updated safety and efficacy of puxitatug samrotecan (Puxi-Sam, AZD8205) in patients (pts) with endometrial cancer (EC) or ovarian cancer (OC): Phase 1/2a BLUESTAR study.

Linda R. Mileschkin, Stephanie Gaillard, Robin Guo, Yoichi Naito, Karen Finkelstein, Anna Tinker, Wendel Naumann, Gun Min Kim, Toon Van Gorp, Marloes Van Dongen, Thatthan Sukombooncharoen, Tatsunori Shimoi, Jing Wang, Joo Ern Ang, Theresa Proia, Sarah Cross, Chris Gibbs, Mohamed Zaid, Andreea Varga, Funda Meric-Bernstam; Peter MacCallum Cancer Centre, Melbourne, VIC, Australia; Johns Hopkins School of Medicine, Baltimore, MD; Memorial Sloan Kettering Cancer Center, New York, NY; Department of General Internal Medicine, National Cancer Center Hospital East, Chiba, Japan; Optimum Clinical Research Group, Albuquerque, NM; BC Cancer, Vancouver, BC, Canada; Levine Cancer Institute, Wake Forest School of Medicine, Charlotte, NC; Yonsei University College of Medicine, Seoul, South Korea; Leuven Cancer Institute, University Hospital Leuven and KU Leuven, Leuven, Belgium; Netherlands Cancer Institute, Amsterdam, Netherlands; Department of Internal Medicine, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand; National Cancer Center Hospital, Tokyo, Japan; Hunan Cancer Hospital and The Affiliated Cancer Hospital of Xiangya School of Medicine, Central South University, Changsha, China; Cancer Research UK Cambridge Centre, Cambridge, United Kingdom; AstraZeneca, Waltham, MA; AstraZeneca, Cambridge, United Kingdom; Oncology R&D, AstraZeneca, Cambridge, United Kingdom; The University of Texas MD Anderson Cancer Center, Houston, TX

Background: B7-H4, a transmembrane glycoprotein that negatively regulates T cells, is highly expressed in EC and OC. Puxi-Sam (AZD8205), a B7-H4-directed topoisomerase I inhibitor antibody-drug conjugate, showed manageable toxicity and promising antitumor activity in BLUESTAR (NCT05123482) dose-escalation. Here, we report updated safety and efficacy results as EC and OC expansion cohorts are fully enrolled. **Methods:** Eligible pts were ≥ 18 years old with relapsed/metastatic B7-H4-positive ($\geq 25\%$ tumor cell staining by central immunohistochemistry) EC or OC and an ECOG PS ≤ 1 . Pts had progressed on prior standard-of-care therapy including platinum-based chemotherapy. Pts with EC received Puxi-Sam at 2.0 or 2.4 mg/kg IV Q3W and pts with OC received Puxi-Sam at 1.6 or 2.4 mg/kg IV Q3W. The primary objectives were to assess safety and tolerability; secondary objectives included assessment of antitumor activity per RECIST 1.1. **Results:** As of October 30, 2025, 93 pts with EC received Puxi-Sam at 2.0/2.4 mg/kg and 78 with OC at 1.6/2.4 mg/kg. Pts with EC had a median age (min-max) of 63.5 (52-78)/65 (34-81) years, respectively, and median prior lines of therapy (LOT) was 1. Pts with OC had a median age of 58 (28-79)/59 (35-74) years, respectively, and median prior LOT was 2. Treatment-related adverse events (TRAE) occurred in 92.9%/88.2% of pts with EC (2.0/2.4 mg/kg); 42.9%/47.1% had Grade ≥ 3 TRAEs, most commonly neutropenia (23.8%/31.4%) and anemia (16.7%/27.5%). TRAEs occurred in 87.9%/97.8% of pts with OC (1.6/2.4 mg/kg); 30.3%/75.6% had Grade ≥ 3 TRAEs, most commonly neutropenia (24.2%/60.0%) and anemia (9.1%/37.8%). One pt (1.1%) with EC and 5 (6.4%) with OC discontinued treatment due to TRAEs. Antitumor activity of Puxi-Sam was most notable in EC at 2.4 mg/kg, with an objective response rate (ORR) of 48% and durable response of 7.1 months; at 2.0 mg/kg in EC, ORR was 34.1%. In OC, ORR was 12.1% at 1.6 mg/kg and 24.4% at 2.4 mg/kg (Table). **Conclusions:** Puxi-Sam showed a favorable safety profile and robust antitumor efficacy, supporting continued development, and is now being investigated in the Phase 3 BLUESTAR-Endometrial01 (NCT07044336) study. Clinical trial information: NCT05123482. Research Sponsor: AstraZeneca.

Efficacy (interim response evaluable pts).

	EC 2.0 mg/kg n=41	EC 2.4 mg/kg n=50	OC 1.6 mg/kg n=33	OC 2.4 mg/kg n=45
ORR, % (95% CI)	34.1 (20.1-50.6)	48.0 (33.7-62.6)	12.1 (3.4-28.2)*	24.4 (12.9-39.5)
Complete response, n	1	1	0	0
Partial response, n	13	23	4	11
Stable disease, n	17	21	22	26
Progressive disease, n	10	5	5	8
Median duration of response, months (95% CI)	6.2 (5.5-NE)	7.1 (4.5-NE)	5.8 (2.8-NE)	7.0 (4.0-NE)
Disease control rate at 12 weeks, % (95% CI)	70.7 (54.5-83.9)	86.0 (73.3-94.2)	54.5 (36.4-71.9)	64.4 (48.8-78.1)
Median progression-free survival, months (95% CI)*	7.0 (4.5-9.0) [§]	8.1 (6.8-9.2) [†]	4.8 (2.8-5.8)	5.7 (4.1-9.5)

*2 pts were non-evaluable.

[†]Full analysis set.

[§]n=42.

[†]n=51.

NE, not estimable.

Updated efficacy, safety, and exploratory biomarker analyses of a phase II trial of abemaciclib plus hormonal therapy in recurrent ovarian (OC) and endometrial cancer (EC).

Jordyn Silverstein, Chi-Hong Tseng, Ivonne Grande, Lisa Del Rio, Christine Kivork, Evelyn Irene Garcia, James Chauv, Kari Kubalanza, Gottfried E. Konecny; University of California Los Angeles, Los Angeles, CA; David Geffen School of Medicine at University of California, Los Angeles, Los Angeles, CA; UCLA, Los Angeles, CA; University of California, Los Angeles, Jonsson Comprehensive Cancer Center, Los Angeles, CA; Ronald Reagan UCLA Medical Center, Los Angeles, CA; University of California Los Angeles Translational Oncology Research, Los Angeles, CA

Background: We evaluated abemaciclib with hormonal therapy in patients with estrogen receptor positive (ER+) EC, low-grade serous OC (LGSOC), and selected high-grade serous OC (HGSOC) with CDK4/6 molecular activation features in a single-center, phase II study. Preliminary results demonstrated a 24-week progression-free survival (PFS) rate of 53% in ER+ EC and 60% in LGSOC (2025 SGO Abstract 256). Here, we report the final clinical outcomes and present the first exploratory biomarker analyses from this study. **Methods:** Abemaciclib was administered at 150mg twice daily in combination with hormonal therapy. The primary endpoint was 24-week PFS; secondary endpoints were median PFS (mPFS), disease control rate (DCR), objective response rate (ORR) and safety. Exploratory analyses evaluated efficacy by TCGA molecular subgroups and tumor next-generation sequencing-defined alterations. PFS was estimated using Kaplan–Meier and compared using log-rank. **Results:** As of December 2, 2025, 43 patients (21 ER+ EC, 14 LGSOC, 8 HGSOC) were evaluable, with a median follow-up of 29 months (mos). Median age was 64 (range 24–78) and median prior lines of therapy was 3 (range 1–13). Among 21 patients with ER+ EC, the 24-week PFS rate was 56.1% (95% CI 34.5–77.7), mPFS was 9.0 mos (2.4–11.3), DCR was 63%, and ORR was 21%, including one complete response. There were 13 (62%) NSMP, two (10%) MSI-high, two (10%) TP53-abnormal, one (5%) POLE-mutated, and three without molecular data. The NSMP group had 24-week PFS rate and mPFS of 59.8% (32–87.3%) and 10.4 mos (2.4–21.0), compared with 20.0% (0–55.0) and 1.9 mos (1.7–9.3) in the non-NSMP group ($p=0.02$). Notably, all responses occurred in the NSMP group. The largest difference was observed between patients with CTNNB1mut with a mPFS of 10.4 months (1.9–NR) compared with 5.2 mos (1.7–9.3) in patients with CTNNB1wt ($p = 0.22$). Among 14 patients with LGSOC, the 24-week PFS rate was 71.4% (47.8–95.1), mPFS was 17.5 mos (3.5–NR), DCR was 79% and ORR was 14%, 5 still on treatment at data cut off. The median time on treatment was 10.5 mos (range 1.7–55.4), 4 patients (28%) were on treatment for more than 3 years, the longest still on treatment after 4.6 years. The most common mutation was KRAS in 7 (50%), with no observed differences by KRAS status (KRASmut 11.9 mos [1.9–NR] mPFS, KRASwt 17.5 mos [3.5–NR] mPFS, $p=0.89$). Despite the 8 patients with HGSOC having CDK4/6 activating mutations the 24-week PFS rate was 12.5% (0–35.4) and the mPFS was 1.6 mos (0.3–1.9). No new safety signals were observed across all subgroups. **Conclusions:** Abemaciclib demonstrated promising clinical activity in patients with LGSOC regardless of KRASmut status and in ER+ EC, with the greatest activity observed in the NSMP group and potentially CTNNB1-mutated cases; however, these exploratory subgroups need larger validation. Clinical trial information: NCT04469764. Research Sponsor: Eli Lilly and Company; NIH T32 National Institute of Health T32 fellowship titled Patient-Centered Outcomes Research Training in Urologic and Gynecologic Cancers (PCORT UroGynCan); T32CA251072.

Effects of short-term fasting compared to free diet in ovarian cancer patients: Results from a two-arm pilot randomized trial.

Claudia Marchetti, Carolina Maria Sassu, Laura Vertechy, Giorgia Russo, Elena Giudice, Serena Maria Boccia, Eleonora Palluzzi, Ilary Ruscito, Adriana Ionelia Apostol, Alessandra Battaglia, Arianna Ferrante, Chiara Anna Cimmino, Marco Fossati, Diana Giannarelli, Maria Cristina Mele, Marco Cintoni, Giovanni Scambia, Anna Fagotti; Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Italy; Humanitas San Pio X, Milan, Italy

Background: Short-term fasting (STF) may enhance chemotherapy efficacy by suppressing insulin-driven pro-survival signaling. Clinical data on the metabolic, oncological, and immunological effects of STF in ovarian cancer (OC) are lacking. **Methods:** In this prospective, pilot randomized trial conducted at our center, women with advanced high-grade serous OC receiving carboplatin/paclitaxel-based neoadjuvant chemotherapy (NACT) were randomized to STF (36h before to 24h after each cycle) or a free diet (FD). Eligibility criteria included body mass index ≥ 19 kg/m². Major exclusions were diabetes mellitus, food allergies, and eating disorders. The primary endpoint was insulin reduction after three NACT cycles. Secondary endpoints included oncological outcomes. Exploratory translational analyses assessed immune profiling. Based on 80% power and a two-sided α of 0.05, 17 patients per arm were required. **Results:** Eighteen patients per arm completed three NACT cycles. Baseline clinical characteristics and insulin levels were comparable between groups. After NACT, insulin increased in FD but decreased in STF (+9.76 vs -1.12 μ IU/mL; $p=0.01$). Patients who did not undergo interval cytoreductive surgery (ICS) after three cycles experienced a greater insulin increase than those who underwent surgery (+11.46 vs +1.35 μ IU/mL; $p=0.033$). At ICS, a chemotherapy response score of 3 was more frequent in STF than in FD (58.8% vs 17.6%; $p=0.03$). After a median follow-up of 18 months, median progression free survival (PFS) was longer in the STF arm compared with FD (38 vs 24 months; $p=0.045$). Translational analyses showed that STF limited immunosuppressive subsets correlated with chemotherapy response. **Conclusions:** The primary endpoint was met. STF induced a favourable metabolic shift and was associated with improved pathological response and prolonged PFS, alongside immune modulation. These findings provide a strong rationale for larger randomized trials evaluating STF in OC. Clinical trial information: NCT07039331. Research Sponsor: None.

Surgical outcomes and metabolic parameters before (baseline insulin levels) and after neoadjuvant chemotherapy (insulin levels and variation after NACT) according to the diet regimen.

	Free Diet Arm N=18	Short-Term Fasting Arm N=18	Overall population N=36	P value
ICS				
Never	1 (5.6)	1 (5.6)	2 (5.6)	0.927
After III cycles	12 (66.7)	13 (72.2)	24 (66.6)	
After VI cycles	5 (27.7)	4 (22.2)	8 (22.2)	
CRS				0.030
1	5 (29.4)	1 (5.9)	6 (17.6)	
2	9 (52.9)	6 (35.3)	15 (44.1)	
3	3 (17.6)	10 (58.8)	13 (38.2)	
Insulin Level - Baseline (μ IU/mL) Mean, SD	8.7 (4.99)	10.7 (7.54)	9.71 (6.38)	0.353
Insulin Level - after NACT (μ IU/mL) Mean, SD	18.5 (12.68)	9.59 (6.66)	14.03 (10.95)	0.014
Insulin Variation after NACT (μ IU/mL) Mean, SD	+9.76 (12.89)	-1.12 (11.0)	+4.32 (13.03)	0.010

CRS, Chemotherapy Response Score; ICS, Interval Cytoreductive Surgery; NACT, Neoadjuvant Chemotherapy; SD, Standard Deviation.

Population-based prediction of cardiovascular mortality in gynecologic cancer survivors using machine learning (RISKHEART).

Luís Felipe Leite da Silva, Andreia Cristina de Melo, Jesse Lopes da Silva, Erito Marques de Souza; Universidade Federal Fluminense, Niterói, Brazil; Division of Clinical Research and Technological Development, Brazilian National Cancer Institute (INCA), Rio De Janeiro, Brazil; Universidade Federal Fluminense, Niteroi, Brazil

Background: General-population cardiovascular disease (CVD) risk scores underperform in cancer survivors by failing to capture treatment-related cardiotoxicity. Gynecologic cancer survivors constitute a distinct phenotype defined by older age and heterogeneous therapies. RISKHEART is an oncology-specific, survivorship-oriented model for individualized cardiovascular risk stratification. **Methods:** Women with primary gynecologic malignancies diagnosed between 2000 and 2020 were identified from the SEER program. Predictors included demographics (age, race, marital status) and SEER-available treatment variables (surgery, radiation, and chemotherapy [yes/no]). Model performance was evaluated using AUC, and explainability was assessed via SHAP. **Results:** The study included 104,384 women with gynecologic cancer. CVD-specific death occurred in 4,962 patients, with cumulative incidence rates of 2.44% at 5 years and 4.75% at 10 years. Affected patients were significantly older at diagnosis than those without CVD death (mean age, 75.0 vs 62.5 years; $P < .001$). CVD mortality differed by marital status and race (both $P < .001$), with widowed patients accounting for a higher proportion of CVD deaths (37.3% vs 17.7%). Endometrial cancer accounted for most CVD deaths (58.2%), whereas ovarian cancer was underrepresented among CVDs deaths relative to its prevalence in the overall cohort (15.1% vs 27.8%). In the independent testing cohort, the RISKHEART model demonstrated good discrimination for 10-year cardiovascular mortality (AUC, 0.786). For 5-year cardiovascular mortality, discrimination was slightly higher (AUC, 0.796), with sensitivity of 0.73 and specificity of 0.74. For the 5-year cardiovascular mortality model, discrimination remained elevated across 2000–2009 (AUC, 0.805) and 2010–2020 (AUC, 0.784). Explainability analyses identified age at diagnosis as the dominant predictor of cardiovascular death, with treatment-related variables contributing more prominently to short-term risk and sociodemographic factors increasing in relative importance over longer follow-up. **Conclusions:** In this large population-based cohort of gynecologic cancer survivors, the RISKHEART ML model demonstrated clinically meaningful discrimination for predicting CVD-specific mortality. This approach may support individualized CVD risk stratification and inform survivorship care. Research Sponsor: None.

Feasibility and concordance of a large language model (ChatGPT-5) as a clinical decision support tool in gynecologic oncology tumor boards: A blinded, multi-observer study.

Hatice Asoglu, Sevgul Kara Kose, Oguzhan Kayim, Ali Abaci, Ganim Khatib, Mehmet Ali Vardar, E. Bagir, Derya Gumurdulu, Mehmet Mutlu Kidi, Ertugrul Bayram, Tolga Koseci, Berksoy Sahin, Ismail Oguz Kara; Cukurova University Department of Medical Oncology, Adana, Turkey; Cukurova University Department of Radiology, Adana, Turkey; Cukurova University Department of Gynecologic Oncology, Adana, Turkey; Medical Faculty, Department of Obstetrics and Gynecology, University of Cukurova, and Department of Gynecologic Oncology, Balcali Hospital, Adana, Turkey; Cukurova University Department of Pathology, Adana, Turkey; Department of Medical Oncology, University of Health Sciences, Adana City Training and Research Hospital, Adana, Turkey

Background: The integration of artificial intelligence (AI) into oncology practice is accelerating; however, the reliability of Large Language Models (LLMs) in complex clinical decision-making remains insufficiently validated. This study evaluated the concordance of ChatGPT-5 with multidisciplinary tumor board (MDT) decisions in gynecologic oncology, assessing accuracy, reproducibility across repeated queries, and specific domains of discordance. **Methods:** We analyzed 97 gynecologic cancer cases requiring multimodal treatment planning, evaluated at the Cukurova University Faculty of Medicine Gynecologic Oncology MDT between 2024-2025. Cases included ovarian (n=34), endometrial (n=41), cervical (n=16), and rare tumors (n=6). Standardized clinical summaries (staging, pathology, molecular markers, comorbidities, patient preferences) were input using a structured prompt template. Each case was queried independently at three time points within the same day to assess reproducibility. Recommendations were evaluated by two blinded medical oncologists using a 5-point Likert scale (1=completely inappropriate, 5=completely appropriate). A composite performance score was calculated as $[(\text{mean Likert score})/5] \times 100$. Inter-rater reliability and concordance were analyzed using Cohen's kappa (κ). **Results:** Inter-rater reliability was high for both MDT ($\kappa=0.748$, $p<0.001$) and AI evaluations ($\kappa=0.802$, $p<0.001$). Concordance between MDT and ChatGPT-5 recommendations was fair (Rater 1: $\kappa=0.267$; Rater 2: $\kappa=0.341$), indicating frequent disagreement in specific clinical nuances despite similar overall quality scores. Mean performance scores were significantly higher for MDT versus AI (Rater 1: $94.2\% \pm 4.8$ vs. $89.8\% \pm 6.3$, $p<0.001$; Rater 2: $93.8\% \pm 5.1$ vs. $90.1\% \pm 5.9$, $p<0.001$). Crucially, ChatGPT-5 demonstrated full consistency across three queries in only 38% of cases (37/97), with a mean reproducibility score of 4.10 ± 0.83 . Subgroup analysis revealed superior AI performance in early-stage (I–II) versus advanced-stage (III–IV) disease ($p=0.024$). However, AI performance was significantly inferior in cases requiring genetic testing recommendations ($p=0.019$), fertility-sparing approaches ($p=0.045$), and novel therapeutics integration ($p=0.012$). **Conclusions:** ChatGPT-5 demonstrates potential as a clinical decision support tool but currently lacks sufficient reliability for independent use in complex gynecologic malignancies. Key limitations include inconsistent reproducibility (62% variability across queries), suboptimal performance in advanced-stage disease, and deficiencies in precision oncology domains. Human expertise remains essential to mitigate risks associated with AI-generated inaccuracies, particularly for novel therapeutic integration. Research Sponsor: None.

Quantitative pathology biomarkers for platinum resistance in ovarian cancer.

Durga Vahini Sritharan, Saahil Chadha, Gregory Aaron Breuer, Nichelle Perera, Daniel Fu, Anand Srinivasan, Arihan Gupta, Alessandro Santin, Elena Ratner, Minhua Wang, Katya Papatla, Sanjay Aneja; Yale School of Medicine, Department of Therapeutic Radiology, New Haven, CT; Yale School of Medicine, Department of Pathology, New Haven, CT; Yale School of Medicine, Department of Obstetrics, Gynecology, and Reproductive Sciences, New Haven, CT

Background: Despite serving as the first-line systemic treatment for high-grade serous ovarian cancer, roughly 20% of patients fail to respond to platinum-based chemotherapy. However, there is a paucity of biomarkers which correlate to platinum resistance. Effective biomarkers would allow for individualized risk profiling and early identification of patients who may benefit from treatment escalation. Quantitative pathologic biomarkers have shown prognostic utility in several cancers and offer a potential low-cost approach to address challenges in assessing platinum resistance. We examined the utility of machine learning (ML)-derived pathologic biomarkers in identifying platinum-resistant ovarian cancer. **Methods:** Our multi-institutional dataset included 158 whole-slide images (WSIs) obtained from resection of primary ovarian cancer, with 86 (54%) in the training cohort and 72 (46%) in the validation cohort. Our dataset included 112 (71%) platinum-sensitive and 46 (29%) platinum-resistant WSIs. The CLAM deep learning framework and CONCH visual-language foundation model were utilized to segment tissue, generate 256 x 256 image patches, and extract 512-dimensional features from each patch. Non-linear dimensionality reduction, employing Uniform Manifold Approximation and Projection (UMAP), was applied to cluster training samples, and validation samples were projected onto the learned low-dimensional space. Samples were stratified into predicted-sensitive and predicted-resistant cohorts based on similarity to training-derived clusters, and clinical characteristics were compared using a two-tailed t-test and chi-square tests. **Results:** UMAP analysis identified distinct phenotypes associated with platinum sensitivity and resistance. At the image level, UMAP-defined phenotypes exhibited high predictive ability. Of the predicted-sensitive images in the validation cohort, 79% showed platinum sensitivity. UMAP-defined phenotypes demonstrated moderate patch-level accuracy in identifying platinum-sensitive samples (training accuracy 69%, validation accuracy 65%). Additionally, clinical correlates to pathology-based predictions were investigated. Predicted-resistant patients were significantly older (median age, 69 years [IQR 59.5–76.26] vs. 62 years [IQR 55–68], $p = .021$) and more frequently higher-staged (IIIC/IV 89% vs. 77%, $p = .087$) compared to predicted-sensitive patients. **Conclusions:** ML-derived pathologic biomarkers can aid in the identification of platinum-resistant ovarian cancer. Our future work will evaluate the relationship between quantitative biomarkers and known clinical predictors of platinum resistance, such as CA-125 and the extent of residual disease at cytoreduction. Integrating multimodal biomarkers in clinical decision-making practices will allow for improved risk stratification and individualized treatment for patients. Research Sponsor: None.

Income inequality and cervical cancer: A comparative analysis of demographics and healthcare burden of women in the lowest and highest income quartiles.

Dhruvi Dipakkumar Pathak, Aishwarya Ramesh, Kesha Pathak, Krupa Savani, Kamleshun Ramphul, Saisree Reddy Adla Jala, Fathima Shehnaz Ayoobkhan; Government Medical College, Surat, India; The New York Medical College Graduate Medical Education Program at St. Mary's General Hospital and St. Clare's Health, Denville, NJ; Gujarat Adani Institute of Medical Sciences, Bhuj, India; Kidney Care Clinic, Surat, India; Independent Researcher, Triolet, Mauritius; Mission Hospital, Asheville, NC; Trinity Health Oakland Hospital/Wayne State University, Pontiac, MI

Background: Cervical cancer disproportionately affects women of lower socioeconomic status, yet comprehensive data comparing the demographic profiles and comorbidity burden across income strata remain limited. This study examines differences in patient characteristics, comorbidities, and healthcare utilization between women in the lowest and highest income quartiles hospitalized with cervical cancer in the United States. **Methods:** We identified women hospitalized with cervical cancer in the United States between 2016 and 2022 using ICD-10 codes C53.x in the National Inpatient Sample. Patients were classified into the lowest (0–25th percentile) and highest (76th–100th percentile) income quartiles based on median household income for their residential ZIP code. We compared demographic characteristics including age, race, socioeconomic distribution, and clinically relevant comorbidities across the two groups. Healthcare utilization was evaluated by analyzing length of stay and inflation-adjusted mean hospital charges. **Results:** We identified 88,240 women hospitalized with cervical cancer; 69.7% were in the lowest income quartile and 30.3% in the highest. Women in the highest income quartile were older (mean age 55.45 vs. 52.62 years, $p<0.001$) and incurred higher inflation-adjusted hospital charges (\$88,955 vs. \$76,121, $p<0.001$), though length of stay was comparable (5.64 vs. 5.82 days, $p=0.134$). Significant racial disparities were evident: the highest income quartile had more White patients (63.2% vs. 46.2%) while the lowest quartile had more Black (29.1% vs. 11.1%) and Hispanic (19.0% vs. 12.2%) patients ($p<0.001$). Women in the lowest income quartile had significantly higher prevalence of smoking (40.2% vs. 31.0%), diabetes (19.8% vs. 13.8%), chronic kidney disease (16.6% vs. 14.0%), obesity (14.4% vs. 11.5%), HIV (2.1% vs. 0.9%), depression (12.1% vs. 10.9%), opioid use disorder (3.1% vs. 1.9%), drug abuse (7.7% vs. 3.5%), and alcohol abuse (2.0% vs. 1.4%) (all $p<0.05$). Conversely, the highest income quartile had higher rates of metastatic cancer (41.8% vs. 38.7%, $p<0.001$). No significant differences were observed in dyslipidemia (17.6% vs. 16.7%, $p=0.165$), cachexia (4.3% vs. 4.6%, $p=0.396$), or palliative care utilization (13.0% vs. 13.5%, $p=0.413$). **Conclusions:** Women in the lowest income quartile comprise the majority of cervical cancer hospitalizations and face disproportionately higher rates of modifiable risk factors and comorbidities. Targeted interventions addressing screening access, preventive care, and comorbidity management in low-income populations are essential to reduce health disparities in cervical cancer. Research Sponsor: None.

Treatment patterns and PD-L1 testing among persistent, recurrent, or metastatic cervical cancer patients in the United States community oncology setting.

Elizabeth A. Szamreta, Ila Sruti, Gregory Patton, Jinhong Guo, Chuck Wentworth, Audrey P. Garrett; Merck & Co., Inc., Rahway, NJ; Ontada, Boston, MA; Willamette Valley Cancer Institute and Research Center, The US Oncology Network, Eugene, OR

Background: Pembrolizumab was approved for persistent, recurrent, or metastatic cervical cancer (PRM-CC) among patients (pts) with PD-L1 expression in October 2021. This followed its June 2018 approval for PD-L1-positive recurrent, metastatic pts who progressed after chemotherapy. This real-world study aimed to describe treatment patterns and PD-L1 testing patterns among pts with PRM-CC between 2018-2024. **Methods:** Electronic medical record data from The US Oncology Network identified adult PRM-CC pts diagnosed between July 2018 and July 2022 and followed through June 2024. Persistent disease was defined as either absence of a complete response or provider-documented progression within 90 days following the completion of initial CC-related treatment. **Results:** There were 216 PRM-CC pts eligible for the study. Overall, median age was 55 years and median duration of follow-up was 12.8 months. Overall, 56% (n = 121) of PRM-CC pts had documented PD-L1 testing during the study observation period, of which 78% (n = 94) had a positive result and 7% (n = 8) had undocumented result. Among PD-L1 positive pts without metastatic disease at initial diagnosis (n = 121), 41% were tested after PRM-CC diagnosis date and had a median time from diagnosis to PD-L1 testing of 1.4 months, and 11% were tested prior to PRM-CC diagnosis date. PD-L1 testing increased from 54% to 69% after October 2021, yet 43% of PD-L1+ patients did not receive pembrolizumab after 2021. 12% (8/69) of pts who received pembrolizumab did not have documented PD-L1 testing. Pembrolizumab was received by 27 pts in 1L (pre-2021: 16, post-2021: 11) and 26 patients in 2L pre-2021: 17, post-2021: 9). Most patients had metastatic disease (74%, n = 159), of which 60% (n = 95) presented with metastatic disease at initial diagnosis. Concurrent chemoradiation prior to metastatic disease was received by 38% (n = 81) of pts. The majority of pts with metastatic disease received first line (1L) treatment (n = 86%, n = 137) and 28% (N = 45) of pts initiated 2L treatment. During the first regimen of 1L, 96 pts received a platinum+taxane-containing regimen (+bevacizumab, n = 72). **Conclusions:** Between 2018-2024, many PRM-CC pts were not tested for PD-L1 although biomarker-driven treatments were available. Among those tested, almost half of PD-L1 positive patients did not receive standard-of-care therapy. The current treatment landscape provides a valuable opportunity to standardize and enhance PD-L1 testing in order to optimize treatment selection and support personalized care in this population. Research Sponsor: Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc.

	Overall	Pembrolizumab initiation-Yes	Pembrolizumab initiation-No
PD-L1 Testing	216	69	147
Tested, N(%)	121 (56.0)	61 (88.4)	60 (40.8)
Positive	94 (77.7)	52 (85.2)	42 (70.0)
Negative	19 (15.7)	4 (6.6)	15 (25.0)
No result	8 (6.6)	5 (8.2)	3 (5.0)
Not Tested, N (%)	95 (44.0)	8 (11.6)	87 (59.2)

Radiotherapy use among locally advanced cervical cancer patients (LACC) in the United States community oncology setting.

Elizabeth A. Szamreta, Ila Sruti, Gregory Patton, Jinhong Guo, Chuck Wentworth, Audrey P. Garrett; Merck & Co., Inc., Rahway, NJ; Ontada, Boston, MA; Willamette Valley Cancer Institute and Research Center, The US Oncology Network, Eugene, OR

Background: Brachytherapy with concurrent chemoradiation +/- pembrolizumab is the current standard of care for LACC. American Society for Radiation Oncology (ASTRO) recommends external beam radiation therapy (EBRT)+brachytherapy, and since 2020 has recommended intensity modulated radiation therapy (IMRT) over other forms of EBRT due to reduced toxicity risk. However, real-world evidence is needed to characterize patient outcomes based on the type of radiation received. **Methods:** Electronic medical record (EMR) data from The US Oncology Network identified adult LACC (FIGO 2018 Stage IB3-IVA) patients (pts) diagnosed between July 2018 – July 2022 and followed through June 2024. Pts were stratified by receipt of IMRT or Volumetric Modulated Arc Therapy (VMAT) and brachytherapy during the observation period. Patient characteristics and provider-documented progression were assessed descriptively. **Results:** This study included 250 LACC pts; 73 (29%) pts received IMRT or VMAT, 177 (71%) pts received other forms of EBRT; and 189 (76%) pts received brachytherapy. Overall, 61 pts (24%) received both IMRT or VMAT and brachytherapy. Among the 148 pts who were diagnosed in 2020 or later, 28% received IMRT or VMAT. Disease progression occurred among 14% of IMRT or VMAT pts and 63% of non IMRT or VMAT patients; progression was similar across brachytherapy and non-brachytherapy patients. **Conclusions:** Advanced radiation techniques such as IMRT or VMAT and brachytherapy are associated with improved outcomes for patients with LACC, yet their combined use only occurs among 1 in 4 LACC patients, which is notably less than clinical trials. These findings present an opportunity to broaden adoption of evidence-based radiation strategies, supporting optimal treatment delivery and improved patient outcomes. Research Sponsor: Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc.

	IMRT or VMAT	non IMRT or VMAT	Brachytherapy	Non-brachytherapy
Patient, N	73	177	189	61
Age (yrs, median)	51	54	51	59
Race (White), N(%)	50 (69)	101 (57)	114 (60)	37 (60)
Race (non-White), N(%)	9 (12)	36 (20)	35 (19)	10 (16)
Race (not documented), N(%)	14 (19)	40 (23)	40 (21)	14 (23)
Stage I-II, N(%)	31 (42)	82 (46)	94 (50)	19 (31)
Stage III, N(%)	23 (32)	65 (37)	64 (34)	24 (39)
Stage IVA, N(%)	6 (8)	10 (6)	11 (6)	5 (8)
Progression, N(%)	24 (14)	46 (63)	55 (29)	15 (25)

Targeting stromal FAK signaling to address chemotherapy and immunotherapy resistance in gastric-type endocervical adenocarcinoma.

Ting Peng, Yingchao Zhao, Peng Wu; Department of Obstetrics and Gynecology, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, Hubei, China; Cancer Center, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, Hubei, China

Background: Gastric-type endocervical adenocarcinoma (GAC) is a rare, HPV-independent cervical cancer subtype with profound resistance to standard chemotherapy and radiotherapy and an exceptionally poor prognosis. Unlike HPV-associated cervical cancers, GAC lacks established molecular targets and effective treatment strategies. Whether patients with GAC can benefit from immunotherapy remains unclear, and the biological mechanisms underlying its intrinsic resistance to both cytotoxic and immune-based therapies are poorly understood.

Methods: We established an integrated translational platform incorporating patient-derived GAC cell lines, organoids, and matched primary cancer-associated fibroblasts (CAFs). These models were integrated with multi-omics profiling of clinical specimens, including single-cell RNA sequencing of 58 cervical lesions across disease states, together with molecular and functional validation assays, to systematically characterize tumor-stroma interactions and identify actionable therapeutic vulnerabilities. **Results:** Multi-omics analyses revealed that GAC converges on a pancreatic ductal adenocarcinoma-like transcriptional and microenvironmental program characterized by stromal dominance and therapeutic refractoriness. Mechanistically, GAC tumor cells reprogram the tumor microenvironment through secretion of LAMA3, activating a CD44/ITGB1-dependent FAK signaling axis in CAFs. Stromal FAK activation drives extracellular matrix remodeling and endothelial dysfunction, establishing a profoundly immunosuppressive niche marked by impaired antigen presentation and enrichment of tissue-resident CD8⁺ T cells (CD8⁺ITGA1⁺). This stromal program mechanistically underlies resistance to both chemotherapy and immunotherapy. In patient-derived GAC organoid-based models, FAK inhibition enhanced responses to chemotherapy and immunotherapy in vitro, supporting a translational rationale for FAK-targeted combination strategies. Based on these findings, we initiated a multicenter, phase II clinical trial evaluating the FAK inhibitor IN10018 in combination with nab-paclitaxel and cadonilimab in patients with metastatic, recurrent, or persistent GAC (NCT06654011). **Conclusions:** Gastric-type endocervical adenocarcinoma is a stroma-driven malignancy in which aberrant stromal FAK signaling is a central mediator of resistance to both chemotherapy and immunotherapy. Targeting this stromal dependency provides a compelling therapeutic strategy and directly informs an ongoing phase II clinical trial addressing a critical unmet need in this aggressive disease. Research Sponsor: Non-communicable Chronic Diseases-National Science and Technology Major Project; 2025ZD0544103; National Natural Science Foundation of China; 82372929.

Retrospective study of guideline concordance in cervical cancer screening surveillance by age, race, and ethnicity.

Maeve Fitzgerald Givens, Edward Gemson, Shifa Hossain, Rulla Tamimi; Weill Cornell Medical College, New York, NY; Weill Cornell Medicine - Cornell University, New York, NY; Weill Cornell Medicine, New York, NY

Background: Nearly one in five new cervical cancer cases occur in individuals aged ≥ 65 , with higher incidence among Black women compared to White women. Despite these disparities, evidence guiding screening and surveillance in older women is limited. This study evaluates guideline concordance for follow-up after abnormal cervical cancer screening and examines variation by age, race, and ethnicity. **Methods:** This retrospective cohort study assessed 1,861,906 cervical cancer screening results (2009–2024) from the TrinetX database. Included patients were female, ≥ 21 years old, and had an HPV test or pap smear. Guideline concordance (i.e., colposcopy within one year of high-risk cervical cancer screenings result) was assessed by running logistic regression models by age group, race, and ethnicity. Logistic regression assessed odds of concordant follow-up by age, race, and ethnicity, using women aged 30–39 and non-Hispanic White women as reference groups, respectively. **Results:** Guideline-concordant follow-up varied by age: 56.87% aged 21–29, 58.84% aged 30–39, 56.36% aged 40–49, 53.93% aged 50–65, and 45.80% aged 65+. Compared with women aged 30–39, both younger and older women were significantly less likely to receive guideline concordant follow-up. Women 65+ had 44% lower odds of concordant follow-up (OR= 0.56, 95% CI 0.53 to 0.60, $p<.001$). Guideline-concordant care also varied by race and ethnicity: 51.11% of non-Hispanic Black, 56.65% of non-Hispanic Asian, 60.36% of non-Hispanic White, 58.43% of non-Hispanic Other, and 51.71% of Hispanic patients. Compared to non-Hispanic White women, all other groups had significantly lower odds of follow-up, with non-Hispanic Black women having 30% lower odds (OR = 0.70, 95% CI 0.68 to 0.72, $p<.001$) and Hispanic women having 28% lower odds (OR= 0.72, 95% CI 0.71 to 0.74, $p<.001$) of concordant follow-up. **Conclusions:** Overall, the rate of guideline concordant follow-up after high-risk cervical cancer screening results was low (57.83%) and declined with age, with lowest rates among women ≥ 65 (45.80%). All other age groups had significantly lower odds of concordance than those 30–39, with those 65+ having the lowest odds of concordance. Significant disparities were also observed by race and ethnicity, particularly among non-Hispanic Black and Hispanic women. Further research is needed to assess the decreased surveillance rates after high-risk cervical cancer screening results at the population level and specific attention should be focused on groups who have been under-surveilled. Research Sponsor: None.

Efficacy and safety of cadonilimab (CD) in combination with disitamab vedotin (RC48) or nab-paclitaxel (NP) in the treatment of recurrent or metastatic cervical cancer (r/mCC): A prospective, double-cohort, multicenter, open-label, phase II clinical study.

Min Zheng, Haifeng Gu, Jian Zhou, Jianwei Wang, Lili Liu, Yun Zhou, Baoyue Pan, Qingna Chen, Huijuan He, Weijun Ye, Yan Ding, Li Zhou, Li Sun, Mingyi Li, Xiping Cao, Jin-Xin Bei; Sun Yat-sen University Cancer Center; State Key Laboratory of Oncology in South China; Collaborative Innovation Center for Cancer Medicine, Guangzhou, China; Sun Yat-sen University Cancer Center, Guangzhou, Guangdong, China; Sun Yat-sen University Cancer Center, State Key Laboratory of Oncology in South China, Guangdong Provincial Clinical Research Center for Cancer, Guangzhou, China; Sun Yat-sen University Cancer Center, Guangzhou, China; Department of Pathology, Sun Yat-sen University Cancer Center; State Key Laboratory of Oncology in South China; Guangdong Provincial Clinical Research Center for Cancer, Guangzhou, China; Department of Gynecologic Oncology, Sun Yat-sen University Cancer Center, Guangzhou, China; Gansu Provincial Cancer Hospital, Lanzhou, China; Department of Gynecologic Oncology, Cancer Hospital of Shantou University Medical College, Shantou, China; Cancer Centre/National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital & Shenzhen Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Shenzhen, China; Guangzhou Institute of Cancer Research, the Affiliated Cancer Hospital, Guangzhou, Guangdong, China; State Key Laboratory of Oncology in South China, Collaborative Innovation Center for Cancer Medicine, Guangdong Key Laboratory of Nasopharyngeal Carcinoma Diagn, Guangzhou, China

Background: The prognosis for patients(pts) with r/mCC is poor. The available second-line treatment regimens are limited, highlighting the need for more effective therapies. CD is a dual-target immune checkpoint inhibitor targeting PD-1 and CTLA-4 and RC48 is an antibody-drug conjugate targeting HER2. Here, we report updated results from a phase II study of CD plus RC48 or NP in r/mCC. **Methods:** This is a prospective, multicenter, open-label, phase II trial with two parallel cohorts(AK001). Eligible patients had r/mCC with progression after 1-3 prior lines of chemotherapy. Patients were assigned by HER2 immunohistochemistry (IHC): cohort I (HER2 IHC 1+ - 3+) received CD (6mg/kg) plus RC48 (2.5mg/kg) biweekly; cohort II (HER2 IHC 0) received CD (10mg/kg) plus NP (260mg/m²) triweekly. The primary endpoint of the study was objective response rate (ORR). Key secondary endpoints included duration of response (DOR), progression-free survival (PFS), overall survival (OS) and safety. A Simon's two-stage design was applied, with the ORR from the innovaTV 204 study as a historical control, which was 24%. Assuming the ORR for cohort I is 50% and for cohort II is 40%, with a power of 0.8 and a one-sided α of 0.05, and considering a dropout rate of 10%, the total sample size calculated was 32 for cohort I and 42 for cohort II. **Results:** As of the data cutoff (January 15, 2026), 62 pts were enrolled, including 53 evaluable pts (26 in cohort I and 27 in cohort II) across 5 large academic centers in China. Median follow-up was 12.03 months (range, 1.87 - 26.57). For cohort I, the ORR was 57.7% (95% CI, 36.9% - 76.6%) and median DOR was not reached (95% CI, 3.97 - NR). Median PFS was 8.23 (95% CI, 3.41 - 13.06) months and 12-month PFS rate was 45%. For cohort II, the ORR was 55.6% (95% CI, 35.3% - 74.5%) and median DOR was 4.57 (95% CI, 2.30 - 6.83) months. Median PFS was 5.87 (95% CI, 4.55 - 7.19) months and 12-month PFS rate was 38%. Toxicity was tolerable in both cohorts. Grade 3-4 treatment-related adverse events occurred in 15.4% of pts in cohort I and 21.4% of pts in cohort II. **Conclusions:** Our current results support a potential HER2 expression-guided option for second-line treatment of r/mCC. CD plus RC48 demonstrated favorable efficacy and a manageable safety profile, and may emerge as a novel effective combination for the treatment of HER2 positive cervical cancer. Long-term benefits and further analysis of the role of this combination therapy in r/mCC will be critical to advancing treatment strategies. Clinical trial information: ChiCTR2300076740. Research Sponsor: Akeso Biopharma; RemeGen Co, Ltd.

Antitumor activity assessed by RECIST version 1.1.

	Cohort I (n=26)	Cohort II (n=27)
ORR	15(57.7%)	15(55.6%)
95%CI	36.9 - 76.6	35.3 - 74.5
DCR	24(92.3%)	20(74.1%)
95%CI	74.9 - 99.1	53.7 - 88.9
Best Overall Response		
CR	3(11.5%)	0
PR	12(46.2%)	15(55.6%)
SD	9(34.6%)	5(18.5%)
PD	2(7.7%)	7(25.9%)

Impact of adjuvant sequential chemoradiotherapy on long-term overall survival in early-stage cervical cancer: Final analysis of the STARS phase III randomized trial.

He Huang, Qidan Huang, Hua Tu, Ting Deng, Yanling Feng, Ting Wan, Yanna Zhang, Xinping Cao, Xin Huang, Min Zheng, Jundong Li, Guandi Chen, Hu Li, Liguang Ma, Yi Le Chen, Hongying Yang, Li Li, Shuzhong Yao, Qing Liu, Jihong Liu; Sun Yat-sen University Cancer Center; State Key Laboratory of Oncology in South China; Collaborative Innovation Center for Cancer Medicine, Guangzhou, China; Sun Yat-sen University Cancer Center; State Key Laboratory of Oncology in South China; Collaborative Innovation Center for Cancer Medicine, Guangzhou, Guangdong, China; Sun Yat-sen University Cancer Center, Guangzhou, China; Guangdong Provincial People's Hospital, Guangzhou, China; Pan Yu Central Hospital, Guangzhou, China; Shenzhen Baoan Shajing People's Hospital, Guangzhou Medical University, Shenzhen, China; Hunan Provincial Tumor Hospital, Changsha, China; Peking University Cancer Hospital Yunnan, Yunnan Cancer Hospital, The Third Affiliated Hospital Kunming Medical University, Kunming, China; Cancer Hospital Affiliated To Guangxi Medical University, Nanning, China; Department of Obstetrics and Gynecology, The First Affiliated Hospital, Sun Yat-sen University, Guangzhou, China

Background: The STARS trial (NCT00806117) previously demonstrated that adjuvant sequential chemoradiotherapy (SCRT) significantly improved disease-free survival (DFS) compared with radiotherapy (RT) or concurrent chemoradiotherapy (CCRT) in early-stage cervical cancer patients with pathological risk factors. This pre-specified analysis reports the mature overall survival (OS) results. **Methods:** In this open-label, phase III trial, 1,048 cervical cancer patients with FIGO stage IB1–IIA2 and postoperative pathological risk factors were randomized (1:1:1) to receive RT alone, CCRT (RT with weekly cisplatin), or SCRT (paclitaxel–cisplatin chemotherapy before and after RT). The second endpoint was OS, analyzed by intention-to-treat. Subgroup analyses were performed based on risk stratification: intermediate-risk (deep stromal invasion or lymphovascular space invasion) and high-risk (node-positive or parametrial involvement). **Results:** With a median follow-up of 90 months, SCRT significantly improved OS compared to both RT (10-year OS 89.0% vs 81.0%; HR 0.54, 95% CI 0.35–0.83; $P=0.005$) and CCRT (89.0% vs 83.0%; HR 0.64, 0.41–0.98; $P=0.040$) in intention to treat population. No significant difference was observed in OS between CCRT and RT (HR 0.85, 0.58–1.24; $P=0.404$). The survival benefit of SCRT was consistent across key subgroups: it was most pronounced in intermediate-risk patients (HR 0.54 vs RT, 95% CI 0.31–0.93; $P=0.027$) and showed a clinically meaningful trend in high-risk patients (HR 0.61, 95% CI 0.30–1.24). However, CCRT showed no overall benefit in these risk-based populations but was markedly effective in the subgroup with deep stromal invasion without lymphovascular invasion (HR 0.20 vs RT, 95% CI 0.05–0.85; $P=0.029$) in per-protocol population. SCRT achieved higher protocol completion than CCRT (73.4% vs 62.3%) and was an independent favorable prognostic factor for OS (HR 0.54) in multivariable analysis, along with lymph node metastasis and adenocarcinoma histology. **Conclusions:** The long-term STARS trial update confirms adjuvant SCRT as the optimal strategy, demonstrating both DFS and OS superiority in early-stage cervical cancer with postoperative risk factors. The significant 10-year survival benefit strongly supports adopting SCRT where radiotherapy access is limited. Clinical trial information: NCT00806117. Research Sponsor: Sun Yat-sen University Clinical Research 5010 Program (Number 2007041).

Impact of para-aortic lymphadenectomy on prognosis and quality of life in pre-operative IB2-IIA2 cervical cancer: A multi-center cohort study.

Xinqu Qu, Junjun Qiu Sr., Xingyu Chang, Keqin Hua; Obstetrics and Gynecology Hospital of Fudan University, Shanghai, China

Background: The indication of para-aortic lymphadenectomy (PALD) in preoperative IB2-IIA2 (FIGO 2018) cervical cancer remains unclear. We aimed to access the impact of PALD on the prognosis and life quality in preoperative IB2-IIA2 cervical cancer patients. **Methods:** This cohort study, a target trial emulation, was conducted at the Obstetrics and Gynecology Hospital of Fudan University, including cervical cancer patients with a preoperative stage of IB2-IIA2 from 2019 to 2023 (clinical trial ChiCTR2400092255). Propensity score matching at a 1:1 ratio (PALD versus non-PALD) was applied to balance baseline characteristics. Primary outcomes were progression-free survival (PFS), overall survival (OS), and cancer-specific survival (CSS). Secondary outcomes included perioperative complications and adverse events (AEs). Kaplan-Meier and subgroup analyses were conducted, and Cox proportional hazard models were established. External validation was performed at another three tertiary hospitals in China. **Results:** Of the 2609 patients included, 683 (26.2%) underwent PALD during radical surgery. Propensity score matching yielded a cohort of 1250 patients with balanced covariates. Patients who underwent PALD demonstrated similar PFS (hazard ratio 1.27; 95% CI, 0.89-1.80; $P=0.188$), OS (hazard ratio 1.17; 95% CI, 0.71-1.93; $P=0.544$), and CSS (hazard ratio 1.20; 95% CI, 0.70-2.06; $P=0.512$) as those who did not. Additionally, no significant differences were detected in survival associated with receiving PALD among subgroups defined by lymph node status based on preoperative imaging, the para-aortic lymph node (PALN) metastasis prediction model, and other postoperative pathological risk factors. External validation drew consistent conclusions regarding the effect of PALD on survival. Moreover, the PALD group compared with non-PALD group showed more intraoperative hemorrhage ($P=0.005$), longer operation time ($P=0.004$), and a higher tendency for chylous fistula ($P=0.077$). **Conclusions:** PALD, compared with non-PALD, was not associated with survival benefits for IB2-IIA2 cervical cancer patients yet was associated with increased surgical complications. Research Sponsor: None.

Azenosertib plus paclitaxel for platinum-resistant ovarian cancer: Results from a phase 1b study.

Meena Okera, Catherine M. Shannon, Gary Edward Richardson, Siqing Fu, Angeles Alvarez Secord, Cara Amanda Mathews, Premal H. Thaker, Stephanie V. Blank, Bradley Corr, Yong Sang Song, Zivko Vranjes, Catherine Lee, Dongliang Zhuang, Thejonatha Annareddy, Naomi Molloy, C. Matthias Wilk, Joyce F. Liu; Cancer Research SA, Adelaide, SA, Australia; Mater Hospital Brisbane, South Brisbane, QLD, Australia; Cabrini Hospital, Melbourne, VIC, Australia; The University of Texas MD Anderson Cancer Center, Houston, TX; Duke Cancer Institute, Durham, NC; Women & Infants Hospital of Rhode Island, Legorreta Cancer Center, Alpert Medical School of Brown University, Providence, RI; Washington University of St. Louis, St. Louis, MO; Department of Obstetrics/Gynecology and Reproductive Sciences, Icahn School of Medicine at Mount Sinai, New York, NY; University of Colorado, Aurora, CO; Seoul National University Hospital, Seoul, South Korea; University Clinical Center of Republic of Srpska, Banja Luka, Bosnia and Herzegovina; Zentalis Pharmaceuticals, San Diego, CA; Dana-Farber Cancer Institute, Boston, MA

Background: Most patients (pts) with ovarian cancer develop platinum-resistant disease following surgery and platinum-based chemotherapy and have a poor prognosis. Paclitaxel (PAC) monotherapy is the most efficacious chemotherapy for platinum-resistant ovarian cancer (PROC) but clinical benefits require further improvement. Azenosertib (Azeno) is a potentially best-in-class, novel, selective and orally bioavailable small molecule inhibitor of the WEE1 tyrosine kinase. Herein we report results from a Phase 1b study of Azeno plus PAC for PROC. **Methods:** MUIR (NCT04516447) is an open-label Phase 1b study evaluating the safety, efficacy and preliminary clinical activity of Azeno plus chemotherapy (Part 1 dose escalation) for PROC. Eligible pts were aged ≥ 18 years, had ECOG PS score ≤ 2 , histologically/cytologically confirmed high-grade serous epithelial ovarian, fallopian tube, or peritoneal carcinoma, and measurable disease per RECIST v1.1; pts had received 1–4 prior lines of systemic therapy and had platinum-resistant disease. Pts were assigned to 1 of 4 cohorts: carboplatin, gemcitabine, pegylated liposomal doxorubicin, or PAC (80 mg/m² IV on Days 1, 8 and 15 of 28-day cycles). Azeno plus PAC is the focus of this analysis where Azeno was orally administered 200 mg (continuously) or 200, 250 and 300 mg (intermittently 5 days on, 2 days off [5:2]) for 28-day cycles. Primary objectives were safety and tolerability. Clinical activity was a key secondary objective assessed by objective response rate (ORR) and duration of response (DOR) per RECIST v1.1, and progression-free survival. Exploratory objectives included analysis of baseline tumor and plasma biomarkers with optional biopsies/blood plasma. **Results:** As of December 1, 2025, 46 pts received Azeno (continuously 200 mg, n=7 and intermittently 5:2: 200 mg, n=15; 250 mg, n=12; 300 mg, n=12) plus PAC. Median age was 66 years (range 45–83), median number of prior lines of therapy was 2 (range, 1–4), and all pts received prior PAC. Most common treatment related adverse events (TRAEs) were fatigue (61%), anemia (59%), nausea (52%), and neutropenia (50%); most frequent grade ≥ 3 TRAEs were neutropenia (30%) and anemia (20%). Serious TRAEs occurred in 20% of pts. Overall, confirmed ORR was 39.1% (95% CI, 25.1–54.6) with a median DOR of 5.6 months (95% CI, 5.6–9.2) (Table). **Conclusions:** Azeno plus PAC showed promising clinical activity and tolerability in pts with PROC. ORR and median DOR were improved when compared historically with PAC monotherapy supporting the continued evaluation of this regimen in PROC and other indications. Clinical trial information: NCT04516447. Research Sponsor: Zentalis.

OR and median DOR.

	Azeno 200 mg + PAC (n=7)	Azeno 5:2 200 mg + PAC (n=15)	Azeno 5:2 250 mg + PAC (n=12)	Azeno 5:2 300 mg + PAC (n=12)	All (N=46)
ORR, % (95% CI)	57.1 (18.4–90.1)	20.0 (4.3–48.1)	50.0 (21.1–78.9)	41.7 (15.2–72.3)	39.1 (25.1–54.6)
Median DOR, months (95% CI)	7.8 (5.6–NE)	5.6 (3.7–NE)	9.2 (3.8–NE)	5.6 (5.2–NE)	5.6 (5.6–9.2)

NE, not evaluable.

Global disparities in current clinical trials in cervical cancer.

Sneha Ahuja, Carl Jay Jainar, Sara Moufarrij, Edward Christopher Dee, Luisa Jacomina; Memorial Sloan Kettering Cancer Center, New York, NY; Benavides Cancer Institute, University of Santo Tomas Hospital, Manila, Philippines; Department of Radiation Oncology, Memorial Sloan Kettering Cancer Center, New York, NY; Department of Radiation Oncology, Benavides Cancer Institute, University of Santo Tomas Hospital, Manila, Philippines

Background: Cervical cancer is one of the most disproportionately distributed cancers worldwide, with highest incidence and mortality rates occurring in low- and middle-income countries (LMICs). Although clinical trials provide the crucial foundation for the development of standards of care, oncology research is disproportionately concentrated in high-income settings. **Methods:** We assessed the current global landscape of cervical cancer clinical trials to determine whether trial activity aligns with disease burden and to characterize various disparities in trial representation. Interventional phase II and III cervical cancer clinical trials registered on ClinicalTrials.gov between January 1, 2014, and December 31, 2025, were identified. Trials were further categorized by intervention class, patient population, funding source, and location. Representation of trials in relation to disease burden for cervical cancer was determined using trial-to-age-standardized incidence rate (ASIR) from Global Cancer Observatory estimates. Countries were classified by World Bank Income Level and disease burden, where high burden countries had an ASIR above the global ASIR of 14.1. Non-parametric statistical tests were used to compare trial-to-ASIR ratios across groups. **Results:** A total of 269 eligible trials were included. Most studies were phase II (62.5%) and evaluated systemic or combination therapies (83.6%). The majority of trials were institutionally funded (55.0%), with industry sponsorship accounting for 33.5% of studies. Clinical trial activity was concentrated in a small number of countries, with single-country trials conducted predominantly in China (60.2%) and the United States (13.0%), while multinational trials were largely conducted in high-income countries. When adjusted for disease burden, most high-burden countries had few or no trials relative to incidence, resulting in significantly lower trials per ASIR compared with non-high-burden countries ($P < .001$). Significant disparities were also observed across income groups, with high-income countries demonstrating substantially higher trial-to-ASIR ratios than lower-income countries ($P < .001$). **Conclusions:** The global distribution of cervical cancer clinical trials remains misaligned with disease burden, with high-burden and lower-income countries underrepresented in research participation. Funding patterns and trial sponsorship may further influence where trials are conducted. Addressing these disparities will be essential to ensure equitable evidence generation and improve global cervical cancer care. Research Sponsor: None.

Genomic landscape and patient demographics in endocervical adenocarcinoma: Insights from the AACR Project GENIE.

Rechuma Hafter, Elazar Gaon, Akaash Surendra, Suraj Puvvadi, Beau Hsia, Abubakar Tauseef; Hunter College CUNY, New York, NY; Hunter College, New York, NY; Arizona State University, Tempe, AZ; Creighton University School of Medicine (Phoenix Regional Campus), Phoenix, AZ; Department of Medicine, Creighton University Medical Center, Omaha, NE

Background: Endocervical Adenocarcinoma (EA) makes up 20–25% of cases of cervical cancer, and has an 80–90% association with HPV infection. Treatment outcomes of EA have significant disparities: cases of EA arising from HPV have a much higher survival rate than survival rate for non-HPV-related EA. While survival outcomes with modern treatments such as radical hysterectomy are positive for HPV associated cases, increasing frequency of diagnosis and treatment heterogeneity, along with variability in diagnostic timing emphasize the need to define molecular drivers for targeted therapies. Using the AACR GENIE database, this study characterizes EA's mutational landscape to identify genetic markers and therapeutic targets. **Methods:** The American Association for Cancer Research Project Genomics Evidence Neoplasia Information Exchange database was accessed using cBioPortal (v18.0–public) on November 29, 2025 to identify all patients with EA. The most common somatic point mutations, demographic correlations, and mutual exclusivities were analyzed using a two-sided T-test and non-parametric tests, with Benjamini–Hochberg false discovery rate correction. **Results:** This study included 257 samples from 245 patients. The patient cohort was 61.2% non-Hispanic and 13.9% Hispanic. The cohort was 10.2% Asian, 61.2% White, 4.1% Black, and 12.2% unknown/other patients. A majority of the samples used were obtained from primary tumors (60.3%), while 80 (31.1%) were from metastatic tumors. The most common mutations were identified in PIK3CA (n=68; 26.4%), TP53 (n=51; 19.8%), KRAS (n=41; 15.9%), SMAD4 (n=37; 14.4%), ERBB2 (n=35; 13.6%), ARID1A (n=32; 12.4%), KMT2D (n=26; 10.1%), GNAS (n = 26; 10.1%), ERBB3 (n = 23; 8.9%), KMT2C (n = 21; 8.1%), STK11 (n = 20; 7.8%), MED12 (n = 18; 7.0%), and ATM (n = 17; 6.6%). Several mutations were uniquely observed in Black patients, HFE, RAD54B, ADAMTS20, ADGRB3, and BCL3, with n = 1 for each observed mutation. Among exclusively primary tumor samples, the HSD3B2 mutation was identified (n = 1). RXRA (p < 0.05), TBX3, and TET1 (p > 0.05) mutations with n = 3 each were exclusively observed in the metastatic samples. Frequencies of recurrent alterations in key genes such as KRAS (15.2%) and PRKDC (7.5%), showed substantial overlap and no significant differences between the groups. No significant mutual exclusivity patterns were identified among profiled genes. **Conclusions:** To the best of our knowledge, this is the first GENIE database analysis of EA, addressing a significant knowledge gap regarding its genomic landscape. These findings suggest PIK3CA and TP53 as targets for targeted inhibitors or immunomodulators. Further research is warranted to validate these genomic associations and translate them into precision medicine therapeutics for patients with endocervical adenocarcinoma. Research Sponsor: None.

GT101 autologous TIL therapy in patients with recurrent and metastatic cervical cancer: A phase 1 study.

Pin Wang, Haifeng Qin, Yongsheng Wang, Yuyao Yi, Fang Gao, Dongling Zou, Yongsheng Li, Xiubao Ren, Dongmei Ji, Jian Zhang, Shasha Wang, Zhen Zeng, Jing Yu, Liqing Ma, Lili Lu, Wensheng Huang, Bowen Li, Derun Shen, Yanbin Liu, Yarong Liu; University of Southern California, Los Angeles, CA; The Fifth Medical Centre of Chinese PLA General Hospital, Beijing, Beijing, China; West China Hospital of Sichuan University, Chengdu, Sichuan, China; Gynecological Oncology Center, Chongqing University Cancer Hospital, Chongqing, China; Phase I Clinical Trial Center, Chongqing University Cancer Hospital, Chongqing, China; Tianjin Medical University Cancer Institute and Hospital, Tianjin, China; Fudan University Shanghai Cancer Center, Shanghai, China; Grit Biotechnology, Shanghai, China

Background: Adoptive cell therapy with autologous TILs has shown durable clinical benefit in selected advanced solid tumors after progression on standard therapies. We report results from a phase I, open-label, single-arm, multicenter trial (NCT05430373) evaluating GT101 in patients with recurrent or metastatic cervical cancer. Primary objectives were safety; second objectives included preliminary efficacy and PK. **Methods:** Eleven patients with recurrent or metastatic cervical cancer received a lymphodepletion regimen followed by GT101 infusion and high-dose IL-2. The primary endpoint was safety, including treatment-emergent adverse events (TEAEs), serious adverse events (SAEs) and adverse events (AEs), graded per CTCAE v5.0. Secondary endpoints included objective response rate (ORR), disease control rate (DCR), progression-free survival (PFS), duration of response (DoR), and overall survival (OS), assessed by RECIST v1.1. Flow cytometry of immune cells and T cell receptor (TCR) sequencing were performed on peripheral blood samples collected from patients before and after treatment. **Results:** As of September, 2025, 11 patients were treated (median age was 48 years; median two prior lines of therapy). Following FC lymphodepletion, patients received GT101 at doses $\geq 5 \times 10^9$ viable cells (median 4.1×10^{10}), followed by high-dose IL-2 (600,000 IU/kg, up to 6 doses). Most AEs were Grade 1-2. Grade ≥ 3 AEs were primarily related to lymphodepletion and IL-2, and included lymphopenia, leukopenia, neutropenia, anemia, pyrexia, and thrombocytopenia; most resolved or improved to Grade ≤ 2 within 14 days. The ORR was 45.5% (5/11), with DCR of 90.9% (10/11). Median DoR was 6.4 month. Four patients (36.4%) achieved confirmed PR, one patient (9.1%) achieved a CR, and five patients (45.5%) had stable disease (SD). Median PFS was 4.83 months; OS follow-up is ongoing. One patient with stage IIIC2 cervical squamous cell carcinoma achieved a confirmed CR lasting 14.5 months, with tumor burden reduced from a baseline sum of diameters of 71.57 mm to complete resolution by Week 12. Pharmacokinetics and Correlation Analyses: Peripheral blood analyses demonstrated peak circulating T cells 5-7 days post-infusion, followed by contraction to near-baseline by two weeks. Responders exhibited lower proportions of CD39⁺PD-1⁺ T cells. TIL infusion increased T-cell clonal diversity in all patients, with greater expansion observed in non-responders who has lower baseline diversity; persistence of TIL-derived clones did not differ consistently between groups. **Conclusions:** GT101 demonstrated a manageable safety profile with no treatment-related SAEs or dose-limiting toxicities and showed clinically meaningful and durable antitumor activity in recurrent or metastatic cervical cancer. These findings support further clinical development, and a pivotal phase II study is ongoing. Clinical trial information: NCT05430373. Research Sponsor: None.

Neoadjuvant chemotherapy and individualized de-escalation surgery for fertility preservation in stage IB1-IIA2 cervical cancer: A multicenter prospective study (FIND study).

Yanling Feng, Yuanming Shen, He Huang, Ting Deng, Yun Zhou, Xuemei Li, Ling Xi, Chuyao Zhang, Qidan Huang, Ting Wan, Hua Tu, Jieping Chen, Zejian Lin, Wenjing Wang, Jihong Liu; Sun Yat-sen University Cancer Center; State Key Laboratory of Oncology in South China; Collaborative Innovation Center for Cancer Medicine, Guangzhou, Guangdong, China; Women's Hospital, School of Medicine, Zhejiang University, Hangzhou, China; State Key Laboratory of Oncology in South China, Collaborative Innovation Center for Cancer Medicine, Department of Gynecologic Oncology, Sun Yat-sen University Cancer Center, Guangzhou, China; Sun Yat-sen University Cancer Center; State Key Laboratory of Oncology in South China; Collaborative Innovation Center for Cancer Medicine, Guangzhou, China; Department of Gynecologic Oncology, Sun Yat-sen University Cancer Center, Guangzhou, China; Department of Gynecologic Oncology, Liaoning Cancer Hospital, Shenyang, China; Department of Gynecologic Oncology, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China; Sun Yat-sen University Cancer Center, Guangzhou, China; Sun Yat-sen University Cancer Center, Guang Zhou, China

Background: Radical trachelectomy (RT) has long been the standard fertility-sparing surgery (FSS) for early-stage cervical cancer (most validated for tumor $<2\text{cm}$), produced satisfied oncologic outcomes but adverse pregnancy outcomes. Neoadjuvant chemotherapy (NACT) offers a potential pathway for tumor downstaging, which may further expand the population eligible for FSS. Based on this, this study aimed to evaluate the oncologic and reproductive outcomes of an individualized, NACT-based fertility-preserving strategy in patients with early-stage cervical cancer (FIGO 2018 IB1–IIA2) (CSEM009, NCT02624531). **Methods:** This prospective, non-randomized clinical study enrolled patients aged 18–40 years with pathologically confirmed stage IB1–IIA2 squamous, adenocarcinoma, or adenosquamous carcinoma and a strong desire for fertility preservation. All patients underwent pretreatment pelvic MRI. Patients with a baseline tumor diameter $<1\text{ cm}$ proceeded directly to simple trachelectomy (ST). Those with tumors $\geq 1\text{ cm}$ received 2–3 cycles of platinum-based NACT. Individualized surgery was performed based on Post-NACT MRI: cervical conization (CON) for complete response, ST for residual disease $\leq 2\text{ cm}$, and RT for residual disease 2–4 cm. Lymph node assessment involved sentinel lymph node biopsy (SLNB) or systematic lymphadenectomy. Primary end-points were 5-year overall survival (OS), 5-year progression free survival (PFS), and reproductive outcomes. **Results:** From June 2015 to June 2023, 99 eligible patients were enrolled. Among them, 84 received NACT, and 80 ultimately underwent FSS. Median follow-up duration was 67 months (range: 7–122). For the entire cohort of 99 patients, 5-year PFS and OS were 88.9% and 93.9%, respectively. In the FSS group ($n=80$), 5-year PFS and OS were 91.3% and 96.3%. In FSS patients, univariate analysis identified lymphovascular space invasion (LVSI) as significantly associated with recurrence and mortality ($p<0.05$). Patients with initial tumors $\leq 2\text{ cm}$ ($n=42$), 2–4 cm ($n=29$), and $\geq 4\text{ cm}$ ($n=9$) had 5-year PFS rates of 95.2%, 86.2%, and 88.9%, and 5-year OS rates of 97.6%, 93.1%, and 100%, respectively. Nineteen patients failed to undergo FSS with 5-year PFS 78.9% and 5-year OS 84.2%. Of 40 FSS patients attempting pregnancy, 19 (47.5%) achieved at least one pregnancy, resulting in 17 cumulative deliveries: 3 after conization and 14 after ST. No successful pregnancies occurred after RT. **Conclusions:** This prospective study demonstrates that fertility-sparing strategy involving NACT and individual less radical FSS provides favorable long-term oncologic safety and meaningful reproductive potential in patients with FIGO 2018 IB1–IIA2 cervical cancer. Clinical trial information: NCT02624531. Research Sponsor: None.

Quality of life outcomes following hypofractionated radiotherapy in locally advanced cervical cancer.

David Francisco Cantu De Leon, Lenny Nadia Gallardo Alvarado, Guillermo Moreno-Flores, Rebeca Ramirez-Morales, Ma Delia Perez-Montiel Gomez, Carlos Pérez Plasencia, Didier Prada, Isabel Sollozo-DuPont; Instituto Nacional de Cancerología, Mexico, DF, Mexico; Instituto Nacional de Cancerología, Mexico City, Mexico; FES-Iztacala, Mexico, DF, Mexico; Icahn School of Medicine at Mount Sinai, New York, NY; Instituto Nacional de Perinatología, Mexico, DF, Mexico

Background: Cervical cancer remains a significant global health burden, particularly in low- and middle-income countries where access to radiotherapy is often limited. While concurrent chemoradiotherapy is the standard of care, hypofractionated radiotherapy has emerged as a potential strategy to improve treatment efficiency without compromising outcomes. Our purpose was to assess the impact of hypofractionated radiotherapy on quality of life in comparison with conventional fractionation in patients with locally advanced cervical cancer.

Methods: Health-related quality of life was evaluated using EORTC QLQ-C30 and QLQ-CX24 questionnaires in patients with FIGO stage IB3–IIIC1 cervical cancer enrolled in a phase II randomized trial. All patients received concurrent chemotherapy and were assigned to either standard external-beam radiotherapy (50 Gy in 25 fractions) or hypofractionated radiotherapy (37.5 Gy in 15 fractions), followed by radical hysterectomy with bilateral pelvic lymphadenectomy. QoL scores were calculated using standard EORTC methodology. Higher scores indicate better functioning or greater symptom burden, and changes were interpreted based on established thresholds for clinical relevance. Outcomes were compared between groups across predefined time points using ANOVA. Statistical significance was defined as $p < 0.05$. **Results:** A total of 91 patients were included (49 standard fractionation, 42 hypofractionation). No significant differences in global QoL were observed between treatment groups. However, QoL varied significantly over time, with the greatest deterioration occurring between completion of concomitant chemoradiotherapy and surgery. Quality-of-life scores recovered to baseline levels by three months after treatment completion in both groups. **Conclusions:** Hypofractionated radiotherapy was not associated with worse quality-of-life outcomes compared with conventional fractionation. These findings support hypofractionation as a feasible alternative for locally advanced cervical cancer, particularly in resource-limited settings. Further studies with larger cohorts and longer follow-up are warranted to confirm these results. Clinical trial information: NCT03750539. Research Sponsor: None.

Comparison of key health-related quality-of-life domains by treatment arm.

Domain	BaselineStd* / Hypo&	End QT/RTStd / Hypo	Post-SurgeryStd / Hypo	3 MonthsStd / Hypo	p value
Global Health Status / QoL	66.9 (23.7) / 65.8 (21.0)	65.7 (20.7) / 64.6 (17.0)	70.5 (18.5) / 64.0 (18.3)	79.1 (12.5) / 74.4 (21.7)	0.497
Physical Functioning	81.6 (19.7) / 88.0 (14.6)	80.2 (18.6) / 82.2 (20.8)	75.2 (20.5) / 79.0 (17.5)	86.4 (19.4) / 86.8 (13.6)	0.216
Nausea and Vomiting	87.1 (21.2) / 83.8 (27.8)	72.4 (30.5) / 67.2 (28.5)	82.6 (23.3) / 88.3 (21.0)	94.8 (10.2) / 91.1 (16.8)	0.001
Diarrhea	90.1 (15.5) / 86.6 (28.5)	77.7 (20.6) / 67.7 (28.3)	81.4 (21.3) / 84.4 (25.8)	92.5 (14.1) / 91.1 (14.9)	0.001

Mean (SD) scores using EORTC QLQ-C30 and CX-24.

Trends in rural-urban disparities in U.S. cervical cancer mortality before and after the HPV vaccine introduction: A CDC analysis, 1999-2023.

Jasvinder Kumar, Hameer Ali, Ayesha Mudassar, Umm-e- Aimen, Anushah Faheem Ilyas, Zain Ali, Noor Fatima, Muhammad Idrees, Steve Oguguo Nwokeocha, Jeffrey P. Allerton; Bassett Medical Center/Bassett Healthcare Network, Cooperstown, NY; Chandka Medical College, Larkana, Pakistan; King Edward Medical University, Lahore, Pakistan; Faisalabad Medical University, Faisalabad, Pakistan; Karachi Medical and Dental College, Karachi, Pakistan; Wah Medical College, Wah, Pakistan; Peoples University of Medical and Health Sciences for Women, Nawabshah, Pakistan; Hematology & Oncology, University of Washington/ Fredhutch Cancer Institute, Seattle, WA; PGY 2 IM, Bassett Medical Center, Cooperstown, NY; Bassett Medical Center, Cooperstown, NY

Background: Cervical cancer mortality has declined in the United States following the introduction of HPV vaccination. However, disparities by urbanization, geography, and race may persist. Rural women remain up to 40% more likely to die from cervical cancer. Understanding rural-urban trends is essential to guiding equitable prevention strategies. **Methods:** CDC WONDER mortality data for females ≥ 15 years with cervical cancer (ICD-10 C53) were analyzed. Age-adjusted mortality rates (AAMR) per 100,000 population were analyzed. Urbanization data were available till 2020 and were used for urban-rural stratification (NCHS classification). Temporal trends were assessed using joint point regression to determine average annual percent change (AAPC). **Results:** Between 1999 and 2023, 102,205 cervical cancer deaths were identified. The overall AAMR declined from 1.52 to 1.28 during the pre-vaccine era (1999–2005; AAPC = -2.95% , 95% CI -4.0 to -1.8) and further to 1.09 during the post-vaccine era (2006–2023; AAPC = -0.86% , 95% CI -1.0 to -0.7). Rural-urban mortality (AAMR) ratio increased in post-vaccine era from 1.13 vs 1.15 with 1.47% increase in disparity. By urbanization, declines were greatest in central metropolitan areas (AAMR 1.72 to 1.48 pre-vaccine; 1.14 post-vaccine; AAPC = -1.40% , 95% CI -1.6 to -1.2), while small metro (1.36 to 1.29 pre-vaccine; 1.11 post-vaccine; AAPC = -0.93% , 95% CI -1.2 to -0.6) and micropolitan areas (1.70 to 1.44 pre-vaccine; 1.32 post-vaccine; AAPC = -0.34% , 95% CI -1.3 to 0.6) showed slower improvement which widened mortality gap. Subgroup analyses showed the steepest mortality declines among women aged ≥ 75 years (AAPC = -3.66%), among Black women (AAPC = -2.81%), and in the Northeast region (AAPC = -2.16%). **Conclusions:** U.S. cervical cancer mortality declined after the HPV vaccine introduction; however, rural-urban, racial, and regional disparities persisted. Declines were slower in small metropolitan and nonmetropolitan areas and highest among Black individuals, underscoring the need for targeted vaccination, screening efforts and access-to-care. Research Sponsor: None.

HPV-stratified tissue factor expression and multi-omic correlates of overall survival after tisotumab vedotin in cervical cancer.

Shaina Bruce, Sharon Wu, Wen Gu, Michael Dean, Theodore Nicolaides, Ninad Kulkarni, Ryan Jaehne, Kathleen N. Moore, Britt Kristina Erickson, Robert Louis Coleman, Ramez Nassef Eskander, Rebecca Christian Arend, Joyce F. Liu, Thomas J. Herzog, Matthew James Oberley; Penn State Health, Hershey, PA; Caris Life Sciences, Phoenix, AZ; CARIS Life Sciences, Phoenix, AZ; National Cancer Institute, National Institutes of Health, Bethesda, MD; Caris Life Sciences, Irving, TX; CARIS Life Sciences, Irving, TX; Fred and Pamela Buffett Cancer Center at the University of Nebraska Medical Center, Omaha, NE; University of Minnesota, Masonic Cancer Center, Minneapolis, MN; Texas Oncology, US Oncology Research, The Woodlands, TX; UC San Diego Moores Cancer Center, La Jolla, CA; The University of Alabama at Birmingham, Birmingham, AL; Dana-Farber Cancer Institute, Boston, MA; GOG Foundation and University of Cincinnati Cancer Center, Cincinnati, OH

Background: Cervical cancer (CxC) is heterogeneous, and the impact of HPV status on outcomes with tisotumab vedotin (TV; tissue factor [TF/F3]–targeted ADC) remains incompletely defined. We evaluated HPV–stratified associations between TF expression and real-world overall survival (OS) after TV and explored molecular correlates of long vs short survival. **Methods:** 274 CxC patients who received TV (HPV+, n=106; HPV–, n=45) underwent DNA and RNA sequencing. HPV16/18/31/33/45 status was determined from whole exome sequencing (WES). Real-world OS was calculated from first TV claim to death/last contact. Hazard ratio (HR) was estimated by Cox proportional hazards, with p-value using log-rank test. TFH was defined as TF (F3) expression (RNA-seq normalized expression) $\geq$ the cohort-specific median (median split) among TV-treated cases with available data. For transcriptomic comparisons, LS (long survival) and SS (short survival) were defined as above-median vs below-median OS after TV within each HPV stratum, respectively. **Results:** Among TV-treated patients with available TF/OS data, TFH vs TFL showed no statistically significant OS difference in the overall cohort (n=195; TFH n=98 vs TFL n=97; median OS 11.73 vs 9.79 months; HR 0.765; log-rank p=0.142) or in the HPV+ cohort (n=69; TFH n=35 vs TFL n=34; median OS 10.22 vs 10.35 months; HR 0.602; log-rank p=0.138). In contrast, in the HPV– cohort (n=27; TFH n=14 vs TFL n=13), TFH was associated with improved OS (median OS 21.81 vs 9.79 months; HR 0.251, 95% CI 0.065–0.977; log-rank p=0.032). Transcriptomic profiling suggested HPV–dependent survival: in HPV– patients, LS was enriched for cell-cycle/DDR, and energy metabolism pathways (e.g., p53 pathway NES 1.86; FDR-adjusted p<0.0001), whereas in HPV+ patients, SS was enriched for inflammatory pathways (e.g., interferon- γ response NES –2.25; FDR-adjusted p<0.0001; TNF–NF κ B) and LS for tumor-intrinsic metabolic/drug-handling and coagulation-related pathways (e.g., Xenobiotic metabolism, NES 2.13, FDR-adjusted p=0.0021; Coagulation). In the HPV+ cohort, exploratory genomic correlates of survival included enrichment of ARID1A pathogenic mutations (3/18, 16.7% LS vs 0/41, 0% SS; p=0.0073) and AKT2 amplifications (2/17, 11.8% LS vs 0/39, 0% SS; p=0.0292), consistent with tumor-intrinsic pathway alterations in LS. **Conclusions:** TF expression and HPV status may interact in TV-treated cervical cancer. While TFH was not associated with OS in the overall or HPV+ cohorts, TFH was associated with improved OS in HPV– disease. HPV-stratified transcriptomic analyses further suggest distinct biological contexts of benefit and lack thereof, supporting the need to HPV–stratified biomarker analyses for evaluating TV benefit in CxC, potentially extending to other ADCs, and motivating validation in independent datasets. Research Sponsor: None.

The impact of re-adoption of open radical hysterectomy on postoperative outcomes in the United States: An interrupted time series analysis.

Alex Ede Rosenthal Powers, William Manning, Christina Onyebuchi, Alicia Youssef, Amy Bregar, Jose Alejandro Rauh-Hain, Alexander Melamed; Massachusetts General Hospital, Boston, MA; The University of Texas MD Anderson Cancer Center, Houston, TX

Background: The Laparoscopic Approach to Cervical Cancer (LACC) trial, published in 2018, demonstrated inferior disease-free and overall survival outcomes with minimally invasive radical hysterectomy compared to open surgery for cervical cancer, establishing open radical hysterectomy (ORH) as the standard of care. This study evaluates the impact of the rapid adoption of ORH after publication of the LACC trial on postoperative outcomes. **Methods:** We categorized 2013–2017 as the *pre*-LACC period, 2019–2022 as the *post*-LACC period, and 2018 as the washout period. We included patients who underwent radical hysterectomy for cervical cancer in a Commission on Cancer-accredited program with the highest utilization of ORH (top quartile, > 83%) in the post-LACC period. We fit linear probability models with cluster-robust standard errors to estimate the causal association between ORH adoption, postoperative length of stay, 30-day readmission rates, and 90-day mortality, using pre-LACC trends to estimate a counterfactual outcome for 2019 and comparing these with outcomes from the post-LACC period. **Results:** 2,982 patients were treated in the 107 rapid adopter hospitals. Mean age was 46.5 (SD 12). Most patients were white (67%), followed by Hispanic (14%), and Black (11%). Most patients had grade 1 or 2 (60%) tumors with squamous cell (52%) or adenocarcinoma (40%) histology. Thirty-two percent of patients had positive LVSI and 12% of patients had positive lymph nodes. The proportion of ORH was 45% vs 94% in the pre- vs post-period and ORH utilization was 65 percentage points (p.p.) higher than the estimated 2019 counterfactual ORH utilization. In the pre-period, MIS use increased significantly over time (4.1 p.p. per year, 95% CI 1.9–6.3, $p < 0.001$) while mean length of postoperative stay declined (0.3 days per year, 95% CI 0.1–0.5, $p = 0.003$). Rapid adoption of ORH in 2019 (+65.1 p.p., 95% CI 53.4–76.8, $p < 0.001$) was associated with a 1.7 day (95% CI 1.0–2.5, $p < 0.001$) increase in the duration of postoperative hospitalization, from 1.5 to 3.3 days. There was no significant association with a change in 30-day readmission rates (3.6% pre vs 1.9% post, 1.7 p.p. decrease, 95% CI –5.3 to +1.8, $p = 0.35$). Only 13 patients (0.4%) died within 90 days of surgery over the entire study period, precluding analysis of postoperative mortality. **Conclusions:** Rapid adoption of ORH following the LACC trial was associated with a moderate increase in postoperative length of stay, but no change in 30-day readmission rate. Research Sponsor: None.

Optimal adjuvant therapy for early-stage cervical cancer (ESCC) with intermediate-risk factors: A target trial emulation of GOG-0263 based on the NCDB.

Ifeyinwa Ejisoby-Nwosu, Naba Ali, Kristin Ann Ward, Sarah Dilley, Sagar Anil Patel, Yuan Liu; Emory University, Atlanta, GA; Emory University School of Medicine, Atlanta, GA; Department of Radiation Oncology, Emory University, Atlanta, GA; Department of Biostatistics and Bioinformatics, Emory University, Atlanta, GA

Background: Optimal adjuvant therapy for early-stage cervical cancer (ESCC) patients with intermediate-risk factors remains uncertain, specifically whether the addition of concurrent chemotherapy (CRT) to radiation therapy (RT) confers a survival benefit. The GOG-0263 randomized phase III trial compared adjuvant RT vs CRT in patients with FIGO Stage I-IIA cervical cancer who had undergone radical hysterectomy. We sought to emulate this trial using real-world data from the National Cancer Database (NCDB) to evaluate the benefit of CRT versus RT on overall survival (OS) in intermediate risk ESCC. **Methods:** Using the NCDB, we conducted a target trial emulation of GOG-0263 for patients diagnosed from 2004-2020 with pathologic T1-T2a2 No Mo cervical cancer who underwent radical hysterectomy. Eligible patients had intermediate risk factors, defined as tumor size ≥ 2 cm with lymph-vascular invasion (LVI) or tumor size ≥ 4 cm. OS, defined from the date of definitive surgery, was compared between patients who received adjuvant RT alone versus adjuvant CRT. Kaplan-Meier methods and Cox proportional hazards models, along with an inverse probability treatment weighting (IPTW) schema, were implemented to assess the treatment effect. Subgroup and sensitivity analyses were conducted to identify specific disease characteristics that maximize the benefit of CRT and to evaluate the impact of potential immortal time bias. **Results:** Among 1,171 eligible patients, 537 (45.9%) received CRT and 634 (54.1%) received RT alone, with median ages of 44 years (IQR: 36-55) and 46 years (IQR: 39-57) and median follow-up times of 7.5 years (IQR: 4.8-10.5) and 6.6 years (IQR: 4.2-9.9), respectively. There was no significant difference in OS between CRT and RT in unadjusted (HR 0.94; 95% CI, 0.71-1.25), adjusted (HR 0.89; 95% CI, 0.67-1.18), or weighted analyses (HR 0.88; 95% CI, 0.66-1.17). Five-year OS was similar between groups (86.4% vs. 86.6%). No subgroup demonstrated a significant survival benefit from CRT. **Conclusions:** In this real-world emulation of GOG-0263, addition of concurrent chemotherapy to adjuvant RT was not associated with improved OS for intermediate-risk ESCC. These findings support emerging trial evidence and supplement the conclusion of the GOG-0263 trial. The indication of this study suggests that chemotherapy may be safely omitted in this population under a doctor's careful discretion, thereby potentially reducing treatment-related toxicity and preserving patients' quality of life without compromising survival. These findings highlight the need for improved risk stratification and patient selection to identify those most likely to benefit from treatment intensification with concurrent chemotherapy in addition to adjuvant RT. Research Sponsor: National Cancer Institute/U.S. National Institutes of Health; P30CA138292.

Evaluation of imiquimod treatment outcomes in vulvar melanoma.

Alyssa Osheim, Katherine Riley, Sabrina Zheng, Johana Monzon, Aaron Malekan, Sarah Pasyar, Madeleine Hines Salge, Kelly Nelson; (UT Health Houston) McGovern Medical School, Houston, TX; McGovern Medical School, University of Texas Health Science Center at Houston, Houston, TX; (TTU HSC El Paso) Paul L. Foster School of Medicine, El Paso, TX; Davidson College, Davidson, NC; SUNY Downstate Health Sciences University, Brooklyn, NY; The University of Texas MD Anderson Cancer Center, Houston, TX; Department of Dermatology, The University of Texas MD Anderson Cancer Center, Houston, TX

Background: Vulvar and vaginal melanomas account for approximately 10% of vulvar malignancies and less than 1% of all melanomas. Compared to cutaneous melanoma at other sites, vulvovaginal melanoma is associated with significantly worse outcomes. Wide local excision is the standard treatment for vulvar melanoma, but anatomical challenges and the “field effect” complicate complete resection. The field effect refers to a margin of pre-cancerous intra-epithelial cells extending beyond the visible tumor and is thought to contribute to local recurrence. Imiquimod, an immune-modifying cream indicated for genital warts and some types of early keratinocyte carcinomas, is used off-label as an adjunct therapy to prevent marginal recurrence of vulvar melanoma in situ. Its benefit in this setting remains unclear due to limited outcome data, and it is associated with significant side effects. More research is needed to clarify the role of imiquimod and explore alternative therapies. This case series aims to evaluate recurrence and survival outcomes following imiquimod treatment and inform clinical management in this understudied cancer subtype. **Methods:** Patients were identified by two criteria: (1) confirmed vulvar melanoma and (2) treatment with imiquimod. Cases were drawn from a previously published institutional cohort focused on adjuvant radiation therapy in vulvovaginal melanoma and from MD Anderson’s electronic medical records. Regional progression-free survival and overall survival were defined as study endpoints. Data included demographics, clinical characteristics, and recurrence and mortality outcomes. Kaplan–Meier analysis compared progression-free and overall survival between patients treated with imiquimod and those who were not. **Results:** Among 124 patients, 19 received imiquimod. The imiquimod group showed a modest improvement in regional progression-free survival, but no significant difference in overall survival ($p = 0.1753$ and $p = 0.2775$, respectively). Imiquimod was associated with notable side effects, including burning, itching, and blistering. **Conclusions:** This case series highlights the limited evidence supporting imiquimod as an effective adjunct therapy for vulvar melanoma. Although there was a trend toward delayed regional progression, differences were not statistically significant, and side effects raise concerns about patient quality of life. These findings underscore the need for more effective and tolerable strategies. A systematic review is underway, and multi-institutional efforts aim to expand the dataset. Greater evidence is essential to guide treatment decisions, optimize outcomes, and ensure survivor-centered care in this rare and understudied cancer. Research Sponsor: National Institutes of Health, National Cancer Institute; R25 CA056452.

Association of steroid exposure with overall survival and hypersensitivity reaction risk in paclitaxel-treated patients with gynecologic cancers.

Mohammad Harris Jalili, Benjamin Ascherman, Eun Jeong Oh, Codruta Chiuzan, Sara Kim, Veena S. John; Zuckerberg Cancer Center, Northwell Health, Lake Success, NY

Background: Paclitaxel remains a first-line agent in chemotherapy regimens for gynecologic cancers but is associated with hypersensitivity reactions (HSRs) in up to 40% of patients. Though this risk is largely mitigated by dexamethasone-based premedications, preclinical studies suggest that dexamethasone can induce treatment resistance through enhanced DNA repair capacity, immune suppression, or inhibition of apoptosis, raising concern that pre-treatment could compromise paclitaxel efficacy. Furthermore, the effect of cumulative steroid exposure on survival outcomes remains unknown. This study evaluates the impact of cumulative steroid exposure on overall survival (OS) and explores factors associated with HSRs among paclitaxel-treated patients with gynecologic cancers. **Methods:** This IRB-approved retrospective cohort study included patients with gynecologic malignancies treated with paclitaxel-based chemotherapy at the R.J. Zuckerberg Cancer Center, Northwell Health Cancer Institute, New York, between May 2023 and December 2024. Treatment characteristics and outcomes data were analyzed using univariable and multivariable zero-inflated Poisson regression models for HSRs and Cox regression models for OS. **Results:** A total of 163 patients who completed at least three cycles of paclitaxel-based chemotherapy were included. The median age (range, 38–87) was 66 years. Patients were 49% White, 18% Asian, 17% Black, 6% Hispanic, and 11% other or unknown. Cancer types included endometrial cancer (53%), ovarian/peritoneal (42%), cervical (4%), and vaginal (1%). At initial diagnosis, 30% of patients had AJCC stage I disease, 31% stage II–III, 9% stage IV, and 30% had insufficient staging data. Most patients (85%) were newly diagnosed. Twenty one percent of patients developed at least one HSR. Body surface area, race, and prior exposure to paclitaxel were not independently associated with HSRs. In contrast, stage IV disease at diagnosis was associated with a higher rate of HSR compared with stage I disease, with a rate ratio of 2.83 (95% CI 1.01–7.93; $p=0.048$) after adjustment for key confounders. Cumulative dexamethasone exposure did not impact OS in either univariable or multivariable analyses. **Conclusions:** HSRs occurred in 21% of paclitaxel-treated patients and were independently more common among those with stage IV disease. This suggests that greater disease burden may reflect differences in immune responsiveness that predispose to HSRs. While dexamethasone is commonly used to improve treatment tolerability and reduce the risk of HSRs, cumulative exposure did not impact OS. Further studies are needed to clarify the mechanisms underlying paclitaxel-associated HSR and to define the optimal role of steroid premedication. Research Sponsor: None.

Association of post-treatment vaginal structural changes with psychosexual dysfunction in young cervical cancer survivors: Evidence from a low- and middle-income country.

Suriana Sultana; National Institute of Cancer and Research Hospital, Dhaka, Bangladesh

Background: Vaginal stenosis is a known late side effect of pelvic radiotherapy for cervical cancer. In low- and middle-income countries (LMICs), the extent of vaginal changes and their effects on sexual and emotional health are poorly studied due to cultural stigma and limited counseling. This study examined objective vaginal changes and their association with psychosexual distress among young cervical cancer survivors. **Methods:** This cross-sectional mixed-method study included 300 women aged ≤ 45 years who completed pelvic radiotherapy, with or without surgery and/or brachytherapy, 6–24 months earlier at Delta Hospital and collaborating centers. Participants completed a bilingual interviewer-administered questionnaire on counseling, intimacy, psychosocial distress, and perceived barriers. A standardized clinical examination was used to assess vaginal changes, including vaginal length, elasticity, adhesions, dryness, and dyspareunia, graded using LENT-SOMA and CTCAE v5.0 criteria. Outcomes were compared between women treated with definitive chemoradiation and those who underwent surgery followed by adjuvant radiotherapy $\pm$ brachytherapy. **Results:** The mean post-treatment vaginal length was 4.1 ± 1.2 cm. Reduced vaginal elasticity and adhesions were found in 68% of participants. Severe vaginal shortening (≤ 2 cm) or blind-ending occurred more often in women who received surgery followed by adjuvant radiotherapy and brachytherapy (approximately 40%) compared with those treated with definitive chemoradiation ($p < 0.05$). The psychosexual impact was marked: 80% of women reported no return to penetrative intimacy or regular vaginal dilation, and 85% reported loss of sexual interest. The most common barriers were fear of injury or cancer recurrence (72%), pain during intercourse (65%), sociocultural stigma (48%), and partner separation or dysfunction (36%). Although 52% recalled receiving some counseling, only 15% actively discussed sexual health concerns, and fewer than 10% accessed specialized psychosexual care. **Conclusions:** Objective vaginal shortening and fibrosis are strongly linked to psychosexual distress and avoidance of intimacy among young cervical cancer survivors, especially after multimodality treatment. In low- and middle-income countries, unstructured counseling alone is not sufficient. Survivorship care should include regular vaginal assessment and culturally sensitive, partner-inclusive psychosexual counseling. Research Sponsor: None.

Real-world outcomes comparing the use of GLP-1 receptor agonists in patients with endometrial cancer and comorbid obesity: A propensity score matched analysis from a global federated health research network.

Yajur Arya, Arshi Syal, Colton Jones, Himil Mahadevia, Angimar Uriepetro Palma, Reema Tawfiq, Trevanne Rose Matthews Hew; Mayo Clinic Florida, Jacksonville, FL; The University of Texas San Antonio, San Antonio, TX; Jefferson Einstein Philadelphia Hospital, Philadelphia, PA

Background: Glucagon-like peptide-1 (GLP-1) receptor agonists are widely used for the treatment of type 2 diabetes and obesity. Emerging evidence suggests that these agents may have potential anti-tumor activity as GLP-1 signaling may influence pathways involved in cell proliferation and inflammation. Endometrial cancer is the most common gynecologic malignancy, and obesity represents a well-established, modifiable risk factor that may adversely affect oncologic outcomes through chronic inflammation and metabolic dysregulation. Our study aims to evaluate the impact of GLP-1 receptor agonists on outcomes among patients with endometrial cancer and comorbid obesity. **Methods:** A retrospective cohort study was conducted using the TriNetX Global Collaborative Network, covering January 2000 to December 2025, encompassing data from 168 global healthcare organizations. Patients aged 18 and above with endometrial cancer and comorbid obesity were identified and then stratified into two groups based on treatment with GLP1 agonists or not. The two groups were then propensity-matched based on age, ethnicity, medical comorbidities, and stage of cancer. Outcomes were assessed for five years from treatment initiation and included overall mortality, myocardial infarction (MI), ischemic stroke; development of peritoneal, lymph node, and visceral metastases; sepsis, pancreatitis, and ED visits. Time-to-event analyses were performed using Kaplan-Meier methods and Cox proportional hazards models. **Results:** After propensity matching, 6352 patients were included in each cohort with balanced baseline characteristics. Our analysis found that patients with endometrial cancer and comorbid obesity who received GLP-1 agonists had a significantly lower risk of overall mortality (Hazard Ratio [HR]: 0.45, 95% CI: 0.39-0.51, p-value <0.001), development of peritoneal metastases (Risk Difference [RD]: -2.16%, 95% CI: -2.74% to -1.58%, p-value <0.001), nodal metastases (RD: -0.41%, 95% CI: -0.72% to -0.09%, p-value =0.01), visceral metastases (RD: -3.76%, 95% CI: -4.60% to -2.93%, p-value =0.01), and sepsis with and without shock (RD: -1.42%, 95% CI: -2.14% to -0.70%, p-value <0.001) compared to patients who did not receive GLP-1 agonists. There was no statistically significant difference in the rates of MI, ischemic stroke, ED visits, and pancreatitis between the two cohorts. **Conclusions:** In this large real-world analysis, patients with endometrial cancer and comorbid obesity who received GLP-1 agonists had lower rates of overall mortality; peritoneal, lymph node, and visceral metastases, and sepsis with or without shock. Additional longitudinal cohort studies are imperative to explore the associations between these agents and inform clinical practice guidelines in this patient population. Research Sponsor: None.

A phase 1 dose-escalation and -expansion study of AFN0328, a novel mRNA-based immunotherapy, in patients with HPV16/18-associated high-grade squamous intraepithelial lesions.

Yunxia Cao, Beicheng Sun, Ying Zhou, Yan Chen, Lin Liu, Yan Wang, Yunfang Yan, Li Ma, Xiuyun Zhang, Fengqiu Yao, Xiaoli Wang, Cheng Peng, Xiaohong Ruan, Da Chen, Lihua Song, Yucai Wang; First Affiliated Hospital of Anhui Medical University, Hefei, China; Department of Obstetrics and Gynecology, Core Facility Center, The First Affiliated Hospital of USTC, Division of Life Sciences and Medicine, University of Science and Technology of China, Hefei, Anhui, China; First Affiliated Hospital of USTC, Division of Life Sciences and Medicine, University of Science and Technology of China (USTC), Hefei, Anhui, China; University of Science and Technology of China, Hefei, China; Department of Obstetrics and Gynecology, The First Affiliated Hospital of USTC, Division of Life Sciences and Medicine, University of Science and Technology of China, Hefei, China; Jiangmen Central Hospital, Hefei, Anhui, China; AlphaNa Bioscience Co., Ltd., Hefei, China., Hefei, Anhui, China; Anhui Anke Biotechnology (Group) Co, Hefei, Anhui, China

Background: Persistent infection with high-risk human papillomavirus (HPV), particularly HPV16 and HPV18, drives the development of high-grade squamous intraepithelial lesions (HSIL), an obligate precancerous condition. The standard care of cervical HSIL requires either surgical excision (LEEP or cold-knife conization), or in some circumstance, watchful waiting. AFN0328 is a novel mRNA-based immunotherapy encoding HPV16/18-related antigens, designed to elicit antigen-specific immune responses and interrupt viral antigen-driven disease progression. **Methods:** Safety, tolerability and preliminary efficacy of AFN0328 were assessed in patients with HPV16- and/or HPV18-associated HSIL (CIN2/3) in an ongoing, multicenter, open-label Phase 1 trial. The study comprised two sequential parts: Part 1 employed a classic 3+3 dose-escalation design to assess safety and determine the maximum tolerated dose (MTD); Part 2 is a dose-expansion cohort at selected doses (150 µg and 300 µg) to further characterize safety, tolerability, and preliminary efficacy. AFN0328 was administered intramuscularly at 0, 4, and 12 weeks. The primary endpoints included safety and tolerability (dose-limiting toxicities within 28 days post-first dose, adverse events graded per CTCAE v5.0). For Part 2, the efficacy endpoints included viral clearance rate at Week 24 and Week 36, and histopathological regression at Week 36. Secondary endpoints included pharmacokinetic parameters, HPV16/18-specific IgG antibody titers, and pharmacodynamic markers (cellular immune responses and serum cytokines). **Results:** As of December 29, 2025, 23 patients had received at least one dose of AFN0328. No DLTs, serious adverse events, or grade ≥3 treatment-related adverse events (TRAE) were observed. PK analyses of first and last doses showed that circulating mRNA encoding HPV-related antigens peaked within 48 hours and declined gradually, with detectable levels persisting for up to at least 4 weeks across dose levels. All evaluable patients developed specific IgG responses and viral clearance was observed in evaluable patients during follow-up. **Conclusions:** AFN0328 demonstrated favorable safety and tolerability with robust immune responses in HPV16/18-associated HSIL, supporting further clinical development as an immunotherapy for HPV-driven precancerous disease. Clinical trial information: CTR20244013. Research Sponsor: None.

Summary of safety and immunogenicity outcomes.	
Outcome	Result
Patients treated	23
Dose-limiting toxicities	0
Grade ≥3 treatment-related AEs	0
Most common TRAEs	Injection-site reactions, fever
Specific IgG response rate	100%*
Observed viral clearance	Yes*

*Observed in evaluable patients during interim follow-up.

Limb compression therapy and chemotherapy-induced peripheral neuropathy in women with gynecologic cancers: A prospective self-controlled study (NEURO-GLOVE Trial)—Updated long-term analysis.

Kadriye Başkurt, Galip Can Uyar, Enes Yeşilbaş, Fatma Zehra Altunc, Damla Emirhan Cevik, Ismet Murat Melek, Yasemin Eren, Omur Berna Cakmak Oksuzoglu, Kadriye Bir Yucel, Osman Sütçüoğlu; Etlik City Hospital, Department of Medical Oncology, Ankara, Turkey; Etlik City Hospital, Department of Neurology, Ankara, Turkey; Gazi University Hospital, Department of Medical Oncology, Ankara, Turkey

Background: No established strategy prevents taxane-induced CIPN. We evaluated if dual-site mechanical compression reduces CIPN severity at 3 and 6 months post-treatment. **Methods:** In this prospective, self-controlled study (Dec 2023–Dec 2024), 76 women receiving carboplatin–paclitaxel were enrolled. During infusions, compression was applied to the non-dominant hand (two surgical gloves) and ipsilateral foot (Class II stocking); contralateral limbs served as controls. The primary endpoint was the incidence of Grade ≥ 2 sensory/motor neuropathy (CTCAE v5.0) at End-of-Treatment (EOT), 3 months, and 6 months. **Results:** Among 76 patients (median age 61), Grade ≥ 2 CIPN was lower in compression vs control limbs at Cycle 3 (27/76 [35.5%] vs 41/76 [53.9%]; $P=.001$) and EOT (45/76 [59.2%] vs 53/76 [69.7%]; $P=.021$). Benefits persisted at 3 months (22/76 [28.9%] vs 40/76 [52.6%]; $P=.015$) and 6 months (15/74 [20.3%] vs 25/74 [33.8%]; $P=.002$). Longitudinal analysis showed significant time-by-limb interactions for hand sensory ($P=.003$), foot sensory ($P=.018$), and motor domains ($P=.041$). EORTC QLQ-CIPN20 sensory scores showed high accuracy (AUC 0.92 at Cycle 3; 0.97 at EOT). **Conclusions:** Compression significantly reduces acute and persistent CIPN. Sustained benefits at 3 and 6 months suggest prevention of irreversible damage, supporting compression as an effective neuroprotective strategy. Clinical trial information: NCT07105553. Research Sponsor: None.

Limb-specific incidence of moderate-to-severe chemotherapy-induced peripheral neuropathy by EORTC QLQ-CIPN20 across time.						
Time point	Limb	Moderate-severe CIPN†, n/N (%)	Discordant cases ‡, n	McNemar p (compression vs control)	RD %, Control-Compression (95% CI)	P value vs baseline §
Baseline	Compression	0/76 (0.0)	—	—	—	—
	Control	0/76 (0.0)				
Cycle 3	Compression	27/76 (35.5)	Compression only: 2 Control only: 16	0.001	+18.4% (4.5 to 32.4)	<0.001
	Control	41/76 (53.9)				
EOT	Compression	45/76 (59.2)	Compression only: 1 Control only: 9	0.021	+10.5% (3.5 to 24.5)	<0.001
	Control	53/76 (69.7)				
3-month follow-up	Compression	22/76 (28.9)	Compression only: 2 Control only: 20	0.015	+23.7% (10.0 to 37.4)	<0.001
	Control	40/76 (52.6)				
6-month follow-up	Compression	15/74** (20.3)	Compression only: 0 Control only: 10	0.002	+13.5% (1.5 to 25.4)	<0.001
	Control	25/74 (33.8)				

Systemic inflammation and tumor immune microenvironment biomarkers (FOXP3, CD68, CD163) stratified by BRCA/HRD status in high-grade serous ovarian carcinoma: Associations with PFS and OS.

Carolina Ibañez Cáceres, Gregoria Viveros, Cristóbal Valdes, Mauricio Cuello, Elisa Orlandini, Jorge Branes, Jose Bennett, Nicolas Saez, Gareth I. Owen, Cesar Sanchez, Francisco Acevedo, Sebastian Ramirez, Benjamin Walbaum; Pontificia Universidad Católica de Chile, Santiago, Región Metropolitana, Chile; Pontificia Universidad Católica de Chile, Santiago, Metropolitana, Chile; Clínico Pontificia Universidad Católica de Chile, Santiago, Metropolitana, Chile; Pontificia Universidad Católica de Chile, Santiago, Chile; Pontificia Universidad Católica de Chi, Región Metropolitana, Chile; Pontificia Universidad Católica de Chile, Región Metropolitana, Chile; Pontificia Universidad Católica de Chile, Santiago, Chile; Pontificia Universidad Católica de Chile, Santiago, Chile

Background: Outcomes in high-grade serous ovarian carcinoma (HGSOC) may be influenced by systemic inflammation and the tumor immune microenvironment. We evaluated the prognostic impact of systemic inflammatory markers and intratumoral immune biomarkers, including FOXP3⁺ regulatory T cells and tumor-associated macrophages (CD68 and CD163), in the context of BRCA/HRD status. **Methods:** We conducted a retrospective cohort study of patients with HGSOC with available baseline systemic inflammatory markers and tumor immunohistochemistry. Systemic inflammation was assessed using neutrophil-to-lymphocyte ratio (NLR >3.5) and lactate dehydrogenase (LDH >220). Intratumoral FOXP3, CD68, and CD163 expression was evaluated by immunohistochemistry. BRCA/HRD status was coded as positive versus negative. Progression-free survival (PFS) and overall survival (OS) were analyzed using multivariable Cox proportional hazards models. **Results:** Twenty-nine patients were included, with 27 PFS events and 25 OS events. In multivariable analysis for PFS, elevated systemic inflammation was independently associated with worse outcomes: NLR >3.5 (HR 5.88, 95% CI 1.35–25.54; $p=0.018$) and LDH >220 (HR 6.70, 95% CI 1.33–33.74; $p=0.021$). Within the tumor microenvironment, higher intratumoral CD68 was associated with inferior PFS (HR 1.10, 95% CI 1.04–1.17; $p=0.001$), whereas higher CD163 was associated with improved PFS (HR 0.92, 95% CI 0.87–0.97; $p=0.002$). BRCA/HRD positivity was not independently associated with PFS. For OS, BRCA/HRD positivity was strongly protective (HR 0.14, 95% CI 0.03–0.60; $p=0.008$), while NLR >3.5 remained independently associated with worse OS (HR 4.27, 95% CI 1.17–15.68; $p=0.028$). High FOXP3 expression was associated with improved OS (HR 0.06; $p=0.032$). CD68 and CD163 showed borderline associations with OS. **Conclusions:** In this HGSOC cohort, baseline systemic inflammation was associated with inferior PFS, and elevated NLR predicted worse OS. Intratumoral immune biomarkers showed distinct prognostic patterns, suggesting that the balance and functional state of myeloid and regulatory immune compartments influence outcomes. BRCA/HRD positivity remained strongly favorable for OS. These findings support further investigation of integrated systemic and tumor immune profiling in larger, prospectively annotated cohorts. Research Sponsor: Fondef 152220002. Centro para la Prevención y el Control del Cáncer, CECAN.

Genomic signature–based risk score for PARP inhibitor response in *BRCA*-mutated ovarian cancer: A whole-exome sequencing analysis.

Junhwan Kim, Jong Kwang Kim, Myong Cheol Lim, Sang-Soo Seo, Sang-Yoon Park, Junyoung Shin, Chong Woo Yoo, Sokbom Kang; Center for Gynecologic Cancer, National Cancer Center, Goyang-Si, South Korea; National Cancer Center, Goyang, South Korea

Background: To identify whole-exome sequencing (WES)–based genomic signatures associated with response to poly(ADP-ribose) polymerase (PARP) inhibitors and develop a prediction model for PARP inhibitor effectiveness in *BRCA*-mutated advanced ovarian cancer, given the heterogeneous real-world treatment outcomes. **Methods:** This retrospective cohort study included patients with advanced ovarian cancer harboring *BRCA1/2* mutations who received olaparib or niraparib as first-line maintenance therapy between 2020 and 2022 at the National Cancer Center, South Korea. Among them, patients with at least one year of follow-up from the reference date (August 1, 2024) and sufficient additional tumor samples for WES were identified. Baseline characteristics were collected, and progression-free survival (PFS) and overall survival (OS) from the initiation date of PARP inhibitors were extracted from electronic medical records. Formalin-fixed, paraffin-embedded tumor samples of eligible patients underwent DNA extraction and WES. Prognostic modeling incorporated clinical and genetic variables using Cox proportional hazards regression with the least absolute shrinkage and selection operator (Lasso) method with leave-one-out cross-validation. Model performance was assessed using time-dependent area under the curve (AUC(t)). **Results:** Fifty-five patients were included. The median patient age was 57 years (range, 39–72). High-grade serous carcinoma comprised 96.4%. Neoadjuvant chemotherapy (NACT) was performed in 40.0%. Complete remission after adjuvant chemotherapy occurred in 87.3%. Olaparib was administered in 76.4% and niraparib in 23.6%. NACT-exposed samples had lower Mutant-Allele Tumor Heterogeneity (MATH) scores than non-NACT-exposed samples, indicating reduced intratumor heterogeneity ($P < 0.001$). Recurrence during PARPi maintenance occurred in 11 patients (20.0%) (olaparib: 5/42 [11.9%]; niraparib: 6/13 [46.2%]). No deaths were observed. The median PFS was 37.9 months (range, 4.2–54.5), and the median OS was 43.3 months (range, 20.2–60.1). Mutations significantly associated with progression-free survival included *POLN* (HR, 2.02; 95% CI, 1.12–3.67), *ABCC10* (HR, 4.57; 95% CI, 1.13–18.5), *GTPBP6* (HR, 2.07; 95% CI, 1.04–4.12), and *TCTEX1D1* (HR, 0.19; 95% CI, 0.05–0.82). A genomic risk score model incorporating these mutations stratified patients into low- and high-risk groups with strong prognostic discrimination for progression-free survival (HR, 4.44; 95% CI, 2.26–8.68; log-rank $P < 0.001$; AUC(t), 0.87). **Conclusions:** The genomic signature-based risk score model independently predicted PARP inhibitor effectiveness. External validation is warranted. Research Sponsor: National Cancer Center, Republic of Korea; NCC2510290-2.

ErbB family members as mediators of acquired resistance to immunotherapy in high-grade serous ovarian cancer.

Mengyao Xu, Fabian Bernhard Thaddäus Kraus, Oladapo O. Yeku; Massachusetts General Hospital Cancer Center, Boston, MA; Department of Obstetrics and Gynecology and Comprehensive Cancer Center Munich, University Hospital, LMU Munich, Munich, Germany; Massachusetts General Hospital, Harvard Medical School, Boston, MA

Background: Efforts to improve immunotherapy for ovarian cancer (OC) have focused on optimizing T-cell effector-based strategies such as immune checkpoint inhibitors (ICIs), bispecific T-cell engagers (BiTEs), or chimeric antigen receptor (CAR)-T cells, or combining them with other therapeutic modalities. Relatively little is known about how adaptive resistance occurs or how to improve the intrinsic susceptibility of ovarian cancer cells to T cell-mediated cytotoxicity. **Methods:** An OC organoid derived from a patient who relapsed on immunotherapy (MGH538) was generated. OVCAR3 immune-edited cell line (OVCAR3^{IE}) was generated by treating OVCAR3 wild-type (OVCAR3) tumor-bearing mice with activated T-cells, anti-PD-1, and anti-CTLA4 antibodies. Peritoneal tumors were then harvested and cultured *in vitro*. BiTEs-resistant cell line (OVCAR3^R) was generated by treating OVCAR3 cells with anti-MUC16 BiTEs *in vitro* until the cells were resistant. Comparative RNA sequencing analysis was performed on OVCAR3, OVCAR3^{IE}, and OVCAR3^R. Protein expression was assessed by Western blot analysis. To evaluate cytotoxicity, OVCAR3, OVCAR3^{IE}, and OVCAR3^R were co-cultured with MUC16-specific CAR-T cells and MUC16-directed BiTEs, alone or in combination with pharmacologic inhibitors targeting EGFR, RAS, and Bcl-xL, including a Bcl-xL degrader DT2216. **Results:** MGH538, OVCAR3^{IE} and OVCAR3^R were confirmed to be resistant to T-cell directed cytotoxicity compared to OVCAR3. RNA sequencing analysis revealed significant differences in the transcriptome profiles of immune-naïve and immunotherapy-exposed OC cells. In particular, significant changes in the RNA expression levels of three out of four ErbB family members (EGFR (ErbB1), ErbB2 and 3) were detected. In Western blot analysis, this finding was paralleled by significant changes in the ratio of phospho-ERK to ERK, an important component of ErbB downstream signaling. In functional assays, EGFR inhibition with gefitinib significantly enhanced CAR-T cell-mediated killing in OVCAR3, OVCAR3^{IE} and OVCAR3^R cells. Furthermore, blocking downstream EGFR signaling with a Ras inhibitor also restored sensitivity to immunotherapy. Finally, blocking anti-apoptotic signaling with Bcl-family inhibitor navitoclax, or the Bcl-xL inhibitor DT2216 restored susceptibility to both CAR-T cell and BiTEs-mediated killing. **Conclusions:** Adaptive resistance to T-cell mediated cytotoxicity appears to be mediated, at least in part, by upregulation of ErbB family members and consequent downstream Ras signaling and resistance to apoptosis. While further functional *in vitro* and therapeutic *in vivo* studies are warranted to investigate the translational potential of our findings, EGFR signaling may represent a promising target for clinical combination strategies. Research Sponsor: None.

Development of payload-resistant human ovarian cancer cell lines to better understand antibody-drug conjugate sequencing and resistance mechanisms.

Janina Pearce, Payton De La Cruz, Samantha Buyungo, Areta Bojko, Cara Amanda Mathews, Paul Disilvestro, Nicole James; Program in Women's Oncology, Department of Obstetrics and Gynecology, Women and Infants Hospital, Brown University, Providence, RI; Department of Pathobiology, Brown University, Providence, RI; Women and Infants Hospital, Providence, RI

Background: Within gynecologic oncology, limited data exist regarding mechanisms of resistance to antibody-drug-conjugates (ADC) or the impact on response to future ADC treatment. The purpose of this study was to develop and characterize payload-resistant human ovarian cancer cell lines, and to determine the effect of payload resistance on subsequent ADC exposure.

Methods: Three commercially available human high grade serous ovarian cancer cell lines (PEA1, PEA2, and OVCAR8) were each exposed separately to three commercially available payloads with corresponding, clinically approved ADCs (deruxetecan/trastuzumab deruxetecan, SN38/sacituzumab govitecan, and DM4/mirvetuximab soravtansine). Cell viability assays were performed to confirm and quantify resistance after completion of treatment for payload-resistant cell lines, and western blot analyses performed to evaluate changes in HER2, TROP2, and FOLR1 expression between payload-resistant cells and their controls. Lastly, paired payload-resistant and -sensitive cell lines were then exposed to ADCs with different payloads for 48 hours, and cell viability assays were performed. **Results:** The development of payload-resistant cell lines demonstrates notable variability in timelines for attaining resistance, both across the three cell lines and within individual cell lines across different payload exposures. Compared to payload-sensitive controls, payload-resistant cells displayed similar morphologic changes including increased surface area; however, demonstrated variable differences in HER2, TROP2, and FOLR1 protein expression. Additionally, different payload-resistant cell lines responded differently to subsequent ADC exposure. As a specific example, DM4-resistant PEA1 cells were more sensitive to subsequent exposure to sacituzumab govitecan compared to DM4-sensitive controls at various doses ($p < 0.0001$, see Table). **Conclusions:** This study illustrates challenges in developing payload-resistant cell lines, and highlights variability in molecular changes with payload resistance. The data demonstrate subsequent ADC susceptibility in some payload-resistant cell lines, highlighting the complexities of changes that occur with drug treatment. Our data suggests that HGSOc patients that received mirvetuximab soravtansine may be more susceptible to future treatment with sacituzumab govitecan. Future work is underway to expand these findings to determine ideal sequencing of these different ADCs, and to determine other off-target effects that may influence non-ADC treatment response. Research Sponsor: None.

Viability of DM4-resistant versus sensitive PEA1 human ovarian cancer cells after exposure to sacituzumab govitecan (SG).

	DM4 resistant		Control		p value
	Average % viability	SEM	Average % viability	SEM	
SG 400nM	52.01	1.63	98.98	1.01	< 0.000001
SG 600nM	45.43	0.65	96.87	0.49	< 0.000001

Geographical heterogeneity in modeled CA-125 KELIM values: Insights from more than 50,000 real-world calculations on the Biomarker Kinetics platform.

Benoit You, Pauline Corbaux, Aurore Carrot, Gilles Freyer, Olivier Colombari; Centre Hospitalier Lyon Sud, and GINECO, Pierre-Benite, France; EA3738 CICLY, Lyon University, Saint Etienne University Hospital, Oullins, France; UCBL EA3738 CICLY, Oullins, France; Lyon University Hospital (HCL), Pierre-Bénite, France; Laboratoire EA 3738 UCBL/HCL CICLY Equipe 3, Oullins, France

Background: The modeled CA-125 KELIM is a pragmatic indicator of primary tumor chemosensitivity during neoadjuvant (NACT) or adjuvant chemotherapy (post-primary cytoreductive surgery: ADJUVANT) in ovarian cancer. In a recent GCIG meta-analysis, Japanese patients with stage III–IV high-grade serous carcinoma had higher median KELIM values than Western populations (Corbaux.et.al., Proc ESGO 2025). To further assess potential geographical variations in chemosensitivity, we analyzed KELIM values calculated via the free online platform www.biomarker-kinetics.org, which performs approximately 30,000 calculations annually worldwide. **Methods:** All CA-125 KELIM calculations performed on the BK platform between April 2024 and January 2026 were extracted. Median KELIM values were compared separately for NACT and adjuvant settings across continents and countries. **Results:** During the 21-month study period, 50,055 KELIM calculations were recorded worldwide (NACT 59%; ADJUVANT 41%), originating from Asia (n=27,280; 55%), Europe (n=16,461; 33%), North America (n=3,690; 7%), South America (n=1,363; 3%), and rest of globe. Marked geographical variations in KELIM distribution were observed. In the NACT setting, median KELIM values (standardized by the classical cutoff) were significantly higher in patients from Asia (median 1.06, 95%CI [1.05–1.07]), Middle-East (median 0.96 [0.89–1.0.6]), and North America (median 0.91 [0.89–0.94]) compared to those from Europe (median 0.85 [0.84–0.86]) ($P < 0.0001$). Within Asia, KELIM values were similarly elevated in China (n=10,617; median 1.07 [1.06–1.08]) and Japan (n=3,092; median 1.05 [1.03–1.07]) ($P=NS$). Similar results were noted in the ADJUVANT setting (Asia median 0.91, North America 0.80, vs Europe 0.75; all $P < 0.0001$). Weighted median ($\tau = 0.5$) quantile regression confirmed significantly higher standardized KELIM values in Asia (+0.21), Middle East (+0.12), and North America (+0.06) compared with Europe in the NACT setting. Similar outcomes were found in ADJUVANT setting : Asia (+0.16), Middle East (+0.28), and North America (+0.04) compared to Europe. **Conclusions:** Consistent with the GCIG meta-analysis, this global extraction of >50,000 KELIM calculations in the last 2 years confirms substantial geographic variability in tumor chemosensitivity, with higher median standardized KELIM values observed in patients from Asia and, to a lesser extent, the Middle East, while those from Europe exhibited the lowest values. These findings suggest potential important worldwide differences in primary tumor sensitivity to 1st-line carboplatin-paclitaxel chemotherapy and support the need for further biological and clinical investigations across diverse geographic and ethnic populations. Research Sponsor: None.

YL205, a novel anti-Napi2b antibody drug conjugate (ADC), in patients with ovarian cancer: Preliminary result from a first-in-human trial.

Xiaohua Wu, Haifeng Liu, Jing Wang, Tao Zhu, Yanzhou Wang, Peng Peng, Genhai Zhu, Qingshui Li, Juan Li, Qin Xu, Ge Lou, Yu Kang, Mengxia Li, Meng Yao, Ruihua Wang, Steve Chin; Fudan University Shanghai Cancer Center, Shanghai, China; Department of Oncology, Jilin Cancer Hospital, Changchun, China; Department of Gynecologic Oncology, Hunan Cancer Hospital, Changsha, China; Tongji Medical College of HUST Tongji Hospital, Wuhan, Hubei, China; The Southwest Hospital of Army Medical University, Chongqing, China; Peking Union Medical College Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China; The First Affiliated Hospital of Hainan Medical University, Haikou, Hainan, China; Cancer Hospital of Shandong First Medical University (Shandong Cancer Institute, Shandong Cancer Hospital), Jinan, China; Fujian Cancer Hospital, Fuzhou, China; Harbin Medical University Cancer Hospital, Harbin, China; Obstetrics & Gynecology Hospital of Fudan University, Shanghai, China; Chinese People's Liberation Army Army Characteristic Medical Center, Chongqing, China; MediLink Therapeutics (Suzhou) Co., Ltd., Suzhou, China; Medilink Therapeutics (Suzhou) Co., Ltd., Suzhou, China

Background: Sodium-dependent phosphate transport protein 2b (NaPi2b) is a rapidly internalizing sodium-phosphate transporter which is highly overexpressed in ovarian cancer (OC). The prognosis of patients (pts) with heavily pretreated ovarian cancer remains poor, highlighting a significant unmet need. YL205 is a unique antibody-drug conjugate comprising a NaPi2b-directed antibody conjugated to a potent topoisomerase 1 inhibitor payload developed with TMALIN platform. The preliminary safety and efficacy of YL205 monotherapy in ovarian cancer from a multi-center, open-label, phase I/II trial are presented. **Methods:** Pts with advanced solid tumors, mainly OC, who had failed standard therapy or no available standard therapy were enrolled in the trial YL205-CN-101-01. It consists of dose-escalation (BF-BOIN design), followed by dose-expansion. Pts received YL205 IV at 1.0~3.0 mg/kg once every 3 weeks. Primary objectives were to assess safety and tolerability. **Results:** As of the data cut-off on Dec. 12, 2025, 48 OC pts were dosed with YL205 monotherapy in China and United States with median follow up time of 5.5 months (range 0.2-17.2). Pts had median age of 54.2 yo (range 32-70), 68.8% with ECOG PS 1, 37.5% with ≥ 4 prior lines of therapy. Previous therapies included bevacizumab (89.6%), PARP inhibitors (43.8%), and mirvetuximab soravtansine (2.1%). No maximum tolerated dose (MTD) was defined. Grade 3 TRAEs occurred in 27.1% of pts. 14.6% of pts developed SAEs related to tx. The most common TRAEs were neutropenia (60.4%; $G \geq 3$: 12.5%), anaemia (60.4%, $G \geq 3$: 4.2%), nausea (47.9%, $G \geq 3$: 0), vomiting (33.3%, $G \geq 3$: 0), decreased appetite (27.1%, $G \geq 3$: 0) and thrombocytopenia (25.0%, $G \geq 3$: 6.3%) across all dose levels. Among 43 efficacy evaluable pts, confirmed ORR was 46.5% (95% CI: 31.2 – 62.3), and DCR was 95.3% (95% CI: 84.2 – 99.4). At the date cutoff, the median progression-free survival (PFS) data was immature, 62.5% (15/24) of patients with a response remain on treatment. NaPi2b expression as evaluated by H-score was found to be low (0-100) in 1 pt, medium (101-201) in 11 pts (101-200) and high (201-300) in 35 pts whose tumor tissues available at baseline. No correlation trend was observed between NaPi2b expression and response. **Conclusions:** YL205 demonstrated a manageable safety profile in heavily pretreated ovarian cancer patients, with preliminary efficacy observed irrespective of NaPi2b expression intensity. The promising clinical data supports further investigation of this ADC in OC. Clinical trial information: NCT06459973. Research Sponsor: None.

A first-of-its-kind multi-omic assay using lipids and proteins to identify early-stage ovarian cancer in symptomatic individuals.

Abigail McElhinny, Rachel Culp-Hill, Brendan Giles, Shannon Kilkenny, Charles Nichols, Yu Han, Moises Zapata, Enkhtuya Radnaa, Maria Wong, Mattie Goldberg, Vuna Fa, Kim Ekroos, James R. White; AOA Dx, Denver, CO; Lipidomics Consulting Ltd, Esbo, Finland; Resphera Biosciences, Baltimore, MD

Background: Ovarian cancer (OC) is often diagnosed at advanced stages, leading to one of the highest mortality rates for gynecologic malignancies. While 85% of patients are symptomatic even at early stages, symptoms are vague and overlap with benign conditions. Existing diagnostic tools such as CA125 and HE4 lack sufficient sensitivity and specificity to detect early-stage disease, even in symptomatic individuals. As a result, there is a critical unmet need for a highly sensitive diagnostic tool designed for patients presenting with vague abdominal symptoms. **Methods:** Here, we report the first large-scale, prospective U.S. clinical trial evaluating a targeted multi-omic assay of symptomatic women, its intended-use population. Assay performance was assessed in a subset of an independent, prospectively recruited, multi-site study enrolled across the United States, supplemented with samples from a commercial vendor (N=346). The cohort comprised patients diagnosed with OC across stages and subtypes (N=116: 50 early-stage I/II, 66 late-stage III/IV) and a symptomatic control group (N=230), comprising individuals with benign adnexal masses (BAN; N=116) and symptomatic individuals with vague abdominal symptoms who were followed longitudinally for 12 months to confirm absence of malignancy (symptomatic normal; N=114). Serum lipids including selected phospholipids, sphingolipids, and ceramides were quantified by mass spectrometry. Proteins were measured using clinically validated immunoassays. An ensemble machine learning modeling approach was applied using targeted feature subsets from a refined panel of 23 lipid and 5 protein markers, with outputs weighted to reflect anticipated disease prevalence in the intended-use population. **Results:** The assay demonstrates consistently high diagnostic performance, achieving 96.5% sensitivity with 80.6% specificity for OC vs. symptomatic control, and 92% sensitivity for early-stage OC in the same comparison. Integrating lipid and protein biomarkers into a targeted multi-omic model therefore results in a substantial improvement in OC detection, especially early-stage, over current standard-of-care biomarkers. **Conclusions:** In a large, prospectively collected cohort reflecting real-world symptomatic patients, this first-of-its-kind, targeted multi-omic assay accurately distinguishes OC from non-malignant conditions in symptomatic women with dramatic improvement in early-stage detection. These findings support the feasibility and clinical utility of a multi-omic assay in addressing a longstanding diagnostic gap for symptomatic women, clearing a path to earlier triage and diagnosis. Research Sponsor: None.

Preoperative assessment of peritoneal carcinomatosis with [⁶⁸Ga]Ga-FAPI-46 PET/CT.

Ayca Arcay Ozturk, Gabriel Libérale, Anne-Leen Deleu, Raluca Poenaru, Erwin Woff, Polastro Laura, Ana Veron, Laurine Verset, Jean Christophe Noël, Mutaz Kassas, Zena Wimana, Sigrid Vercauteren, Clementine Marin, Paulus Kristanto, Loubna Taraji, Patrick Flamen; Department of Nuclear Medicine, Institut Jules Bordet, Hôpital Universitaire de Bruxelles, Université Libre de Bruxelles, Brussels, Belgium; Department of Digestive Surgery and Digestive Surgical Oncology, Institut Jules Bordet, Hôpital Universitaire de Bruxelles, Université Libre de Bruxelles, Brussels, Belgium; Department of Nuclear Medicine, Institut Jules Bordet, Hôpital Universitaire de Bruxelles, Université Libre de Bruxelles, Brussels, Belgium; Department of Medical Oncology, Institut Jules Bordet, Hôpital Universitaire de Bruxelles, Université Libre de Bruxelles, Brussels, Belgium; Department of Radiology, Institut Jules Bordet, Hôpital Universitaire de Bruxelles, Université Libre de Bruxelles, Brussels, Belgium; Department of Pathology, Institut Jules Bordet, Hôpital Universitaire de Bruxelles, Université Libre de Bruxelles, Brussels, Belgium; Department of Pathology, Institut Jules Bordet, Hôpital Universitaire de Bruxelles, Université Libre de Bruxelles, Brussels, Belgium; Department of Medical Physics, Institut Jules Bordet, Hôpital Universitaire de Bruxelles, Université Libre de Bruxelles, Brussels, Belgium; Clinical Biostatistics Unit, Hôpital Universitaire de Bruxelles (HUB), Université Libre de Bruxelles (ULB), Brussels, Belgium

Background: Accurate preoperative mapping of peritoneal carcinomatosis (PC) is essential for selecting patients for cytoreductive surgery (CRS) and guiding treatment planning. Conventional imaging including [¹⁸F]FDG PET/CT may underestimate PC tumour burden. This study evaluated [⁶⁸Ga]Ga-FAPI-46 PET/CT for preoperative PC assessment using a surgico-pathological reference standard and compared its performance with MRI and [¹⁸F]FDG PET/CT. **Methods:** In this prospective phase II study (FAPeCa, NCT06061874), patients with colorectal or ovarian cancer with known or suspected PC underwent [⁶⁸Ga]Ga-FAPI-46 PET/CT, [¹⁸F]FDG PET/CT (FDG PET), and MRI within 4 weeks before diagnostic laparoscopy and/or CRS. PC extent was quantified using a 10-segment adaptation of the Peritoneal Cancer Index (PCI). Reference standard was intraoperative PCI with histopathological confirmation, with pathology adjudicating discordant findings. Agreement between imaging-derived total PCI and the reference-standard PCI was assessed using intraclass correlation coefficient (ICC, two-way mixed, absolute agreement). Segment-level diagnostic performance was evaluated after dichotomisation (PCI 0 vs ≥1). Subgroup analyses were performed according to recent chemotherapy (<3 months). **Results:** Sixty-one patients were enrolled. Median (IQR) total PCI values were 11 (18.5) for the reference standard, 12 (15.5) for FAPI PET, 6 (15.5) for MRI, and 4 (6.5) for FDG PET; FAPI-PCI was higher than MRI-PCI and FDG-PCI (Wilcoxon signed-rank, $p < 0.001$). Agreement with the reference standard was highest for FAPI PET (ICC 0.81; BCa 95% CI 0.67–0.89), followed by MRI (ICC 0.76; BCa 95% CI 0.63–0.85) and FDG PET (ICC 0.54; BCa 95% CI 0.29–0.74). In the recent chemotherapy subgroup, FAPI PET maintained good agreement with the reference standard (ICC 0.75, BCa 95% CI 0.56–0.86), whereas agreement declined to moderate for MRI (ICC 0.65, BCa 95% CI 0.41–0.82) and was lower for FDG PET (ICC 0.46, BCa 95% CI 0.17–0.75). Segment-level sensitivity, specificity, and accuracy were 77.6%, 71.2%, and 74.8% for FAPI PET; 67.0%, 84.4%, and 74.7% for MRI; and 47.5%, 91.8%, and 67.2% for FDG PET. Overall segment-level sensitivities and specificities differed across the three modalities (Cochran's Q, $p < 0.001$). **Conclusions:** [⁶⁸Ga]Ga-FAPI-46 PET/CT demonstrated the strongest agreement with surgico-pathological PCI and maintained good agreement after recent chemotherapy. It showed higher detectability than MRI and [¹⁸F]FDG PET/CT, albeit at the expense of lower specificity. These findings support [⁶⁸Ga]Ga-FAPI-46 PET/CT as a promising modality for preoperative PC mapping. Clinical trial information: NCT06061874. Research Sponsor: None.

Trastuzumab deruxtecan (T-DXd) + bevacizumab (BEV) as first-line (1L) maintenance therapy in patients (pts) with human epidermal growth factor receptor 2 (HER2)–expressing ovarian cancer (OC): Results from the DESTINY-Ovarian01 (DO-01/ENGOT-ov89/GOG-3112/APGOT-OV13) safety run-in (SRI).

Antonio Gonzalez Martin, Kasumi Yamamoto, Xiaohua Wu, Tsukasa Baba, Destin Black, Scott Jordan, Akira Kikuchi, Eiji Kondo, Satoru Nagase, Shu Soeda, Takashi Uehara, Lin-Hung Wei, Mayu Yunokawa, Veronica Mariotti, Laura-Carolin Hasenkamp, Steven Hua, Hanan Abdel-Monem, David Shao Peng Tan, Joyce F. Liu, Kosei Hasegawa; GEICO and Cancer Center Clinica Universidad de Navarra, Madrid, Spain; Department of Gynecologic Oncology, Hyogo Cancer Center, Akashi, Japan; Fudan University Shanghai Cancer Center, Shanghai, China; Department of Obstetrics and Gynecology, Iwate Medical University, Morioka, Japan; Trials 365, LLC, Shreveport, LA; Broward Health Medical Center, Fort Lauderdale, FL; Department of Gynecology, Niigata Cancer Center Hospital, Niigata, Japan; Department of Obstetrics and Gynecology, Mie University Hospital, Tsu, Mie, Japan; Department of Obstetrics and Gynecology, Yamagata University Hospital, Yamagata, Japan; Department of Obstetrics and Gynecology, Fukushima Medical University School of Medicine, Fukushima, Japan; Department of Gynecology, NHO Hokkaido Cancer Center, Sapporo, Japan; Department of Obstetrics and Gynecology, National Taiwan University Hospital, Taipei, Taiwan; Department of Advanced Medical Development, Cancer Institute Hospital of Japanese Foundation for Cancer Research, Tokyo, Japan; Oncology Research and Development, Daiichi Sankyo, Inc., Basking Ridge, NJ; Clinical Development, Daiichi Sankyo Europe GmbH, Munich, Germany; NUS Centre for Cancer Research, National University of Singapore and National Cancer Institute, Singapore and National University Hospital (NUH), Singapore, Singapore; Dana-Farber Cancer Institute, Boston, MA; Saitama Medical University International Medical Center, Hidaka, Saitama, Japan

Background: HER2 immunohistochemistry (IHC) expression scores of 3+, 2+, or 1+ occur in up to ~6%, ~28%, and ~21% of OC cases, respectively. In DESTINY-PanTumor02, T-DXd, a HER2-directed antibody–drug conjugate, showed clinically meaningful antitumor activity in pts with heavily pretreated HER2-expressing OC, establishing HER2 as a targetable biomarker. BEV + chemotherapy, followed by maintenance BEV ± poly (ADP-ribose) polymerase inhibitors (PARPi), is a recommended 1L treatment; however, an unmet need remains for PARPi-ineligible pts with HER2-expressing OC. We report the SRI results from DO-01 (NCT06819007), a randomized, open-label, phase 3 trial evaluating T-DXd + BEV vs BEV alone as 1L maintenance therapy in pts with HER2-expressing OC. **Methods:** Pts with newly diagnosed, advanced, high-grade, locally or centrally determined HER2-expressing (IHC 3+/2+/1+) epithelial OC, with no disease progression after 1L chemotherapy + BEV, and ineligible for PARPi, were enrolled and received T-DXd 5.4 mg/kg + BEV 15 mg/kg intravenously every 3 weeks. Pts were treated for ≥2 cycles. Preliminary safety of T-DXd + BEV was assessed by dose-limiting toxicity (DLT; ~30% maximum acceptable rate) and the frequencies of treatment-emergent adverse events (TEAEs) and TEAEs of special interest. **Results:** At data cutoff (DCO; October 23, 2025), 21 pts received a median of 4 cycles (range, 2–8) of T-DXd + BEV; no pt withdrew before cycle 2. Median age was 57 years (range, 22–71) and 19 pts (90.5%) were Asian; 7 (33.3%) and 14 pts (66.7%) had FIGO stages III and IV at baseline, respectively. Median treatment duration was 3.0 mo (range, 1.4–5.5). At DCO, 20 pts (95.2%) completed DLT evaluation and remained on treatment; 1 withdrew after the DLT evaluation period. DLTs occurred in 2 pts (10.0%). TEAEs are shown in the Table. Grade ≥3 drug-related TEAEs occurred in 9 pts (42.9%). Drug-related TEAEs led to dose reduction in 5 pts (23.8%) and dose delay in 6 pts (28.6%). No drug-related TEAEs led to discontinuation or death. Most common drug-related TEAEs (>50%) were nausea (76.2%), leukopenia (52.4%), and neutropenia (52.4%). No cases of adjudicated drug-related interstitial lung disease or left ventricular dysfunction were reported. **Conclusions:** The preliminary safety profile of T-DXd + BEV was consistent with the known safety profiles of the individual agents, and no new safety signals were identified, supporting continued investigation of T-DXd + BEV in DO-01. Clinical trial information: NCT06819007. Research Sponsor: Daiichi Sankyo, Inc.

Pts with events, n (%)	T-DXd + BEV N = 21
Drug-related TEAEs	21 (100)
Drug-related grade ≥3 TEAEs	9 (42.9)
Drug-related TEAEs leading to discontinuation	0
Drug-related TEAEs leading to dose reduction	5 (23.8)
Drug-related TEAEs leading to dose delay	6 (28.6)
TEAEs with outcome of death	0

Integrating a small extracellular vesicle protein-based ovarian cancer score with O-RADS Ultrasound to improve preoperative risk stratification of adnexal masses.

Qunxian Rao, Na Di, Yiru He, Lingling Chen, Jingjie Shen, Shan Zhang, Ruolan Xie, Yunhan Jiang, Yaoxu Chen, Dadong Zhang, Zhongqiu Lin; Department of Gynecologic Oncology, Sun Yat-sen Memorial Hospital, Sun Yat-sen University, Guangzhou, China; Department of Ultrasound, Sun Yat-sen Memorial Hospital, Sun Yat-sen University, Guangzhou, Guangdong, China; Department of Clinical and Translational Medicine, 3D Medicines Inc., Shanghai, China

Background: Accurate preoperative differentiation of adnexal masses remains a major clinical challenge. Although the Ovarian-Adnexal Reporting and Data System (O-RADS) standardizes ultrasound-based risk assessment, approximately 30–35% of adnexal masses are classified as indeterminate (O-RADS 3/4), often resulting in diagnostic uncertainty, unnecessary surgery, or delayed referral to gynecologic oncologists. Conventional serum biomarkers such as CA125 are limited by poor specificity and biological heterogeneity. The small Extracellular vesicle (sEV)-associated biomarkers have emerged as a promising approach to improve diagnostic accuracy by more closely reflecting tumor-related molecular signals. This study evaluated whether a serum sEV-based Ovarian Cancer Score (OCS) provides independent and incremental diagnostic value when integrated with O-RADS ultrasound. **Methods:** This retrospective diagnostic study included 250 consecutive patients with adnexal masses treated at Sun Yat-sen Memorial Hospital. All patients underwent standardized transvaginal ultrasound with O-RADS classification and serum CA125 testing. OCS was assessed using a chemiluminescent immunoassay based on serum sEV-derived CA125, HE4, and C5a. Final histopathology served as the reference standard. Diagnostic performance was evaluated overall and stratified by O-RADS category. Univariate and multivariate logistic regression analyses were performed to identify independent predictors of malignancy. **Results:** Overall, OCS demonstrated significantly higher diagnostic accuracy for malignancy than serum CA125 alone. In masses with clearly benign or malignant imaging features (O-RADS 2 and 5), OCS maintained an accuracy of approximately 90% (87.5% and 94.6%). Within the clinically challenging O-RADS 3/4 subgroup ($n = 115$), OCS achieved a diagnostic accuracy of 86.1%, substantially outperforming serum CA125 (69.6%). Multivariate analysis identified OCS positivity as the strongest independent predictor of malignancy (OR 106.08, 95% CI 15.37–732.15, $p < 0.001$), exceeding individual high-risk ultrasound features such as ascites or mixed cystic-solid components. Diagnostic performance was further enhanced when OCS was combined with selected ultrasound characteristics. **Conclusions:** A serum sEV-based OCS provides robust and independent diagnostic information that complements O-RADS ultrasound in the preoperative evaluation of adnexal masses. By addressing the diagnostic gray zone of O-RADS 3/4, this integrated approach extends beyond conventional serum biomarkers and may support improved risk stratification and triage decisions. Clinical trial information: NCT06366997. Research Sponsor: None.

Neoadjuvant disitamab vedotin plus carboplatin in HER2-expressing advanced ovarian cancer: A prospective, single-arm, phase II trial.

Yifan Meng, Wei Wei, Qiaqia Li, Fan Yang, Ting Wan, Jundong Li; Department of Gynecologic Oncology, State Key Laboratory of Oncology in South China, Collaborative Innovation Center for Cancer Medicine, Sun Yat-sen University Cancer Center, Guangzhou, China; Sun Yat-sen University Cancer Center, Guangzhou, China; Sun Yat-sen University Cancer Center; State Key Laboratory of Oncology in South China; Collaborative Innovation Center for Cancer Medicine, Guangzhou, China

Background: Standard neoadjuvant paclitaxel-carboplatin for advanced ovarian cancer causes significant neurotoxicity impacting quality of life. Disitamab vedotin (RC48), an anti-HER2 antibody-drug conjugate, demonstrated efficacy and favorable tolerability in HER2-expressing solid tumors. We evaluated RC48 plus carboplatin as neoadjuvant therapy in HER2-expressing advanced ovarian cancer. **Methods:** This single-arm phase II trial (NCT06574763) enrolled patients with newly diagnosed FIGO stage III-IV high-grade serous ovarian, fallopian tube, or primary peritoneal cancer expressing HER2 (IHC 1+ or ERBB2 amplification) who were ineligible for primary cytoreductive surgery. Treatment comprised carboplatin (AUC 5, day 1, Q3W) alone in cycle 1, then RC48 (2.5 mg/kg, day 1, Q3W) plus carboplatin for cycles 2-4. A 6-patient safety run-in determined optimal RC48 dosing. Interval debulking surgery (IDS) was performed 14-28 days after cycle 4. Primary endpoint: complete resection rate (CRR, defined as no macroscopic residual disease at IDS). Secondary endpoints: pathological complete response (pCR), objective response rate (ORR per RECIST v1.1), progression-free survival, overall survival, and safety (CTCAE v5.0). **Results:** From October 1st, 2024 to December 31st, 2025, 33 patients were enrolled; 25 completed neoadjuvant therapy and underwent IDS. Among 24 evaluable patients (1 excluded for mixed histology meeting exclusion criteria), median age was 57 years (range 42-71); all had stage IIIC (n=18, 75%) or IVB (n=6, 25%) disease. The regimen achieved exceptional surgical outcomes: CRR 91.6% (22/24), with 2 patients having minimal residual disease <1 cm. ORR was 87.5% (21/24). pCR rate was 4.2% (1/24). Robust tumor regression was observed: median residual viable tumor in primary lesions 22% (range 0-80%), in omental implants 44% (range 0-80%). With median follow-up of 5.0 months (range 2.3-10.6), no disease recurrence occurred. Grade ≥ 3 treatment-related adverse events occurred in 29.2% of patients, primarily hematological toxicities (neutropenia, thrombocytopenia) that resolved to $\leq$ grade 2 within one week with supportive care. Critically, no patient (0/27, 0%) experienced peripheral neuropathy of any grade. **Conclusions:** Neoadjuvant disitamab vedotin plus carboplatin demonstrated exceptional surgical outcomes with 91.6% complete resection rate and complete elimination of neurotoxicity in HER2-expressing advanced ovarian cancer. The regimen induced substantial pathological regression with a favorable safety profile. These results support RC48-carboplatin as a promising neurotoxicity-sparing alternative to standard paclitaxel-based therapy. Updated survival data will be presented. Clinical trial information: NCT06574763. Research Sponsor: Remegen.

Understanding palliative care gaps in young adult ovarian cancer: A population-based study of 37,880 hospitalizations.

Rigved Virendra Jeurkar, Aishwarya Ramesh, Kamleshun Ramphul, Saisree Reddy Adla Jala; Byramjee Jeejeebhoy Government Medical College, Pune, Mumbai, India; 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; Mission Hospital, Asheville, NC

Background: Palliative care (PaC) improves both quality of life and survival compared to usual care. Despite this, significant implementation gaps persist due to delayed or absent utilization. This study examines the determinants, trends, clinical profiles, and outcomes of PaC among young women hospitalized with ovarian cancer. **Methods:** We identified ovarian cancer patients among young adults aged 18–45 years using the National Inpatient Sample (NIS) from 2016–2022. We first estimated the prevalence of PaC utilization and then developed a multivariable logistic regression model to estimate the association of demographic, clinical, and hospital-level variables with PaC use. The in-hospital mortality burden associated with PaC receipt was also estimated. **Results:** We found 37,880 ovarian cancer young adults with 8.78% using PaC. Several variables were associated with PaC utilization. Clinical comorbidities demonstrated the strongest associations: metastatic cancer (aOR 4.123, 95% CI: 3.385–5.023, $p < 0.001$), frailty (aOR 3.407, 95% CI: 2.803–4.142, $p < 0.001$), and cachexia (aOR 3.817, 95% CI: 2.460–5.922, $p < 0.001$). Depression was also significantly associated with PaC utilization (aOR 1.360, 95% CI: 1.056–1.751, $p = 0.017$). Temporal trends revealed increasing PaC utilization in more recent years compared to 2016, with significantly higher odds in 2020 (aOR 1.412, 95% CI: 1.005–1.985, $p = 0.047$) and 2021 (aOR 1.565, 95% CI: 1.122–2.184, $p = 0.008$). Weekend admissions were associated with 38.2% higher odds of PaC receipt (aOR 1.382, 95% CI: 1.107–1.727, $p = 0.004$), and each additional year of age increased odds by 1.5% (aOR 1.015, 95% CI: 1.001–1.029, $p = 0.034$). Insurance status significantly influenced PaC receipt. Compared to Medicare beneficiaries, patients with private insurance had 36.6% lower odds of receiving PaC (aOR 0.634, 95% CI: 0.452–0.890, $p = 0.008$), while self-pay patients had 51.1% lower odds (aOR 0.489, 95% CI: 0.293–0.816, $p = 0.006$). Additionally, patients from the highest income quartile had 25.7% lower odds of PaC compared to those in the lowest income quartile (aOR 0.743, 95% CI: 0.555–0.996, $p = 0.047$). Race, hospital location/teaching status, hospital region, and hospital bed size were not significantly associated with PaC receipt. The overall in-hospital mortality rate was 3.0%, with stark differences by PaC receipt: 21.5% among those receiving PaC versus 1.22% among those not receiving PaC (aOR 16.532, 95% CI: 11.205–24.389, $p < 0.001$). **Conclusions:** Among hospitalized young adults with ovarian cancer, fewer than 1 in 10 received PaC. Services concentrated among patients with metastasis, frailty, and cachexia, suggesting late rather than early integration. Significant disparities by insurance and income highlight access barriers requiring intervention for equitable PaC integration into comprehensive cancer care. Research Sponsor: None.

Ocular toxicity and safety profile of mirvetuximab soravtansine in ovarian cancer: A systematic review and meta-analysis of clinical trials and real-world studies.

Priyanka Nagdev, Heena Arshad, Fatima Ali; UNC HBR, Morganton, NC; Sargodha Medical College, Sargodha, Pakistan; St. Vincent, Evansville, IN

Background: Mirvetuximab soravtansine (MIRV) is a folate receptor alpha (FR α)-targeting antibody-drug conjugate approved for FR α -positive, platinum-resistant ovarian cancer. Ocular adverse events are a characteristic toxicity of MIRV; however, the incidence and severity of ocular and selected non-ocular toxicities across clinical trials and real-world studies have not been comprehensively synthesized. **Methods:** This systematic review and meta-analysis study was conducted according to PRISMA guidelines and registered in PROSPERO (CRD420251270297). MEDLINE/PubMed, Embase, Scopus, and CENTRAL were searched from inception through December 2025 for prospective phase I–III trials and real-world observational studies evaluating MIRV in epithelial ovarian, fallopian tube, or primary peritoneal cancer. Two reviewers independently screened studies and extracted data. Primary outcomes included any-grade and grade ≥ 3 ocular adverse events, as well as ocular toxicity-related dose reductions and treatment discontinuations. Secondary outcomes included grade ≥ 3 pneumonitis and thrombocytopenia. Clinical trial and real-world data were analyzed separately. Random-effects meta-analyses of proportions were performed using logit transformation, with heterogeneity assessed using the I^2 statistic. Analyses were conducted in R version 4.5.2. **Results:** Fourteen studies comprising approximately 750 patients were included. In pooled analyses of clinical trials, any-grade ocular adverse events were common (56.2%; 95% CI, 5.2–96.8) with substantial heterogeneity contributing to wide confidence intervals, whereas grade ≥ 3 ocular adverse events were rare (1.41%; 95% CI, 0.47–4.13) with no observed heterogeneity. Dose reduction due to ocular toxicity occurred in 31.2% (95% CI, 18.0–48.4) of patients, while treatment discontinuation due to ocular adverse events was less frequent (9.98%; 95% CI, 0.70–63.58). Severe non-ocular toxicities were uncommon, with pooled incidences of 1.41% (95% CI, 0.47–4.13) for grade ≥ 3 pneumonitis and 1.44% (95% CI, 0.09–19.44) for grade ≥ 3 thrombocytopenia. Across three real-world studies involving 289 patients, treatment discontinuation due to ocular adverse events was rare (0.35%; 95% CI, 0.00–20.54), with safety findings consistent with those from clinical trials. **Conclusions:** MIRV is associated with frequent, but predominantly low-grade, ocular adverse events, which are commonly managed with dose modification, while severe ocular and non-ocular toxicities are rare. Real-world evidence supports the tolerability profile observed in clinical trials, highlighting the importance of proactive ocular monitoring to optimize treatment continuity. Research Sponsor: None.

Updated efficacy of dalpiciclib and nonsteroidal aromatase inhibitors (NSAIs) in estrogen receptor–positive (ER+) recurrent/metastatic (R/M) ovarian cancer and uterine neoplasms.

Huijuan Yang, Wei Jiang, Yi Fu, Lina Yin, Shuai Liu, Zhongyi Yang, Boer Shan, Lin Zhou, Xuan Pei; Department of Gynecologic Oncology, Fudan University Shanghai Cancer Center; Department of Oncology, Shanghai Medical College, Fudan University, Shanghai, China; Department of Radiology, Fudan University Shanghai Cancer Center; Department of Oncology, Shanghai Medical College, Fudan University, Shanghai, China; Department of Nuclear Medicine, Fudan University Shanghai Cancer Center; Department of Oncology, Shanghai Medical College, Fudan University, Shanghai, China

Background: Initial results from our trial showed the anti-tumor activity and good tolerance of CDK4/6 inhibitor dalpiciclib combined with NSAIs in patients (pts) with ER+ R/M ovarian cancer and uterine neoplasms (SGO, 2024, #S283; IGCS, 2025, #397). Here, we report updated results. **Methods:** This single-center, single-arm, open label, phase 2 trial enrolled pts with ER+, R/M ovarian cancer and uterine neoplasms which met the following criteria: pretreated low-grade serous ovarian carcinoma (LGSOC), pretreated uterine endometrioid carcinoma (EC), uterine leiomyosarcoma (LMS), or untreated low-grade endometrial stromal sarcoma (LGESS). Pts received dalpiciclib (150mg po d1-21 q28d) and NSAIs (mainly letrozole 2.5mg po qd) until disease progression, unacceptable toxicity or consent withdrawn. The primary end-point was 12-week progression-free survival (12wPFS) rate. A Simon's two-stage design was used (one-sided $\alpha=0.05$, power=80%), and the null hypothesis ($P=0.2$) would be rejected if totally >10 of 33 pts achieved primary endpoints. **Results:** As the data cutoff (Jan 5, 2026), 35 pts with a median of one prior therapy for R/M disease were enrolled, including 11 with LGSOC, 15 with EC, 8 with LGESS and 1 with LMS. With a median follow-up of 11.4 months (range, 0.1–52.2), 22 of 29 efficacy-evaluable pts had reached the primary endpoint, with a 12wPFS rate of 75.9% (95% CI 56.5–89.7), suggesting the value of further investigation. Detailed efficacy results are shown in Table 1. Grade 3–4 treatment-related adverse events (TRAEs) occurred in 82.9% (29/35) of pts, mostly neutrophil count decreased (71.4%), white blood cell count decreased (45.7%) and platelet count decreased (14.3%). Sixteen pts had dose reduction of dalpiciclib, mostly due to hematologic toxicities. No serious adverse events or treatment-related deaths occurred. Twelve pts were still on-treatment, with 3 pts treated for >4 years. **Conclusions:** The trial achieved its positive primary endpoint, showing meaningful efficacy of dalpiciclib + NSAIs in ER+ R/M ovarian cancer and uterine neoplasms. No new safety signals were observed. Clinical trial information: ChiCTR2000040597. Research Sponsor: None.

Efficacy results of evaluable pts.

	Overall N=29	LGSOC n=9	EC n=11	LGESS n=8	LMS n=1
12wPFS rate [95%CI]	75.9% (22/29) [56.5-89.7]	77.8% (7/9) [40.0-97.2]	63.6% (7/11) [30.8-89.1]	100% (8/8) [63.1-100]	0% (0/1) [0-97.5]
Clinical Response					
Partial response (PR)	5 (17.2%)	1 (11.1%)	2 (18.2%)	2 (25.0%)	0 (0%)
Stable disease (SD)	17 (58.6%)	6 (66.7%)	5 (45.5%)	6 (75.0%)	0 (0%)
SD $\geq$ 24 weeks	14 (48.3%)	5 (55.6%)	4 (36.4%)	5 (62.5%)	0 (0%)
Progressive disease (PD)	7 (24.1%)	2 (22.2%)	4 (36.4%)	0 (0%)	1 (100%)
ORR (CR+PR, 95% CI)	17.2% (5.85-35.8)	11.1% (0.28-48.3)	18.2% (2.28-51.8)	25.0% (3.19-65.1)	0% (0-97.5)
CBR (CR+PR+SD $\geq$ 24 weeks, 95% CI)	65.5% (45.7-82.1)	66.7% (29.9-92.5)	54.5% (23.4-83.3)	87.5% (47.4-99.7)	0% (0-97.5)

Phase II study of sintilimab combined with nab-paclitaxel in the treatment of platinum-resistant recurrent ovarian cancer.

Nan Zhang, Yanhua Bai, Hong Zheng, Yunong Gao, Tong Shu, Hongguo Wang, Yan Cai; Peking University Cancer Hospital and Institute, Beijing, China; Peking University Cancer Hospital & Institute, Beijing, China; Department of Gynecologic Oncology, Key Laboratory of Carcinogenesis and Translational Research (Ministry of Education/Beijing), Peking University Cancer Hospital and Institute, Beijing, China; Key Laboratory of Carcinogenesis and Translational Research (Ministry of Education), Department of Gynecologic Oncology, Peking University Cancer Hospital & Institute, Beijing, China

Background: Platinum-resistant recurrent ovarian cancer (PROC) remains a major therapeutic challenge with limited effective treatment options. This single-arm phase II trial aimed to evaluate the efficacy, safety, and tolerability of sintilimab combined with nab-paclitaxel in patients with platinum-resistant recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer. **Methods:** A total of 28 patients were enrolled and received intravenous sintilimab (200 mg, day 1) plus nab-paclitaxel (260 mg/m², day 1) every 3 weeks. The primary endpoint was objective response rate (ORR); secondary endpoints included progression-free survival (PFS), disease control rate (DCR), overall survival (OS), and safety. **Results:** The median age was 57 years (range: 37–74 years), with 96.4% having high-grade serous histology, 67.9% being BRCA wild-type, 57.1% with prior bevacizumab exposure, and 50% with a PD-L1 combined positive score (CPS) ≥ 1 . After a median follow-up of 11.8 months, the ORR was 35.7% (10 partial responses), DCR was 64.3%, median PFS was 4.28 months, and median OS was 15.83 months. Patients with CPS ≥ 1 had a higher ORR (42.9% vs. 28.6%) and DCR (71.4% vs. 57.1%) than those with CPS < 1 , but no significant difference in PFS (3.83 vs. 4.13 months, $p = 0.18$). Similar trends were observed for CPS ≥ 5 and CPS ≥ 10 , with ORRs of 44.4% and 50.0%, respectively, but no significant PFS differences (all $p > 0.05$). Notably, patients with tumor-infiltrating lymphocytes (TILs) $\geq 10\%$ exhibited a significantly higher ORR (72.7% vs. 12.5%, $p = 0.005$) and longer median PFS (15.57 months vs. 3.4 months, $p = 0.005$). Treatment-related adverse events (TRAEs) were mainly leukopenia (28.6%), neutropenia (25.0%), anemia (46.4%), and peripheral neuritis (28.6%), with rare grade 3–4 toxicities. **Conclusions:** Sintilimab combined with nab-paclitaxel shows promising efficacy and acceptable safety in PROC, with TILs $\geq 10\%$ and a high CD8⁺/CD4⁺ ratio emerge as potential predictive biomarkers, while PD-L1 CPS shows limited utility. This regimen represents a potential new therapeutic option for this difficult-to-treat population and warrants further investigation in randomized controlled trials. Clinical trial information: 2000031890. Research Sponsor: Xisike-CSPC Tumor Research Fund; Y-SY201902-0010.

Treatment duration with avutometinib/defactinib in recurrent low-grade serous ovarian carcinoma by KRAS mutation status.

Anna Shvygin, Qin Zhou, Carol Aghajanian, Dennis S. Chi, Alexia Iasonos, Roisin Eilish O'Cearbhaill, Aaron Praiss, Britta Weigelt, Rachel N. Grisham; Department of Surgery, Memorial Sloan Kettering Cancer Center, New York, NY; Memorial Sloan Kettering Cancer Center, New York, NY; Gynecologic Medical Oncology, Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, NY; Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, NY; Department of Pathology, Memorial Sloan Kettering Cancer Center, New York, NY

Background: Low grade serous ovarian carcinoma (LGSOC) is characterized by MAPK pathway alterations (most commonly *KRAS*, which occurs in 1/3 of tumors) and poor chemosensitivity. Avutometinib (MEK/RAF clamp) in combination with defactinib (FAK inhibitor) has shown durable responses in patients with recurrent LGSOC harboring a *KRAS* mutation and was recently FDA approved for this indication. However, data is lacking regarding the activity of avutometinib + defactinib (A+D) vs single agent MEK inhibitors for treatment of women with recurrent LGSOC. Here we examine patients who were treated with A+D. We also examine the duration of treatment in patients who received a single agent MEK inhibitor followed by A+D. **Methods:** In this single-institution retrospective cohort study, patients with recurrent LGSOC treated with A+D between 2021 – 2025 were included and stratified by tumor *KRAS* mutation status. The primary outcome was median duration of treatment on A+D, compared using Wilcoxon-Rank sum test. Pair-wise comparison of treatment duration in patients who were treated with single agent MEK inhibitors and A+D was performed. **Results:** 26 patients were included in the final analysis. Median age at diagnosis was 49 years (range 20–85). Patients had a median of 4 (range 1–9) prior lines of therapy, including hormonal (92%, n=24), bevacizumab (38%, n=10), and MEK inhibitors trametinib and binimetinib (35%, n=8). Eight (31%) patients harbored a tumor *KRAS* mutation. Among these 26 patients, median duration of treatment with A+D was 16.8 months in the *KRAS*-mutant and 5.5 months in the *KRAS*-wild type cohorts, respectively (p=0.037). Nine patients were treated with both A+D and a MEK inhibitor, three of whom had *KRAS*-mutant tumors. All nine patients received the single agent MEK inhibitor prior to treatment with A+D, with a median of 7 (range 4–8) prior lines of therapy before treatment with A+D. Among the three patients with *KRAS*-mutant tumors, median duration of treatment with single agent MEK inhibitor was 4.4 months (range 0.4–24.2) while with A+D, it was 17.6 months (range 6.1–23.4). **Conclusions:** In this single-institution retrospective cohort, treatment with A+D was associated with a significantly longer median duration of therapy in patients with *KRAS*-mutant recurrent LGSOC compared with *KRAS*-wild type disease. Among patients who received both regimens, A+D appeared to provide longer treatment duration than prior single agent MEK inhibitors in the *KRAS*-mutant subset, though this is limited by small sample size. These findings support improved activity of A+D in *KRAS*-mutant LGSOC and warrant confirmation in larger prospective studies. Research Sponsor: None.

Circulating tumor DNA to add prognostic stratification beyond CA-125 in epithelial ovarian cancer.

Grace Gorecki, Sarah Crafton, Phillip Gallo, Patti Petrosko, Muhammad Anees, William LaFramboise, John Nakayama; Allegheny Health Network, Pittsburgh, PA; Division of Gynecologic Oncology, Department of Obstetrics and Gynecology, West Penn Hospital, Allegheny Health Network, Pittsburgh, PA; Allegheny Health Network Cancer Institute, Pittsburgh, PA; Allegheny Health Network Cancer Institute, Allegheny Health Network, Pittsburgh, PA; Allegheny Health Network Cancer Institute at Allegheny Health Network, Pittsburgh, PA

Background: Ovarian cancer has a high risk of recurrence, particularly in patients with advanced-stage disease. CA-125 is routinely used to assess disease burden and recurrence risk but has limited prognostic accuracy. Circulating tumor DNA (ctDNA) has emerged as a potential biomarker that may better reflect tumor biology and enable earlier identification of recurrence.

Methods: Patients with epithelial ovarian cancer and available plasma ctDNA and CA-125 measurements collected in association with surgical debulking were included. CA-125 was stratified using a standard clinical cutoff of 35 U/mL. Average cfDNA yield (ng/mL) was stratified into high and low ctDNA groups based on the cohort median. Associations were assessed using correlation and categorical analyses. Overall survival (OS) was evaluated using Kaplan–Meier methods and Cox proportional hazards models, including multivariable analyses. **Results:** Among 89 patients, ctDNA concentration was positively associated with CA-125 (Spearman $\rho = 0.25$; $p = 0.017$). Patients with high CA-125 had higher ctDNA levels than those with low CA-125 (mean 21.2 vs 7.6; $p = 0.0044$). High ctDNA concentration was associated with worse OS compared with low ctDNA (log-rank $p = 0.0036$; HR 3.48, 95% CI 1.50–8.06), with median OS (mOS) of 1386 days versus not reached. Patients with both high CA-125 and high ctDNA experienced markedly worse mOS than patients with low ctDNA (log-rank $p = 0.0045$; HR 3.48, 95% CI 1.47–8.21), with a mOS of 827 days versus not reached respectively. This added stratification by ctDNA persisted across multiple sensitivity analyses, including stratification by timing of sample collection relative to surgery, with consistent prognostic associations observed in pre-surgery samples (mOS 953 days; log-rank $p = 0.031$) and post-surgery samples (mOS 569 days; log-rank $p = 0.045$), as well as in analyses of high-grade serous ovarian cancer, advanced-stage disease, and neoadjuvant therapy. In multivariable Cox regression adjusting for CA-125, disease stage, surgical status, and neoadjuvant therapy, ctDNA remained independently associated with OS (HR 1.012, 95% CI 1.003–1.019). **Conclusions:** ctDNA consistently added prognostic value beyond CA-125 despite treatment-related heterogeneity, suggesting that ctDNA concentration captures biologic features of tumor behavior not reflected by CA-125 alone. Importantly, ctDNA remained predictive regardless of the timing of sample collection. These findings support ctDNA as a complementary biomarker for baseline prognostic stratification. Research Sponsor: None.

The HER2 paradox in ovarian clear cell carcinoma: Expression and intrinsic resistance to trastuzumab deruxtecan (T-DXd).

Junsik Park, Soyeon Kim, Jeong-Hyun Kim, Yoo Na Kim, Yong jae Lee, Sunghoon Kim, Jung-Yun Lee; Department of Obstetrics and Gynecology, Soonchunhyang University Bucheon Hospital, Bucheon, South Korea; Department of Obstetrics and Gynecology, Yonsei University College of Medicine, Seoul, South Korea; College of Medicine, Yonsei University, Seoul, South Korea; Yonsei Cancer Center and Severance Hospital, Yonsei University College of Medicine, Seoul, South Korea

Background: Trastuzumab deruxtecan (T-DXd) shows potent activity in HER2-expressing ovarian cancer (OC). However, efficacy across histologic subtypes remains under-characterized. Specifically, data on T-DXd response in ovarian clear cell carcinoma (OCCC), a distinct chemo-resistant entity, are lacking. This study aimed to evaluate T-DXd efficacy in recurrent OC across different histologic subtypes. **Methods:** We retrospectively analyzed 59 patients with recurrent OC who received T-DXd treatment between 2020 and 2025 at Yonsei Cancer Center. HER2 status (IHC), objective response rate (ORR), progression-free survival (PFS), duration of response, and safety were assessed by histology. **Results:** Patients included HGSC (n=38), Mucinous (n=9), OCCC (n=10), and Endometrioid (n=2). Median age was 55; median prior lines of therapy was 3. Notably, 100% of OCCC, mucinous, and endometrioid tumors were HER2 2+/3+, vs. 89.5% in HGSC. Despite high HER2 expression, outcomes diverged. ORR was 55.3% (26/47) for HGSC/Mucinous vs. 0% (0/12) for OCCC/Endometrioid ($P<0.001$). Specifically, HGSC achieved 57.9% ORR (2 CRs) vs. 0% in OCCC. PFS was significantly shorter in the OCCC/Endometrioid group (median 1.2 vs 6.9 months; HR 18.3; $P<0.0001$). OCCC patients showed rapid progression. Regarding safety, among 54 evaluable patients, 36 (66.7%) experienced Grade 3-4 adverse events, and 5 cases (9.3%) of ILD occurred; however, no new safety signals or treatment-related deaths were reported. **Conclusions:** T-DXd showed robust efficacy in recurrent HGSC and mucinous OC but no response in OCCC and endometrioid OC. Thus, HER2 expression alone does not guarantee T-DXd response in OCCC, possibly due to its chemo-refractory nature. Mechanisms of T-DXd resistance in OCCC warrant investigation. Research Sponsor: None.

Tumor response.				
Histology	HGSC (n=38)	Mucinous (n=9)	Endometrioid (n=2)	Clear cell (n=10)
Objective response ¹ (n, %)	22 (58%)	4 (44%)	0 (0%)	0 (0%)
CR	2 (5%)	0 (0%)	0 (0%)	0 (0%)
PR	20 (53%)	4 (44%)	0 (0%)	0 (0%)
SD	14 (37%)	4 (44%)	0 (0%)	0 (0%)
PD	2 (5%)	1 (11%)	2 (100%)	10 (100%)

¹ $P=0.0006$.

A small extracellular vesicle protein-based model for ovarian cancer relapse detection and monitoring.

Zheng Feng, Xingzhu Ju, Liya Xu, Xiaojun Chen, Jin Li, Yaoxu Chen, Qingzhong He, Dadong Zhang, Xiaohua Wu; Department of Gynecologic Oncology, Fudan University Shanghai Cancer Center, Shanghai, China; Department of Oncology, Shanghai Medical College, Fudan University, Shanghai, China; Department of Clinical and Translational Medicine, 3D Medicines Inc., Shanghai, China; Fudan University Shanghai Cancer Center, Shanghai, China

Background: Recurrence surveillance of epithelial ovarian cancer (EOC) is a major clinical challenge, given the suboptimal performance of serum CA125 levels and limitations of radiological assessments. Serum small extracellular vesicle (sEV)-based liquid biopsy provides tumor-enriched and stable biomarkers, with potential to improve the precision of recurrence monitoring and support post-treatment surveillance. This study aimed to develop and preliminarily validate a serum sEV protein-based model to enhance recurrence monitoring in ovarian cancer. **Methods:** The study was designed with two stages (model development and validation) and plans to prospectively enroll 200 patients with EOC (NCT06925126). This analysis reports preliminary stage I data, and patients were categorized into relapse and non-relapse groups based on imaging-confirmed recurrence status. All relapsed patients were platinum-sensitive with low tumor burden. Quantitative assessment was performed on biomarkers derived from sEVs (specifically, E-CA125, E-HE4, and E-C5a) as well as corresponding serum markers measured in routine clinical practice (namely, H-CA125 and H-HE4), utilizing peripheral blood samples. Biomarker distributions were compared between groups, and predictive performance for recurrence detection was evaluated using receiver operating characteristic (ROC) analysis, including area under the curve (AUC), accuracy, sensitivity, and specificity. **Results:** A total of 113 patients were analyzed (42 non-relapsed, 71 relapsed), with a median age of 57 years. The majority (95/113) of patients had high-grade serous ovarian cancer, while other histological types were also included. Levels of E-CA125, E-HE4, H-CA125, and H-HE4 were significantly higher in relapsed patients compared with non-relapsed patients (all $p < 0.01$), while E-C5a showed no discriminative value between the two groups. Among individual sEV biomarkers evaluated, E-CA125 demonstrated the highest performance for recurrence detection (AUC = 0.877), followed by E-HE4 (AUC = 0.689) and E-C5a (AUC = 0.528). Moreover, the sEV protein-based model achieved an accuracy of 77.9% with a sensitivity of 71.8% and a specificity of 90.9%. This performance surpassed that of the conventional serum CA125, which exhibited an accuracy of 50.0%, a sensitivity of 26.8%, and a specificity of 100.0%. These results indicate that the sEV protein-based model may provide added clinical value when serum CA125 monitoring is unreliable after prior therapy. **Conclusions:** The sEV-derived CA125 and the sEV model demonstrate promising performance for recurrence detection in EOC. These findings support the feasibility of a serum sEV-based surveillance strategy that may improve the reliability of post-treatment monitoring. Prospective validation is ongoing to determine its potential role in guiding clinical surveillance and intervention. Clinical trial information: NCT06925126. Research Sponsor: None.

Efficacy prediction for progression-free survival (PFS) and overall survival (OS) by genomic instability score (GIS) cutoffs in patients (pts) with advanced ovarian cancer (aOC): Post hoc results from the phase 3 PRIMA/ENGOT-OV26/GOG-3012 trial.

Bradley J. Monk, Ignacio Romero, David M. O'Malley, Corina Martinez Mena, Lyndsay Willmott, Annika Auranen, Brian M. Slomovitz, Alice Bergamini, Emily N. Prendergast, Thibault de La Motte Rouge, Colleen C. McCormick, Elena Ioana Braicu, Floor Jenniskens Backes, Jose Alejandro Perez-Fidalgo, Richard G. Moore, Giorgio Valabrega, Roisin Eilish O'Cearbhaill, Sunkyoung Kim, Manjinder Bains, Antonio González-Martín; GOG Foundation, Philadelphia, PA, and Florida Cancer Specialists and Research Institute, West Palm Beach, FL; Instituto Valenciano de Oncología, Valencia, Spain; The Ohio State University and the James Comprehensive Cancer Center, Columbus, OH; CHU Saint-Pierre, Brussels, Belgium; Arizona Center for Cancer Care, Phoenix, AZ; Tays Cancer Center and FICAN Mid, Tampere University and Tampere University Hospital, Tampere, Finland; Department of Gynecologic Oncology, Mount Sinai Medical Center, and Department of Obstetrics and Gynecology, Florida International University, Miami Beach, FL; Obstetrics and Gynecology Unit, IRCCS Ospedale San Raffaele and Università Vita-Salute San Raffaele, Milano, Italy; Minnesota Oncology, Minneapolis, MN; Department of Oncology, Eugene Marquis Cancer Center and GINECO, Rennes, France; Legacy Medical Group Gynecologic Oncology, Portland, OR; Arbeitsgemeinschaft Gynäkologische Onkologie (AGO) and Department of Gynecology, Charité Universitätsmedizin, Berlin, Germany; Division of Gynecologic Oncology, The Ohio State University, Columbus, OH; Hospital Clínico Universitario, Biomedical Research Institute INCLIVA, University of Valencia, Valencia, Spain; Division of Gynecologic Oncology, Wilmot Cancer Institute, Department of Obstetrics and Gynecology, University of Rochester, Rochester, NY; University of Turin, A.O. Ordine Mauriziano, Turin, Italy; GOG Foundation, Philadelphia, PA, and Department of Medicine, Memorial Sloan Kettering Cancer Center, and Weill Cornell Medical College, New York, NY; GSK, Atlanta, GA; GSK, London, United Kingdom; Medical Oncology Department, Translational Oncology Group, CIMA, Universidad de Navarra, Cancer Center Clínica Universidad de Navarra, and Grupo Español de Investigación en Cáncer ginecológico (GEICO), Madrid, Spain

Background: GIS is a key component of a companion diagnostic assay for determining homologous recombination deficiency (HRD) status to identify pts with aOC who may benefit from maintenance therapy. While the standard GIS cutoff to classify tumors as homologous recombination-deficient (HRd) is ≥ 42 , this study analyzed PRIMA final analysis data to see if a lower cutoff of ≥ 33 based on the VELIA/GOG-3005 trial could identify additional pts who experienced a PFS benefit with niraparib (nir) first-line maintenance (1LM) vs placebo (PBO).

Methods: Pts with aOC were randomized 2:1 to nir or PBO 1LM. Tumor HRD status and GIS were assessed using the myChoice HRD test (Myriad Genetics). In pts with GIS data, tumor GIS distribution was assessed in the overall population and by HRD/BRCA status. Investigator-assessed PFS at GIS cutoffs < 33 vs ≥ 33 and < 42 vs ≥ 42 was evaluated using Kaplan-Meier methods with Cox proportional hazards modeling (cutoff, 08Apr2024). Two statistical utility tests were performed for each cutoff: 1) to evaluate each cutoff's potential to add incremental value to the explanation of pt response on top of treatment, and 2), in nir-treated pts, to assess each cutoff's ability to predict long-term PFS (≥ 3 y). OS was assessed by increasing GIS cutoffs.

Results: In the overall population (n=568), GIS ranged from 0 to 95, and 64.3% of pts had GIS ≥ 33 (GIS groups: 0 to < 33 , n=203; ≥ 33 to < 42 , n=67; ≥ 42 , n=298). Of pts with BRCA mutation, 9.4% (21/223) of pts had GIS < 42 . Nir 1LM produced a significant PFS benefit vs PBO across all GIS cutoffs, with greater benefit observed in higher GIS groups (Table). The GIS ≥ 33 cutoff improved the Cox model fit vs the ≥ 42 (ie, explaining more PFS variability and showing more powerful association with PFS after treatment adjustment). In nir-treated pts with GIS data (n=387), the ≥ 33 cutoff increased sensitivity (0.8936 > 0.7872), identifying 10.6% more patients with PFS ≥ 3 y, but lowered specificity (0.4369 < 0.5734) vs the ≥ 42 cutoff. Higher GIS cutoffs were also associated with more favorable nir 1LM on OS effects (lower hazard ratios).

Conclusions: In PRIMA, GIS existed along a spectrum, and nir 1LM resulted in a PFS benefit vs PBO across all GIS cutoffs. Pts with higher GIS experienced greater PFS benefit than pts with lower GIS. The GIS ≥ 33 cutoff identified more long-term PFS responders than the GIS ≥ 42 cutoff. Results suggest that GIS cutoffs of ≥ 33 used for HRd status determination may optimize identification of pts with aOC who may benefit from nir 1LM. Clinical trial information: NCT02655016. Research Sponsor: GSK; N/A.

	Tumor GIS			
Investigator-assessed PFS Nir vs PBO, n	<33 133 vs 65	≥ 33 283 vs 141	<42 169 vs 80	≥ 42 247 vs 126
Hazard ratio (95% CI) ^a	0.69 (0.50–0.96)	0.54 (0.42–0.68)	0.67 (0.50–0.89)	0.51 (0.40–0.66)
P value	0.026	<0.001	0.007	<0.001

^aStratified Cox proportional hazards model. Pts with GIS data included.

Platinum re-challenge in platinum-resistant ovarian cancer: Real-world patterns and outcomes.

Prakirthi Yerram, Matt Bye, Khilna Patel, Nicole Nasrallah, Michael A. Curry, Emily Castellanos; Flatiron Health, New York, NY; Flatiron Health, Durham, NC

Background: Platinum-resistant ovarian cancer (PROC), defined as recurrence within 6 months of completing platinum-based chemotherapy, has limited treatment options and poor outcomes. Although guidelines recommend non-platinum therapy, platinum rechallenge still occurs in real-world practice, despite limited evidence. This study examines real-world patterns and outcomes of platinum rechallenge versus non-platinum therapy at first PROC occurrence overall and by biomarker status, prior therapy, and time to PROC. **Methods:** Using the US-based, EHR-derived deidentified Flatiron Health Research Database, ovarian cancer patients diagnosed after January 1, 2017 (data cutoff August 31, 2025) were selected. Patients with PROC, defined as progressing ≤ 6 months after platinum, that received subsequent therapy were included; primary platinum refractory patients (< 3 months) were excluded. Patients were grouped by first PROC therapy (platinum rechallenge vs non-platinum therapy), and rwPFS and rwOS were assessed overall and by BRCA/HRD status, use of prior first-line maintenance (1LM), number of prior platinum lines, and time to PROC. Associations were assessed using Kaplan-Meier estimates and IPTW-adjusted Cox models accounting for demographics, ECOG PS, practice type, insurance, index year, biomarkers, and prior 1LM and platinum exposure. **Results:** Among 29,194 patients with ovarian cancer, 2,907 had PROC. Of these, 528 received platinum rechallenge and 2,379 received non-platinum therapy (71% received chemotherapy $\pm$ bevacizumab) as subsequent treatment. Baseline characteristics in both groups were similar; the platinum rechallenge group had fewer patients with BRCA mutations (BRCAm) (9.3% vs 12%) and no residual disease (36% vs 40%) but more with only one prior platinum line (56% vs 48%). Median rwPFS was 5.8 mo with platinum rechallenge vs 3.9 mo with non-platinum therapy (adjusted HR 0.72, 95% CI, 0.64 to 0.81; $P < .001$), and median rwOS was 13 vs 11 mo (adjusted HR 0.81, 95% CI, 0.72 to 0.92; $P = .001$). In adjusted analyses, rwPFS advantage of platinum rechallenge was consistent across major subgroups, including biomarker-defined populations (BRCA-wild type and HRD-positive non-BRCAm), prior 1LM and platinum exposure, and time to PROC. rwOS benefit was more limited, confined to patients with BRCAm, earlier recurrence, and more heavily pretreated disease, with limited events in several subgroups. **Conclusions:** In this large real-world cohort, platinum rechallenge improved rwPFS and rwOS vs non-platinum therapy in PROC. Consistent rwPFS benefits across most subgroups and selective rwOS advantages, particularly in BRCAm, highlight heterogeneity within PROC populations and support individualized decisions for platinum rechallenge beyond a strict 6-month platinum-free interval. Prospective studies are required to identify patients most likely to benefit from platinum rechallenge. Research Sponsor: Flatiron Health, Inc.

Circulating tumor DNA to enhance detection of high-risk minimal residual disease in ovarian cancer relative to second look laparoscopy.

Helen D. Clark, Sanghoon Lee, Anne Knisely, Yi Chen, Kathleen Keough, Charles Abbott, Mario Tanguma, Pamela T. Soliman, Jeffrey Andrew How, Lois M. Ramondetta, Travis T. Sims, David M. Boruta, Shannon Neville Westin, Aaron Shafer, Roni Nitecki Wilke, Gwyn Richardson, Anil K. Sood, Sean Michael Boyle, Richard Chen, Amir A. Jazaeri; The University of Texas MD Anderson Cancer Center, Houston, TX; Personalis, Inc., Fremont, CA; Personalis, Inc., Menlo Park, CA

Background: Minimal residual disease (MRD) following frontline treatment of ovarian cancer has been established as a predictor of recurrence and survival. Historically, second look laparoscopy (SLL) has served as the gold-standard method to assess MRD; however the need for surgical evaluation limits widespread adoption and clinical applicability. Circulating tumor DNA (ctDNA) offers a non-invasive alternative for MRD detection and enables longitudinal monitoring with the potential for early identification of recurrence. Presently, the concordance between ctDNA-based detection and surgical assessment remains incompletely characterized. In this retrospective cohort study, we compare the predictive performance of ctDNA versus SLL for detecting clinically significant MRD after frontline treatment for high-grade ovarian cancer. **Methods:** This retrospective, single-institution study included patients with high-grade epithelial ovarian cancer who completed frontline chemotherapy and surgery. All patients underwent SLL to determine surgical MRD status. At the time of SLL, plasma was collected and profiled using NeXT Personal. Using whole-genome sequencing, this ultrasensitive, tumor-informed assay tracks up to 1,800 tumor-specific variants to detect ctDNA at levels down to ~1 part per million. Statistical analyses were conducted using RStudio (version 2026.01.0.392). **Results:** The cohort consisted of 72 patients (median follow up 38.9 months) with high-grade epithelial ovarian cancer, of whom 69 patients (95.8%) were in clinical remission by Ca-125 and imaging. Despite this, 30 patients (41.7%) were positive for MRD by ctDNA and 33 patients (45.8%) were positive for MRD by SLL. On multivariable analysis, ctDNA positivity independently predicted worse PFS (HR 4.35, 95% CI 2.17-8.72, $p < 0.001$). The results of MRD and SLL were concordant in 53 (73.6%) of cases. There were 8 cases in which ctDNA was positive and SLL was negative. To date, 6/8 patients (75%) have recurred. There were 11 cases in which SLL was positive and ctDNA was negative. To date, 6/11 (54.5%) have recurred. Among these discordant cases, individuals with positive ctDNA but negative SLL had significantly worse PFS than cases with concordant negative results (HR 3.03, 95% CI 1.13-8.14, $p = 0.03$). Whereas among cases with positive SLL and negative ctDNA, there was not a significant difference compared with concordant negative cases (HR 1.54, 95% CI 0.58-4.12, $p = 0.39$). **Conclusions:** In this cohort where nearly all patients were in clinical remission, ctDNA was an independent predictor of PFS after frontline therapy in high-grade ovarian cancer. Although discordance occurs between ctDNA and SLL, these data suggest that ctDNA may detect clinically meaningful MRD not captured by SLL and could represent a more clinically relevant prognostic tool in this setting. Research Sponsor: None.

Dose-dense weekly versus standard three-weekly paclitaxel in combination with carboplatin for resectable stage II-IV epithelial ovarian carcinoma: A retrospective cohort study.

Sehrish Sarwar Baloch, Saqib Raza Khan, Anoud Khan, Aryan Tareen, Nawazish Zehra, Danial Hadi, Abdul Wasio, Munira Moosajee, Zarka Samoon; Aga Khan University Hospital, Karachi, Pakistan; Schulich School of Medicine & Dentistry, Western University, London, ON, Canada; Ziauddin Medical College, Karachi, Pakistan; Department of Oncology, Division of Medical Oncology, Schulich School of Medicine and Dentistry, Western University, London, ON, Canada; St Mary's Hospital, Waterbury, CT; Department of Oncology, Aga Khan University Hospital, Karachi, Pakistan; Peter MacCallum Cancer Centre, Melbourne, Australia

Background: Dose-dense weekly paclitaxel combined with carboplatin has demonstrated variable efficacy in first-line treatment of resectable epithelial ovarian cancer across different populations. While Japanese and selected real-world studies suggest improved outcomes, large Western trials have failed to confirm a survival advantage. Data from South Asian populations remains limited. This study compared progression-free survival (PFS), overall survival (OS), and toxicity profiles of dose-dense versus standard three-weekly paclitaxel plus carboplatin in a real-world, resource-constrained setting. **Methods:** This single-center retrospective cohort study included women aged ≥ 20 years with resectable, FIGO stage II–IV epithelial ovarian, fallopian tube, or primary peritoneal carcinoma treated between January 2015 and December 2018. Patients received first-line carboplatin at an AUC of 5 (Area Under Curve 5) with either dose-dense weekly paclitaxel (80 mg/m² on days 1, 8, and 15) or standard three-weekly paclitaxel (175 mg/m²). Kaplan–Meier methods were used to estimate PFS and OS, and comparisons were performed using the log-rank test. Cox proportional hazards models were applied for univariate and multivariate analyses. **Results:** Seventy-two patients were included, 36 in each arm. The majority presented with stage III disease (63.9% in the dose-dense arm vs. 52.8% in the standard arm). High-grade serous carcinoma was the predominant histology in both groups (83% vs. 75%). The distribution of primary versus interval debulking surgery and rates of residual disease were similar between the two arms. The dose-dense regimen was associated with significantly improved PFS compared with the standard schedule (mean PFS 25 vs. 18 months; 95% CI: 23.1–28.4; log-rank $p = 0.01$); median PFS was 32 months in the dose-dense arm, whereas it could not be estimated in the standard arm. OS favoured the dose-dense group (mean OS of 56 vs. 50 months), although this difference was not statistically significant ($p = 0.27$). In the multivariate analysis of the dose-dense cohort, elevated baseline Ca-125 (HR = 6.80; 95% CI: 1.38–34.20; $p = 0.01$) and cytoreduction type (HR = 13.30; 95% CI: 1.90–90.20; $p = 0.008$) were independent predictors of PFS but not for OS. Rates of grade ≥ 3 treatment-related adverse events were comparable between arms, while sensory neuropathy occurred more frequently with dose-dense therapy (39% vs. 28%). **Conclusions:** This real-world analysis supports the use of dose-dense weekly paclitaxel combined with carboplatin for improved PFS, findings consistent with some regional studies. While OS data showed a non-significant trend favouring the dose-dense regimen with some risk of neuropathy, they highlight the need for larger prospective regional studies to better define patient populations most likely to benefit. Research Sponsor: None.

Everolimus and aromatase inhibitors for advanced and recurrent low-grade serous ovarian carcinoma.

Halle Goodwin, Miranda Benfield, Erin Crane, Allison Puechl, Jubilee Brown, Brittany Lees, Yovanni Casablanca, R. Wendel Naumann; Atrium Health Levine Cancer Wake Forest University, Charlotte, NC

Background: Treatment options for advanced and recurrent low grade serous ovarian carcinoma (LGSOC) are limited. Mutations in the PI3K/AKT/mTOR pathway have been described in LGSOC, but the use of everolimus and aromatase inhibitors (AI) has not been studied. Our primary objective was to determine the disease control rate (DCR) of everolimus (used off-label) and an AI in patients with LGSOC. Secondary objectives included progression free survival (PFS) and overall survival (OS). **Methods:** Diagnosis codes and medication lists were used to identify all patients with LGSOC from a single tertiary-care institution who were treated with everolimus and an AI between 2000– 2025. Data were extracted from the electronic medical record including demographics, staging, treatment, CA-125, imaging studies, reported side effects, recurrence, and survival data. Response was defined with RECIST 1.1 when measurable disease was present, otherwise clinical response was used. CA-125 was used independently as an additional measure of response. **Results:** A total of eight patients were identified, six with stage IIIC disease and two with stage IVB disease. Patients had between 0 and 4 debulking surgeries. Prior to treatment with everolimus and an AI, patients had 1–6 prior lines of therapy. All patients had received prior endocrine therapy, and five received chemotherapy. All patients were treated with everolimus 10mg and an AI (6 with letrozole and 2 with anastrozole). Patients remained on this regimen between 2 and 20 months (median = 15 months). One patient continues treatment today after 21 months of treatment. By RECIST criteria, two patients had a partial response, and four patients had stable disease. One patient has had clinically stable disease (soft tissue thickening and a stable CA-125) for 21 months and continues treatment. When comparing initial CA-125 to nadir while on treatment, CA-125 was stable in three patients and decreased 29%–64% (median = 50.5%) in four patients. One patient did not have CA-125 available in the EMR. Overall, the DCR was 87.5% (7 of 8 patients). Median PFS was 16.8 months, and median OS was 26 months. Of the seven patients who discontinued treatment, reasons for discontinuation included progression (n=3), death from disease (n=2), and inability to tolerate (n=2, one with grade 3 pneumonitis). **Conclusions:** In a group of eight patients with advanced LGSOC, everolimus and an AI demonstrated a DCR of 87.5%, a median PFS of 16.8 months, and a median OS of 26 months. While larger retrospective studies or prospective studies are needed, this regimen should be considered for advanced, recurrent LGSOC. Research Sponsor: None.

Exposure–response (E–R) analyses of efficacy and safety with raludotatug deruxtecan (R-DXd), a CDH6-directed antibody-drug conjugate (ADC), to inform dose selection for phase (Ph) 3 development in platinum-resistant ovarian cancer (PROC).

Felipe K. Hurtado, Emily Schapiro, Elizabeth Lusk, Isabelle Laure Ray-Coquard, Lydia Gaba, Kosei Hasegawa, Alexander Philipovski, Izna Ali, Youngjun Yoo, Hiroyuki Inoue, Tsvetomir Mitov, Guillaume Berghold, Yvonne Lau; Daiichi Sankyo, Inc., Basking Ridge, NJ; A2-Ai LLC, Ann Arbor, MI; Centre Léon Bérard, Centre Régional de Lutte Contre Le Cancer de Lyon, Lyon, France; Hospital Clinic, Barcelona and GEICO, Barcelona, Spain; Saitama Medical University International Medical Center, Hidaka, Saitama, Japan; Florida Cancer Specialists/Sarah Cannon Research Institute, Lake Mary, FL; Daiichi Sankyo, Ltd., Tokyo, Japan; Daiichi Sankyo UK Ltd., Uxbridge, United Kingdom; Daiichi Sankyo France SAS, Rueil-Malmaison, France

Background: R-DXd, an ADC, comprises a humanized cadherin 6 (CDH6) IgG1 monoclonal antibody attached to a topoisomerase I inhibitor payload (DXd) via a tumor-selective cleavable linker. R-DXd monotherapy demonstrated promising antitumor activity and a manageable safety profile at doses up to 6.4 mg/kg IV Q3W in patients (pts) with heavily pretreated ovarian cancer (OC) in a Ph 1 study and in pts with PROC in an ongoing Ph 2/3 study. We report findings from E–R analyses of key efficacy and safety endpoints that supported R-DXd dose selection for Ph 3 clinical investigation in patients with PROC. **Methods:** Data were included from (i) the first-in-human Ph 1 study in pts with advanced OC (N=156) or renal cell carcinoma (RCC; N=23) evaluating R-DXd 1.6–9.6 mg/kg Q3W (NCT04707248), and (ii) the dose-optimization part of the Ph 2/3 REJOICE-Ovarian01 study in pts with PROC (N=107) (NCT06161025), in which pts were randomized 1:1:1 to receive R-DXd 4.8, 5.6, or 6.4 mg/kg Q3W. E–R analysis for efficacy was conducted based on pooled data from 241 pts with PROC using BICR-assessed endpoints: ORR (primary endpoint in the Ph 2 part of REJOICE-Ovarian01), best change in target lesion size, DOR, and PFS. Further, E–R analysis for safety was performed for 11 AEs of clinical interest using data from 286 pts treated with R-DXd across tumor types (OC, RCC). ORR and all safety endpoints, except interstitial lung disease (ILD), were analyzed by logistic regression; DOR, PFS, and ILD were analyzed using the Kaplan–Meier method. Numerous patient-specific covariates were evaluated. **Results:** E–R analyses demonstrated positive dose–response relationships for both efficacy and safety. Higher R-DXd exposure was associated with increased probability of achieving objective response, greater reduction in target lesion size from baseline, longer PFS, and longer DOR. Covariate analysis identified that baseline CDH6 expression was positively associated with ORR and tumor response. Higher R-DXd or DXd payload exposure was associated with an increase in drug-related TEAEs, including Grade ≥ 3 (G3+) AEs, any-grade ILD, G2+ gastrointestinal AEs (nausea/vomiting), G3+ cytopenias (anemia, neutropenia, thrombocytopenia), and AEs leading to dose reduction. While higher doses of R-DXd are predicted to maximize efficacy based on the E–R analysis, the 5.6 mg/kg dose provides an overall optimal balance of safety, tolerability, and efficacy compared to 6.4 mg/kg and 4.8 mg/kg. **Conclusions:** Integrated E–R analyses, combined with the totality of data from 286 pts, support selection of 5.6 mg/kg Q3W as the optimal R-DXd monotherapy dose for the Ph 2 extension and Ph 3 parts of REJOICE-Ovarian01, in accordance with the principle of benefit/risk for oncology dose optimization and guidelines from the FDA's Project Optimus. Research Sponsor: Daiichi Sankyo; Merck.

Population pharmacokinetic analysis of raludotatug deruxtecan (R-DXd), a cadherin 6 (CDH6)–directed antibody–drug conjugate (ADC), in patients (pts) with advanced ovarian cancer (OC) or renal cell carcinoma (RCC).

Felipe K. Hurtado, Emily Schapiro, Jonah Lyon, Nicoletta Colombo, Sabrina Chiara Cecere, Kosei Hasegawa, Alexander Philipovskiy, Izna Ali, Youngjun Yoo, Hiroyuki Inoue, Yvonne Lau; Daiichi Sankyo, Inc., Basking Ridge, NJ; A2-Ai LLC, Ann Arbor, MI; European Institute of Oncology, IRCCS, Milan, Italy; IRCCS Fondazione G. Pascale, Naples, Italy; Saitama Medical University International Medical Center, Saitama, Japan; Florida Cancer Specialists/Sarah Cannon Research Institute, Lake Mary, FL; Daiichi Sankyo, Ltd., Tokyo, Japan

Background: R-DXd is a CDH6–directed ADC under clinical investigation for the treatment of pts with advanced or metastatic solid tumors, including platinum-resistant OC (PROC). This analysis was done to characterize the population pharmacokinetics (PopPK) of R-DXd and its small-molecule payload, DXd, in pts with OC or RCC. The analysis used data from two clinical studies of R-DXd: the first-in-human Ph 1 study in pts with OC or RCC (DS6000-A-U101; U101) and an ongoing global, randomized Ph 2/3 study in pts with PROC (REJOICE-Ovarian01).

Methods: A joint PopPK model was developed for R-DXd and DXd, based on pooled data from the dose-escalation and -expansion parts of U101 (156 pts with OC and 23 with RCC; 1.6–9.6 mg/kg IV Q3W) and the dose-optimization primary analysis of REJOICE-Ovarian01 (107 pts with OC; 4.8, 5.6, or 6.4 mg/kg IV Q3W). The analysis was performed using nonlinear mixed-effects modeling in NONMEM (version 7.5.1). The effect of key intrinsic/extrinsic factors on the PK of R-DXd was explored through preliminary covariate analysis. **Results:** The PK of R-DXd and unconjugated DXd were adequately captured by the PopPK model. R-DXd displayed time-varying clearance, resulting in an elimination half-life of approximately 8 days after the first dose and 14 days at steady state. The overall PK profile supports a Q3W dosing interval. Consistent with findings from other mAbs and DXd-based ADCs, covariate analysis identified body weight (BW) as an influential covariate affecting R-DXd and DXd exposure, with the largest effect seen at the extremes of the BW distribution; pts with high BW (101 kg; 95th percentile) showed 26% and 66% higher R-DXd and DXd steady state area under the concentration–time curve (AUC), respectively, relative to a reference pt (61 kg; median BW). Post-hoc estimates of R-DXd and DXd AUC by BW quartiles showed that exposure in pts in the highest BW quartile (>75 kg) trended higher yet remained within the range of pts with average BW (53–74 kg; 25th–75th percentile). Other baseline covariates did not have a clinically important effect on R-DXd or DXd AUC, with effects falling within the predefined range of 80–125% vs reference. These covariates were CDH6 expression (total % membrane staining at any intensity); R-DXd formulation; hepatic function (mild impairment vs normal); renal function (mild-to-moderate impairment vs normal); tumor size; albumin level; number of prior lines of therapy (1 vs 2–3 vs ≥4); tumor type (RCC vs OC); Asian vs non-Asian race. **Conclusions:** R-DXd 5.6 mg/kg IV Q3W, the recommended Ph 3 dose, does not appear to warrant adjustment for any of the patient-specific covariates and clinical characteristics investigated. These findings support the adequacy of this dose for the global population of pts with PROC being recruited in the Ph 3 part of REJOICE-Ovarian01. Research Sponsor: Daiichi Sankyo; Merck.

Multi-modal liquid biopsy integrating cfDNA fragmentomics and serum biomarkers for the differential diagnosis of ovarian tumors.

Zhoumei Liu, Hongying Yang, Ming Wang, Di Xiong, Ning Fu, Ningyou Li, Xinyue Hong, Xiaoying Wu, Shanshan Yang, Rui Liu, Xiaoxi Chen, Haimeng Tang, Xue Wu, Yumei Wu, Xielan Yang; Peking University Cancer Hospital Yunnan, Yunnan Cancer Hospital, The Third Affiliated Hospital Kunming Medical University, Kunming, Yunnan, China; Peking University Cancer Hospital Yunnan, Yunnan Cancer Hospital, The Third Affiliated Hospital Kunming Medical University, Kunming, China; Beijing Obstetrics and Gynecology Hospital, Capital Medical University, Beijing Maternal and Child Health Care Hospital, Beijing, China; Geneseeq Research Institute, Nanjing Geneseeq Technology Inc., Nanjing, China; Nanjing Geneseeq Technology Inc., Nanjing, China; The Capital Medical University Affiliated Beijing Obstetrics and Gynecology Hospital, Beijing, China

Background: Ovarian cancer (OC) remains the leading cause of mortality among gynecological malignancies, primarily due to delayed diagnosis. Current diagnostic modalities, including imaging and serum biomarkers, exhibit suboptimal specificity, leading to unnecessary surgical interventions for benign adnexal masses. This study explores the clinical utility of cell-free DNA (cfDNA) fragmentomics, a high-dimensional genomic feature reflecting chromatin accessibility, in distinguishing malignant from benign ovarian tumors. **Methods:** This multi-center study enrolled 595 participants across three cohorts: a training set (n=236) and an internal validation set (n=172) from Yunnan Cancer Hospital, and an independent external validation set (n=136) from Beijing Obstetrics and Gynecology Hospital. Additionally, a prediction cohort included borderline ovarian tumors (BOT, n=51). Using whole-genome sequencing (WGS), we characterized cfDNA via four fragmentomic dimensions: copy number variations (CNVs), fragment size profiles (FSPs), nucleosome footprints (NFs), and genomic element perturbations (ARTEMIS). An ensemble model was trained to classify malignant ovarian cancer versus benign disease, and a generalized linear model was constructed by integrating fragmentomic scores with CA125 and HE4 levels to further improve the performance. **Results:** The cfDNA-only model demonstrated robust performance with Area Under the Curve (AUC) values of 0.937, 0.930, and 0.932 in the training, internal, and external cohorts, respectively. At 90% sensitivity in training (internal: 88.4%; external: 89.2%), specificities remained stable at 77.12%, 77.91%, and 78.87%. The model exhibited exceptional sensitivity for High-Grade Serous Ovarian Cancer (HGSOC) (>90%) with sensitivity increased with stages; early-stage (I–II) sensitivities were maintained $\geq 77\%$. Integrating the cfDNA fragmentomic score with CA125 and HE4 significantly enhanced AUCs to 0.961 (training), 0.964 (internal) and 0.964 (external). While maintaining high sensitivity ($\sim 90\%$), the combined model substantially increased specificity to 90.1% (training). Among 37 surgically treated stage I–III patients, higher pre-operative predictive scores were significantly associated with shorter disease-free survival (DFS) ($p < 0.05$), independent of age, stage, and histology. In BOT patients, 39.2% were classified as higher malignant-risk, consistent with an intermediate phenotype. **Conclusions:** The integration of cfDNA fragmentomics with traditional biomarkers provides a highly sensitive and specific non-invasive tool for the differential diagnosis of ovarian masses. This multi-modal approach significantly outperforms current clinical standards, offering a promising strategy for early detection and clinical risk stratification in ovarian cancer management. Research Sponsor: Beijing Municipal Health Commission; BCRW202109; Capital Medical University; FCYYMZA202501.

Real-world outcomes of olaparib with versus without bevacizumab in bevacizumab-naïve BRCA1/2-mutated ovarian cancer.

Love Kumar, Jennifer Collins, Courtney Nail, Amir Kamran, Stephen Bush II; Charleston Area Medical Center (CAMC), Charleston, WV; Charleston Area Medical Center Institute for Academic Medicine, Charleston, WV; CAMC Cancer Center, Gynecology, Charleston, WV; Charleston Area Medical Center, Charleston, WV; Gynecologic Oncology, Charleston Area Medical Center Hospital, Charleston, WV

Background: For patients with BRCA1/2-mutated epithelial ovarian, fallopian tube, or primary peritoneal cancer who complete primary platinum-based therapy, maintenance strategies differ based on prior bevacizumab (Bev) exposure. Patients who received Bev during frontline platinum therapy may receive Bev plus olaparib, whereas those without prior Bev exposure are generally treated with olaparib alone. No real-world evidence has evaluated outcomes of adding Bev to olaparib in patients who did not receive Bev during initial treatment. Using a large multi-institutional electronic health record dataset, we compared survival outcomes between olaparib monotherapy and olaparib-Bev combination therapy in this population. **Methods:** Adult patients from 2015-2024 with a diagnosis of ovarian, fallopian tube, or peritoneal cancer who received platinum chemotherapy followed by olaparib were first identified. Patients were then categorized based on bevacizumab exposure around the time of olaparib initiation (-1 to +3 months). This group was compared to patients who did not received Bev at any time. The index date was defined as 3 months after olaparib initiation to align treatment timing and minimize immortal time bias and propensity score matching was performed on age, race, metastatic sites, comorbidities, and prior treatments. Follow-up was then truncated at 3-years. **Results:** Before matching, 111 patients received Bev around the time of olaparib and 1,461 did not. After matching, 110 patients remained in each group with balanced characteristics. Three-year overall survival was significantly lower in the Bev group compared with the no-Bev group (52% vs 73%; HR 2.28, 95% CI 1.4-3.8; $p=0.001$). Treatment switching also occurred more often in the Bev group (54% vs 22%, $p < 0.0001$), with a median time to switching of 16.7 months; the no-Bev group did not reach median time. **Conclusions:** In real-world clinical practice, the addition of bevacizumab to olaparib in patients without prior bevacizumab exposure was associated with worse survival outcomes and earlier treatment switching. These findings may reflect the selection of patients with more aggressive or treatment-resistant disease for combination therapy, or they may suggest that intensifying therapy in this setting does not confer added benefit. Prospective, controlled studies are needed to clarify the underlying reasons for these observations and to better define which patients, if any, derive benefit from this treatment approach. Research Sponsor: None.

A phase II evaluation of sacituzumab govitecan in platinum-resistant ovarian cancer (NCT06028932).

Alessandro Santin, Dana Marie Roque, Eric R. Siegel, Victoria M. Ettore, Michelle Greenman, Sarah Ottum, Blair McNamara, Katya Papatla, Aparna Kailasam, Natalia Buza, Mitchell B. Clark, Pei Hui, Petter Dottino, Elena Ratner, Stefania Bellone; Yale School of Medicine, Division of Gynecologic Oncology, New Haven, CT; Greenebaum Comprehensive Cancer Center, University of Maryland School of Medicine, Division of Gynecologic Oncology, Baltimore, MD; University of Arkansas for Medical Sciences, Little Rock, AR; Yale School of Medicine, Department of Obstetrics, Gynecology, and Reproductive Sciences, New Haven, CT; Yale School of Medicine, Department of Pathology, New Haven, CT

Background: Patients with platinum-resistant ovarian cancer (PROC) have few therapeutic options. More than 60% of high-grade serous ovarian cancers overexpress ($\geq 2+$ by immunohistochemistry) Trop2, a key regulator of growth pathways and marker of aggressive disease. Sacituzumab govitecan (SG) is an antibody-drug conjugate consisting of a Trop-2-specific antibody conjugated with SN-38, an active metabolite of irinotecan. **Methods:** NCT06028932 is a single-institution open-label phase II study. Patients received SG at 10 mg/kg intravenously days 1 and 8 of a 21-day cycle until prohibitive toxicity or progression. The primary endpoint was objective response rate (ORR) by RECIST 1.1. Secondary endpoints included progression-free (PFS) and overall (OS) survival, as well as safety. **Results:** Twenty patients were enrolled. Median age was 67 years (range: 45–84). Most participants (85%, n=17) were White. The median number of prior lines prior to enrollment was 3 (range: 1–8). ECOG performance status was 0 (n=16) or 1 (n=4). Most patients had a poorly differentiated tumor (90%, n=18) with advanced disease (stage III/IV) at initial diagnosis (85%, n=17). Serous histology predominated (75%, n=15), followed by clear cell (15%, n=3), endometrioid (5%, n=1), and carcinosarcoma (5%, n=1). Across a median follow-up of 9.9 months, there were 15 progressions and 4 deaths. ORR was 35% (7/20); there were no complete responses, and stable disease was achieved in 40% (8/20). Median PFS was 8.0 months (95% CI: 3.8–14.8); median OS was not yet reached. No new safety signals were observed. The most common grade 3–4 treatment-emergent adverse events were neutropenia (n=15), hypokalemia (n=3), and anemia (n=2). The most frequent grade 1–2 events included diarrhea (n=59), fatigue (n=27), abdominal pain (n=20), nausea (n=20), alopecia (n=16), anorexia (n=14), and vomiting (n=13). **Conclusions:** SG exhibits encouraging efficacy for PROC with manageable toxicities. Future studies are warranted. Clinical trial information: NCT06028932. Research Sponsor: None.

Preliminary efficacy and safety of first-line anlotinib plus carboplatin/paclitaxel induction therapy followed by anlotinib maintenance in advanced ovarian cancer: Results from the ALTER-GO-010 phase II multicenter trial.

Wenjun Cheng, Yi Jiang, Yingchun Gao, Youguo Chen, Yulang Cai, Huaijun Zhou, Jinjin Yu, Jinhua Zhou; Jiangsu Provincial Hospital, Nanjing, China; Jiangsu Province Hospital, Nanjing, China; Huai'an First People's Hospital, Huai'an, China; The First Affiliated Hospital of Soochow University, Suzhou, China; Department of Obstetrics and Gynecology, Zhongda Hospital Southeast University, Nanjing, China; Nanjing Drum Tower Hospital, Nanjing, China; The Affiliated Hospital, Jiangnan University, Wuxi, China; Department of Obstetrics and Gynecology, The First Affiliated Hospital of Soochow University, Suzhou, Jiangsu, China

Background: Several studies have shown that antiangiogenic drugs combined with chemotherapy as first-line treatment, followed by maintenance therapy with antiangiogenic agents, significantly improve outcomes for ovarian cancer patients. Anlotinib, a highly effective multi-target tyrosine kinase inhibitor targeting VEGFRs, FGFRs, PDGFRs, and c-Kit, has been approved for multiple tumor types in China. The ALTER-GO-010 study is a single-arm, multi-center phase II trial designed to assess the efficacy and safety of anlotinib in combination with carboplatin/paclitaxel as first-line induction therapy, followed by anlotinib maintenance, in patients with newly diagnosed advanced ovarian cancer. **Methods:** Eligible patients with newly diagnosed FIGO stage III–IV primary epithelial ovarian, fallopian tube, or primary peritoneal cancer (ECOG PS 0–1) who have undergone primary or interval debulking surgery will receive 6–8 cycles of chemotherapy (paclitaxel 175 mg/m² + carboplatin AUC 5 every 3 weeks) combined with anlotinib (12 mg orally once daily on days 1–14, 21-day cycle; omitted during the first cycle to prevent delayed wound healing). Following chemotherapy completion, anlotinib will be continued as maintenance monotherapy until disease progression, unacceptable toxicity, or death. Exclusion criteria include prior anti-angiogenic therapy or major surgery within 28 days before anlotinib initiation. The primary endpoint is progression-free survival (PFS). Key secondary endpoints include overall survival, and safety profile. **Results:** As of the data cutoff date (November 30, 2025), 54 patients had received at least one dose of the study drug and were included in the analysis. The median age was 56 years, 98.11% had high-grade serous carcinoma and 1.89% had endometrioid carcinoma. 96.23% had FIGO stage III and 3.77% had stage IV. The data maturity for PFS analysis was 40.7%. The median PFS was 20.76 months (95% CI: 11.58–29.95). Patients without prior history of neoadjuvant therapy had longer mPFS than those with prior therapy. The median OS was not reached. The most common all-grade treatment emergent adverse events (TEAEs) were white blood cell decreased, anemia, neutrophil count decreased, platelet count decreased and lymphocyte count decreased. Grade ≥ 3 TEAEs occurred in 75.5% of patients during the chemotherapy phase and 22.7% during maintenance. No treatment-related deaths were reported. **Conclusions:** The preliminary efficacy and safety data suggest that anlotinib plus carboplatin/paclitaxel induction therapy, followed by anlotinib maintenance, is a promising regimen for newly diagnosed advanced ovarian cancer, with a median PFS of 20.76 months and a favorable safety profile. Clinical trial information: NCT04807166. Research Sponsor: None.

A novel prognostic index for survival prediction in ovarian cancer: Beyond FIGO staging.

Arya Prathap, Prasanth Narayanan, Priyanka Saha, Dripta Ramya Sahoo, Pooja Khandelwal, Priyansh Jain, Sravya Ganti, Abhitesh Singh, Phanindra kumar Swain, Biswajit Sahoo, Kiran Yidagur Gangadharaiah Lokesh Sr., Madhabananda Kar, Dillip Kumar Muduly; AIIMS Bhubaneswar, Bhubaneswar, India; AIIMS, Bhubaneswar, India; Aiiims Bhubaneswar, Baudh Sadar, India; All India Institute of Medical Sciences - Bhubaneswar, Bhubaneswar, India; Aiiims Bhubaneswar, Bhuban, India; All India Institute of Medical Sciences, Bhubaneswar, Bhubaneswar, India; All India Institute of Medical Science (AIIMS), Bhubaneswar, Delhi, India

Background: Prognostication in ovarian cancer is traditionally based on FIGO stage, although survival is influenced by additional patient- and treatment-related factors. We developed a new scoring system integrating age, comorbidities, and disease burden to improve survival prediction. **Methods:** Patients with ovarian malignancies treated with curative intent between June 2016 and November 2024 were identified from a prospectively maintained database. Cox proportional hazards regression was performed for 4-year overall survival (OS). Regression coefficients of significant variables were used to construct a new index. Survival outcomes were assessed using Kaplan–Meier analysis. Predictive performance of new index was compared with FIGO staging using receiver operating characteristic (ROC) analysis. **Results:** Of 221 consecutive patients, 167 treated with curative intent were analyzed. Median age of the cohort was 52 years (IQR 22–78), and FIGO stage IIIC was most common (45.7%). Optimal cytoreduction was achieved in 80.8%, and 71.3% received adjuvant therapy. At a median follow-up of 38.3 months, recurrence and mortality rates were 32.9% and 26.2%, respectively. The new score incorporated age, total surgical PCI, hypothyroidism, diabetes mellitus, and hypertension with regression-derived coefficients of 0.044, 0.114, 0.329, 0.146, and 0.313 respectively. For each patient, a prognostic index (PI) was calculated as the weighted sum of regression coefficients corresponding to that patient's covariate profile, using formula, where $PI (Prognostic\ index) = \sum (\beta_1 \times age) + (\beta_2 \times PCI) + (\beta_3 \times C_1) + (\beta_4 \times C_2) + \dots + (\beta_k \times C_k)$, $C_1 \dots C_k$ = individual comorbidities (eg., diabetes, hypertension, etc), if present = 1, absent = 0). Based on the prognostic index, patients were classified into low- (33.75%), intermediate- (31.3%), and high-risk (31.3%) groups. Compared with the low-risk group, OS was worse in the intermediate-risk group (HR 2.37; 95% CI, 0.95–5.91; $p = 0.06$) and significantly inferior in the high-risk group (HR 7.89; 95% CI, 3.37–18.49; $p < 0.001$). Disease free survival (DFS) also showed a similar trend. The prognostic index demonstrated superior discrimination compared with FIGO staging (C-index 0.73 vs 0.68; AUC 0.71 vs 0.65) and remained robust on bootstrap internal validation. A prespecified subgroup analysis restricted to FIGO stage III patients was performed and demonstrated superior discrimination for overall survival compared with FIGO staging alone (AUC 0.71 vs 0.61), highlighting prognostic heterogeneity beyond anatomic staging. **Conclusions:** The prognostic index demonstrated improved discrimination compared with FIGO staging by integrating patient age, comorbidities, and disease burden. This practical, clinically applicable index may facilitate improved risk stratification beyond anatomic staging and may support individualized management strategies in ovarian cancer. Research Sponsor: None.

Beyond survival: Understanding unmet needs among a diverse cohort of ovarian cancer survivors.

Caroline P. Shermoen, Anne Marie McCarthy, Katie Elkins, Tyasia Cannon, Chelsea Peart, Milka Mengesha, Karen Glanz, Anna Jo Bodurtha Smith, Emily Meichun Ko; University of Pennsylvania, Philadelphia, PA; Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA; Division of Gynecologic Oncology, University of Pennsylvania, Philadelphia, PA

Background: Improvements in therapy have resulted in a growing population of ovarian cancer survivors, with both incidence and survivorship increasing among non-White racial and ethnic groups. Despite increasing survivors, supportive care for ovarian cancer survivors has been reported as insufficient. Existing instruments to address survivorship needs were developed in homogenous populations, predominantly consisting of White patients. The purpose of this study was to gain a deeper understanding of the needs and experiences in a diverse cohort of ovarian cancer survivors. **Methods:** Structured focus groups of ovarian cancer survivors were conducted at a single academic NCI-designated cancer center. During focus groups, participants were guided in discussion about their experience, perspective, and unmet needs as an ovarian cancer survivor. The topics were developed in consultation by providers involved in direct ovarian cancer research and patient care. Thematic analysis was used to systematically code and analyze focus group transcripts, allowing for identification of recurrent patterns and themes within the data. **Results:** Three focus groups of 20 patients were conducted. 12 (60%) patients identified as White, 4 (20%) as Asian, 3 (15%) as Black, and 1(5%) as Hispanic; additional patient characteristics are in Table 1. Participants generally reported their care during treatment was efficient and streamlined; however, gaps in survivorship care emerged. Key themes included poor care coordination with non-oncologic providers, feelings of abandonment after active treatment, limited communication about long-term expectations after surgery and/or chemotherapy, lack of individualized care plans, and uncertainty about where to find reliable resources. Suggested improvements included centralized access to survivorship resources, expanded peer support opportunities, and more tailored, patient-specific communication. **Conclusions:** The study highlights specific gaps in ovarian cancer survivorship among a diverse patient population. Deficits in care coordination, individualized communication, and access to tailored resources may contribute to feelings of abandonment and uncertainty following treatment. Targeted survivorship interventions addressing these areas may help to improve quality of life among an increasingly diverse population of ovarian cancer survivors. Research Sponsor: National Cancer Institute.

Focus group characteristics (N=20).	
Patient Characteristics	# of Participants
Age Range (Years)	
<50	4
50-59	7
60+	9
Time Since Diagnosis (years)	
>10	2
5-10	4
3-5	2
<3	12

Phase II study of utidelone plus fruquintinib for the treatment of platinum-resistant recurrent ovarian cancer (FRUTD trial).

Hao Wen, Zheng Feng, Ruimin Li, Huaying Wang, Xingzhu Ju, Zhong Zheng, Qin hao Guo, Yanping Zhong, Li Tang, Xiaohua Wu; Department of Gynecologic Oncology, Fudan University Shanghai Cancer Center, Shanghai, China; Department of radiology, Fudan University Shanghai Cancer Center, Shanghai, China; Beijing Biostar Pharmaceuticals Co., Ltd., Beijing, China; Fudan University Shanghai Cancer Center, Shanghai, China

Background: Patients (pts) with platinum-resistant ovarian cancer (PROC) have a poor prognosis, and traditional cytotoxic drugs have limitations in efficacy and safety. Therefore, we are exploring the combination of utidelone capsule (UTD2), a novel oral microtubule inhibitor, with fruquintinib capsule (F), a tyrosine kinase inhibitor targeting VEGFR 1,2,3, for the treatment of platinum-resistant recurrent ovarian cancer. **Methods:** This study is an open-label and Simon two-stage phase II clinical trial, aiming to enroll 35 pts with platinum-resistant recurrent epithelial ovarian cancer, fallopian tube cancer, or primary peritoneal cancer. All pts were high-grade serous ovarian cancer, with prior 1–5 lines of systemic therapy, and no more than 3 lines of subsequent therapy after platinum-resistant recurrence. Subjects received F in combination with UTD2 in 21-day cycles. The dose of F was 5 mg once daily, taken orally from day 1 to day 14 of each cycle. The dose of UTD2 was 60 mg/m²/day once daily, taken orally from day 1 to day 5 of each cycle. Primary endpoint was objective response rate (ORR) per RECIST v1.1. In Stage 1, 14 pts received per protocol treatment, and the study would proceed to Stage 2 (enrolling additional 21 patients) if ≥ 2 objective responses (CR/PR) were observed in Stage 1. Secondary endpoints included investigator-assessed progression-free survival (PFS), disease control rate (DCR), duration of response (DoR), overall survival (OS) and Safety. **Results:** From March 18, 2025 to December 22, 2025, 19 pts were enrolled. Median age was 59 years (range, 44–68) with an ECOG PS score of 1. Median prior lines systemic therapy was 3 (range, 1–5) with 1, 2, 3, 4 and 5 lines for 4 pts (21.1%), 2 pts (10.5%), 6 pts (31.6%), 5 pts (26.3%), and 2 pts (10.5%), respectively. Median number of chemotherapy lines after platinum resistance was 1 (range, 0–3), with 0, 1, 2, or 3 lines of chemotherapy for 6 pts (31.6%), 6 pts (31.6%), 5 pts (26.3%), and 2 pts (10.5%), respectively. 14 pts were evaluated for efficacy with an outcome of 1 complete response, 8 partial responses and 5 stable diseases. ORR was 64.3% (95% CI: 38.8–83.7) and DCR was 100%. Median PFS was 7 months (95% CI: 2.8–7.2) and median OS has not reached. The Grade 3 treatment-related AE (TRAE) included neutropenia (n=2), mucositis oral (n=1), palmar-plantar erythrodysesthesia syndrome (n=1), skin ulceration (n=1), diarrhea (n=1), pain (n=1) and neurotoxicity (n=1). There were no $\geq$ Grade 4 TRAE. 1 patient discontinued UTD2+F due to TRAEs. **Conclusions:** Utidelone plus Fruquintinib demonstrated encouraging efficacy for the treatment of PROC with a tolerable safety profile. This study is still actively ongoing, and further data will be provided at time of presentation. Clinical trial information: NCT06973421. Research Sponsor: Beijing Biostar Pharmaceuticals Co., Ltd.

Phase I, multicenter, first-in-human (FIH) global study of SIM0505, an anti-CDH6 (CDH6) antibody-drug conjugate (ADC) in patients with advanced solid tumors.

Xiaohua Wu, Ruijiao Liu, Xiaowei Liu, Yan Zhang, Dihong Tang, Shusuan Jiang, Jundong Li, Daruka Mahadevan, Cesar Augusto Perez, Beryl Manning-Geist, Dmitriy Zamarin, Miguel Gonzalez-Velez, Sarah Premji, Hongxia Wang, Jiajia Li, Rong Sun, Qi Fu, Haolin Sun, Ashley Martz, Udayan Guha; Fudan University Shanghai Cancer Center, Shanghai, China; Affiliated Hospital of Jining Medical University, Jining, China; Cancer Hospital of Shandong First Medical University, Jinan, China; Hunan Cancer Hospital, Changsha, China; Sun Yat-sen University Cancer Center, Guangzhou, China; University of Texas Health, San Antonio, TX; SCRI at Florida Cancer Specialists-Lake Nona, Orlando, FL; Emory University School of Medicine, Atlanta, GA; Icahn School of Medicine at Mount Sinai, New York, NY; Hackensack University Medical Center, Hackensack, NJ; Sarah Cannon Research Institute (SCRI), Nashville, TN; Shanghai Simcere Zaiming Biotechnology Co., Ltd., Shanghai, China; NextCure, Inc., Beltsville, MD

Background: Cadherin 6 is a transmembrane glycoprotein overexpressed in multiple cancers, including ovarian cancer (OC) and uterine serous cancer (USC). SIM0505 is an ADC comprised of an anti-CDH6 humanized IgG1 monoclonal antibody, a stable linker cleaved within tumor cells, and a novel topoisomerase I inhibitor, CPT116. Here, we report initial results from a global FIH study of SIM0505 (NCT06792552). **Methods:** This is a Phase 1 study to evaluate the safety, tolerability, pharmacokinetics, and preliminary anti-tumor activity of SIM0505 in patients (pts) with advanced solid tumors. SIM0505 was administered IV every 21 days from 1.6 mg/kg to 9.6 mg/kg. Dose levels from 3.2–8.0 mg/kg were backfilled. **Results:** As of 26 Dec 2025, 38 pts were enrolled without preselection for CDH6 expression (29 OC, 4 USC, 2 endometrioid endometrial cancer, 3 renal cell cancer) from 1.6 mg/kg to 9.6 mg/kg in the dose-escalation part. The median age was 57.0 years (range 42–78). The median number of prior therapy regimens was 5 (range 1–11). Of the 29 OC pts, 27 (93.1%) were high grade serous and 23 (79.3%) were platinum resistant. 22 (75.9%), 20 (69.0%) and 2 (6.9%) had received bevacizumab, PARPi and mirvetuximab soravtansine (MIRV), respectively. The median treatment duration was 10.6 weeks (range 3.0–33.6). Any-grade and Grade ≥ 3 treatment-emergent adverse events (TEAEs) occurred in 37 (97.4%) and 21 (55.3%) pts, respectively. Any-grade and Grade ≥ 3 treatment-related adverse events (TRAEs) occurred in 35 (92.1%) and 17 (44.7%) pts, respectively. The most common ($\geq 10\%$) Grade ≥ 3 TRAEs were thrombocytopenia (23.7%), neutropenia (21.1%), and white blood cell count decreased (18.4%). One pt at 9.6 mg/kg had dose-limiting toxicity of Grade 4 febrile neutropenia and thrombocytopenia and discontinued treatment. Another patient discontinued treatment due to Grade 2 interstitial lung disease. Serious TRAEs were observed in 6 (15.8%) pts. No TEAEs led to death. MTD was not reached. Among 30 evaluable pts, 11 partial responses (PR, 9 OC and 2 USC) and 13 stable disease were observed. 8 PRs occurred among 14 evaluable OC pts at potential therapeutic dose range of 4.8–8 mg/kg. 9 of 21 Gynecological Cancer Intergroup (GCIG) evaluable pts had CA-125 response. The exposure of SIM0505 was proportional to dose in general, with a half-life of about 8 days. The PK profile was similar to that of total antibody, indicating good stability of the ADC in the circulation. **Conclusions:** SIM0505, a first in class CDH6 CPT116 payload ADC showed manageable safety and tolerability, including at higher dose levels with encouraging efficacy in OC and USC, with a favorable PK profile. These data support initiating the dose optimization portion of the study in gynecological cancers. Clinical trial information: NCT06792552. Research Sponsor: None.

Impact of organ-adjacent extracellular vesicle proteomics from uterine lavage on accurate detection and discrimination of ovarian cancer.

John A. Martignetti, Boris Reva, Dmitry Rykunov, Maria M. Padron-Rhenals, Sabina Swierczek, Katherine Reid, Olga Camacho-Vanegas, Sandra Catalina Camacho, Kelsey Engelman, Deep Pandya, David Doo, Steven Sieber, Paul Fiedler, Stephanie V. Blank, Caitlin Carr, Valentin Kolev, Vaagn Andikyan, Anton Iliuk, Linus T. Chuang, Peter Dottino; MDDx, Inc, Tarrytown, NY; Department of Genetics and Genomic Sciences, Icahn School of Medicine at Mount Sinai, New York, NY; Rudy L. Ruggles Biomedical Research Institute, Nuvance Health, Danbury, CT; Department of Obstetrics/Gynecology and Reproductive Sciences, Icahn School of Medicine at Mount Sinai, New York, NY; Department of Obstetrics, Gynecology, and Reproductive Sciences Yale University School of Medicine, New Haven, CT; Tymora Analytical, West Lafayette, IN

Background: Survival in ovarian cancer (OvCA) exceeds 90% when disease is localized, yet most cases present at advanced stage and effective early detection remains elusive. Blood-based liquid biopsies may be limited by low tumor signal in early disease. We evaluated whether organ-adjacent sampling via uterine lavage extracellular vesicle (EV) proteomics combined with machine-learning (ML) classification could enable accurate detection of OvCA and clinically relevant discrimination from endometrial cancer (EndoCA). **Methods:** Uterine lavage samples were collected under IRB-approved protocols from women undergoing gynecologic evaluation for abnormal uterine bleeding and/or abnormal pelvic imaging. EVs were isolated using an affinity-based capture method and analyzed by liquid chromatography-tandem mass spectrometry. Protein features meeting predefined quality thresholds were analyzed using a novel ML pipeline incorporating entropy-based marker scoring and correlation filtering. Classifier performance was assessed using repeated random two-fold validation and receiver operating characteristic analysis. **Results:** Among 807 participants, diagnoses included OvCA (n=85), benign conditions (n=488), and EndoCA (n=234). An OvCA-versus-benign classifier derived from a 91-protein panel demonstrated strong discrimination (AUC >0.9). Across 100 validation splits, 83 of 85 OvCA cases were correctly classified, including all stage I cases (27/27). A separate 21-protein classifier distinguished OvCA from EndoCA with a sensitivity of 0.94 and specificity of 0.92. **Conclusions:** EV proteomic analysis of uterine lavage specimens enables accurate detection of ovarian cancer, including stage I disease, and reliably distinguishes OvCA from EndoCA in women undergoing gynecologic evaluation. These findings support further prospective clinical validation of organ-adjacent EV proteomics as a translational diagnostic strategy for earlier and more precise classification of gynecologic malignancies. Research Sponsor: None.

Fluorescence-guided surgery with 5-aminolevulinic acid (5-ALA) in ovarian, fallopian tube, and primary peritoneal cancers: Efficacy and safety results from the GINGA study.

Takashi Motohashi, Eiji Kondo, Mitsuya Ishikawa, Suguru Odajima, Muneaki Shimada, Tsutomu Tabata; Tokyo Women's Medical University Hospital, Shinjuku, Tokyo, Japan; Department of Obstetrics and Gynecology, Mie University Hospital, Tsu, Mie, Japan; National Cancer Center Hospital, Chuo-Ku, Japan; Department of Gynecology, the Jikei University Hospital, Minato-Ku, Japan; Tohoku University Hospital, Sendai-Shi, Japan; Tokyo Women's Medical University Hospital, Shinjuku, Japan

Background: Administration of 5-aminolevulinic acid (5-ALA) results in tumor-selective accumulation of protoporphyrin IX, enabling visualization of malignant lesions as red fluorescence under blue light illumination. Although 5-ALA-based photodynamic diagnosis (ALA-PDD) is well established for non-muscle invasive bladder cancer, its role in gynecologic malignancies remains insufficiently characterized. We conducted an investigator-initiated clinical study to evaluate the efficacy and safety of ALA-PDD in ovarian, fallopian tube, and primary peritoneal cancers. **Methods:** From October 2024 to May 2025, patients scheduled for cytoreductive surgery or exploratory laparotomy were enrolled. After exclusion of one patient due to a change in treatment strategy, 22 patients received oral 5-ALA hydrochloride (20 mg/kg) 3–8 hours prior to surgery. Diagnostic performance for detecting peritoneal dissemination under blue light (BL) was compared with that under conventional white light (WL), assessing sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV). Statistical tests were performed using McNemar's-test (sensitivity and specificity) or Chi-square test (PPV and NPV). Safety was evaluated based on the incidence and severity of adverse events. **Results:** Overall sensitivity was comparable between BL and WL (88.8% vs 80.9%), whereas BL demonstrated significantly higher specificity (67.3% vs 51.9%, $p = 0.0229$), indicating fewer false-positive findings. Notably, in patients undergoing interval debulking surgery (IDS; $n = 9$), BL significantly outperformed WL across all diagnostic metrics, including sensitivity, specificity, PPV, and NPV (all $p < 0.05$). These findings suggest that ALA-PDD enables more accurate intraoperative discrimination between malignant and non-malignant lesions following neoadjuvant chemotherapy. All patients experienced adverse events, predominantly Grade ≤ 2 . One case of postoperative ileus was reported; however, no causal relationship with 5-ALA was identified, and no clinically relevant safety signals emerged. **Conclusions:** ALA-PDD appears to enhance intraoperative diagnostic accuracy compared with conventional white light inspection and demonstrates an acceptable safety profile in ovarian, fallopian tube, and primary peritoneal cancers. In IDS patients, ALA-PDD may serve as a clinically meaningful adjunct to achieve precise cytoreduction and support surgical decision-making in the neoadjuvant chemotherapy setting. Clinical trial information: jRCTs031240345. Research Sponsor: None.

Differential impact of *TP53* and *KRAS* pathogenic variants on overall survival in advanced ovarian carcinoma.

Shreyas Kudrimoti, Janet Song, Chen Jiang, Ninah Achacoso, Aleyda V. Solorzano-Pinto, Pamela Tse, Elaine H. Chung, Sachdev P. Thomas, Haruka Itakura, Talayeh Ghezelayagh, Laurel A. Habel, Minggui Pan; Kaiser Permanente Santa Clara Medical Center, Santa Clara, CA; Kaiser Permanente - Santa Clara, Santa Clara, CA; Division of Research, Kaiser Permanente Northern California, Oakland, CA; Kaiser Permanente Division of Research, Oakland, CA; Kaiser Permanente, Oakland, CA; Division of Research, Kaiser Permanente, Oakland, CA; Kaiser Permanente, Vallejo, CA; Stanford University School of Medicine, Stanford, CA; Stanford Women's Cancer Center, Stanford Cancer Institute, Stanford University School of Medicine, Palo Alto, CA; Stanford University, Palo Alto, CA

Background: Advanced epithelial ovarian carcinoma, including high grade serous ovarian carcinoma (HGSOC), clear cell ovarian carcinoma (CCOC), endometrioid ovarian carcinoma (EOC) and mucinous ovarian carcinoma (MOC), frequently presents in advanced stages and is associated with poor outcomes. In addition to common germline mutations in *BRCA1/2*, many patients also harbor *TP53* and *KRAS* pathogenic variants (PVs) in their tumors. However, the role of these genomic alterations in advanced epithelial ovarian cancer remains unclear. **Methods:** Our study examined a large cohort of patients (n = 1060) with advanced epithelial ovarian cancer with genomic profiling performed using next-generation sequencing (StrataNGS). Cox regression modeling was used to examine the associations between *TP53* and *KRAS* PVs and overall survival (OS), adjusting for covariates including age, race/ethnicity, performance status, Charlson Comorbidity Index, and other genomic alterations. **Results:** Our cohort included HGSOC (n = 924), CCOC (n = 66), EOC (n = 42), and MOC (n = 28). Median OS was 33.4, 33.8, 25.1 and 66.8 months for HGSOC, CCOC, MOC and EOC, respectively. In the CCOC group, *TP53* PVs were associated with worse OS (hazard ratio [HR] = 3.23, [95% confidence interval [CI], 1.05–9.89]), while *KRAS* PVs were associated with better OS (HR = 0.29, [95% CI, 0.09–0.89]). In patients with HGSOC 71.3% had *TP53* PVs, whereas 8.0% had *KRAS* PVs. *KRAS* PVs were associated with better OS (HR = 0.72, [95% CI, 0.50–1.02]) in HGSOC. *TP53* PVs were associated with worse OS only within the sub-cohort that also harbored *KRAS* PVs (HR = 3.42, [95% CI, 1.13–10.33]). *TP53* PVs were not associated with OS in the *KRAS* wild-type sub-cohort (HR = 0.95, [95% CI, 0.72–1.25]). Our finding that *TP53* PVs were associated with worse OS in *KRAS* PVs sub-cohort was confirmed by interaction analysis (HR = 2.06, [95% CI, 0.98–4.35]). There was no OS difference between *TP53* gain-of-function versus non-gain-of-function PVs in HGSOC patients. **Conclusions:** In our large study cohort of patients with advanced epithelial ovarian carcinoma, we found that *TP53* and *KRAS* PVs were differentially associated with OS. Surprisingly, *KRAS* PVs were associated with higher OS in HGSOC while *TP53* PVs were associated with worse OS only in conjunction with *KRAS* PVs, highlighting the need to deepen our understanding of the oncogenic role *KRAS* plays in ovarian epithelial carcinoma. Further mechanistic studies to understand the roles of these common mutations in ovarian cancers could provide deeper insights. Research Sponsor: None.

Incidence and genomic characteristics of a low homologous recombination deficiency score subgroup in *BRCA*-mutant ovarian cancer.

Caiyan Liu, Jianguo Zhao, Yaomei Ma, Shasha Liu, Ruijia Sun; Department of Gynecological Oncology, Tianjin Central Hospital of Gynecology Obstetrics, Tianjin, China; Department of Gynecologic Oncology, Tianjin Medical University Cancer Institute Hospital, Tianjin, Tianjin, China; Department of Medical Affairs, 3D Medicines Inc., Shanghai, Shanghai, China

Background: Homologous recombination deficiency (HRD) is a pivotal molecular phenotype in ovarian cancer (OC) and serves as a key biomarker for guiding PARP inhibitor (PARPi) therapy. Current clinical algorithms assess HRD status by integrating pathogenic *BRCA1/2* mutations and genomic scar scores. Nevertheless, a paradoxical phenotype exists: *BRCA* mutations with a low HRD score. The incidence and genomic characteristics of this subgroup remain poorly understood. **Methods:** We retrospectively analyzed a cohort of OC patients tested at a centralized laboratory (2024–2025). A composite genomic instability score was calculated as the sum of three biomarkers: loss of heterozygosity (LOH), telomeric allelic imbalance (TAI), and large-scale state transitions (LST). HRD positivity was defined as the presence of a *BRCA1/2* pathogenic/likely pathogenic variant and/or a HRD score ($\text{LOH} + \text{TAI} + \text{LST}$) ≥ 42 . **Results:** Among 441 ovarian cancer samples, 151 of 310 (34.24%, 151/441) *BRCA* wild-type patients had an HRD score ≥ 42 , primarily driven by other homologous recombination repair (HRR) gene alterations. Conversely, among 131 *BRCA*-mutant patients, 30 (6.80%, 30/441) had an HRD score < 42 . Notably, 13 patients (2.95%, 13/441) with pathogenic *BRCA* variants exhibited remarkably low HRD scores (< 10). This subgroup comprised 10 *BRCA1* and 3 *BRCA2* alterations, including: 4 somatic truncating mutations [Exon11 S1389* (VAF=4.41%; HRD=0), Exon11 D1868Vfs*5 (VAF=4.80%; HRD=4), Exon10 E597* (VAF=17.37%; HRD=3), Exon10 K339Rfs*2 (VAF=30.65%; HRD=6)]; 6 germline truncating mutations [Exon21 Q1785* (VAF=50.29%; HRD=9), Exon13 G1492* (VAF=47.61%; HRD=7), Exon10 L1086* (VAF=46.52%; HRD=2), Exon11 S1882* (VAF=50.83%; HRD=0), Exon10 Q1200* (VAF=49.37%; HRD=0), Exon11 L1908Rfs*2 (VAF=44.44%; HRD=0)]; and 3 germline copy number deletions (HRD=2, 2, 0). We hypothesize potential mechanisms for this discordance: 1) Monoallelic inactivation: Single-allele inactivation (first hit) without a complete loss-of-function second hit, leading to partial HR function retention. 2) Subclonal variants: Low VAF suggests *BRCA* mutations may reside in tumor subclones, not dominating the pan-tumor HRD phenotype, with signals diluted by HR-proficient cells. 3) Time-dependency: *BRCA* inactivation might occur late in tumor evolution, insufficient for accrual of HRD-associated genomic scars at testing. **Conclusions:** This study quantifies a rare subgroup (~3%) of OC with pathogenic *BRCA* mutations but low HRD scores. This suggests monoallelic *BRCA* mutation alone may be insufficient to induce high genomic instability, potentially contributing to primary resistance to PARPis, though validation with clinical outcome data is required. Future studies integrating multi-omics data are needed to precisely evaluate HR pathway status and guide individualized treatment decisions. Research Sponsor: None.

Virtual multiplex immunofluorescence characterization of spatial immune architectures and tertiary lymphoid structures in high-grade serous ovarian cancer.

Junhwan Kim; Center for Gynecologic Cancer, National Cancer Center, Goyang-Si, South Korea

Background: GigaTIME (*Cell*, 2026) is a deep learning-based virtual multiplex immunofluorescence (mIF) model that has been validated using TCGA datasets and enables spatial tumor immune microenvironment (TIME) profiling directly from H&E whole-slide images (WSIs). This study aims to evaluate the feasibility of GigaTIME for characterizing the spatial TIME of high-grade serous ovarian cancer (HGSOC) using public datasets. **Methods:** We analyzed UBC-OCEAN and CPTAC-OV HGSOC H&E WSIs using GigaTIME to generate virtual 21-channel (e.g., DAPI, CK, CD3, CD8, CD20, and Ki67) mIF pixel-level inferred probability maps. Exploratory analyses of 5×5 stitched regions of interest (ROI, 2560×2560 pixels ≈ 1.28×1.28 mm) were performed to detect tertiary lymphoid structures (TLS) via density-based spatial clustering of applications with noise (DBSCAN), identified as CD20⁺ clusters (major axis ≥100 μm) adjacent to CD3⁺ zones, with maturity defined by intra-cluster Ki67⁺ proliferation. Tumor-immune interaction metrics were analyzed in ROIs using Group Degree Centrality (GDC, fraction of tumor cells contacting immune cells) and Cluster Co-occurrence Ratio (CCR, observed/expected contacts). CPTAC-OV HGSOC H&E WSI-derived virtual mIF features were correlated with bulk proteomics using Spearman's rank correlation. Integrated K-means clustering was performed on the combined cohorts after Z-score normalization. **Results:** The UBC-OCEAN cohort (N=195) exhibited an immune-inflamed phenotype with high tumor-immune engagement (mean GDC [mGDC] 0.25) and structural aggregation (mean CCR [mCCR] 1.41), whereas CPTAC-OV (N=222) displayed an immune-excluded phenotype with minimal contact (mGDC 0.05) and near-random distribution (mCCR 1.03). While total TLS density was comparable (UBC-OCEAN 3.92 vs. CPTAC-OV 3.60), UBC-OCEAN exhibited a twofold higher density of mature TLS compared to CPTAC-OV (1.83 vs. 0.77). Integrated clustering (k=2, silhouette=0.71) revealed that High-TLS (N=39) tumors paradoxically exhibited significantly lower mGDC (p=0.016) and mCCR (p=0.001) despite higher TLS density, indicating a spatially segregated and organized immune architecture. In CPTAC-OV validation, virtual CD3 intensity showed a significant positive correlation with bulk proteomics (N=17, $\rho=0.547$, p=0.023), supporting the biological validity of the T-cell-based spatial metrics. **Conclusions:** GigaTIME is feasible for evaluating comprehensive spatial TIME including TLS and demonstrates the heterogeneous immune landscape of HGSOC, providing spatial insights that are not captured by bulk proteomics alone. This warrants the utility of virtual mIF-based profiling as a scalable tool to identify distinct immune phenotypes for personalized immunotherapy at minimal cost. Research Sponsor: None.

Surufatinib combined with toripalimab for the treatment of recurrent ovarian clear cell carcinoma: Update of a prospective single center, single-arm phase II clinical trial.

Huijuan Yang, Yi Fu, Shuai Liu, Jun Wang, Lin Zhou, Wei Jiang, Xuan Pei, Wenbin Shen, Min Sun, Boer Shan; Department of Gynecologic Oncology, Fudan University Shanghai Cancer Center; Department of Oncology, Shanghai Medical College, Fudan University, Shanghai, China; Department of Radiology, Fudan University Shanghai Cancer Center; Department of Oncology, Shanghai Medical College, Fudan University, Shanghai, China; Department of Nuclear Medicine, Fudan University Shanghai Cancer Center; Department of Oncology, Shanghai Medical College, Fudan University, Shanghai, China

Background: Ovarian clear cell carcinoma (OCCC) is a histologically aggressive subtype of epithelial ovarian cancer with limited effective treatment options, particularly for recurrent disease. This study aims to evaluate the efficacy and safety of surufatinib (a kinase inhibitor targeting VEGFR 1, 2, 3, FGFR 1, and CSF-1R) in combination with toripalimab (an anti PD-1 antibody) for recurrent OCCC. Here, we present the latest efficacy and safety data. **Methods:** 23 patients aged 18-75 with histologically confirmed recurrent OCCC, ECOG performance status of 0-2, and failed first or subsequent-line therapy was enrolled (If the patient only had first line chemotherapy, platinum-free interval should be less than 12 months or disease progression occurred during chemotherapy). Patients received orally surufatinib 250 mg once daily in combination with toripalimab 240 mg on day 1 every 3 weeks until disease progression or unacceptable toxicity. Primary endpoint is progression-free survival (PFS), and secondary endpoints include objective response rate (ORR), overall survival (OS), and safety. **Results:** From Jul. 2023 to Dec. 2025, 19 patients (median age 51) were enrolled, with 52.6% (10/19) had an ECOG PS of 0, 73.7% (14/19) were classified as clinical stage of I-II. 57.9% (11/19) had received prior first-line treatment, while the remaining 8 patients had received twice or more. Eight patients had previously received bevacizumab. Among the 19 patients, 10 were platinum-resistant while 9 were platinum-sensitive. The primary metastatic sites were lymph nodes (8/19, 42.1%), lungs (6/19, 31.6%), pelvic cavity (6/19, 31.6%) and peritoneum (5/19, 26.3%). With a median follow-up of 7.1 months, the median PFS was 4.4 months (95% CI: 2.6-8.8). Tumor response was evaluable in 19 patients, with 1 complete response, 4 partial response and 11 had stable disease, resulting in an ORR of 26.3% (95% CI: 9.2-51.2%), and a disease control rate of 84.2% (95% CI: 60.4-96.6%). The most common ($\geq 20\%$) treatment related adverse events (TRAEs) were hyperthyroidism (42.1%), proteinuria (36.8%), hypertension (36.8%), diarrhea (36.8%), anaemia (31.6%), rash (31.6%), increased TSH (26.3%), hypoalbuminaemia (21.1%), increased AST (21.1%) and increased ALT (21.1%). Grade 3 TRAEs ($\geq 10\%$) were mainly hypertension (15.8%), increased AST (15.8%), increased ALT (10.5%). All of AEs were effectively controlled after temporarily discontinuing surufatinib or toripalimab, or reducing the dose of surufatinib, or receiving symptomatic treatment. There were no cases with fatal outcome. **Conclusions:** The combination of surufatinib and toripalimab exhibited potential clinical activity and tolerable toxicity in patients with recurrent OCCC. Clinical trial information: ChiCTR2400083672. Research Sponsor: None.

IGNITE-Cerala: A phase II signal-seeking trial of ceralasertib targeting recurrent high-grade serous ovarian cancer with cyclin E1 overexpression with and without gene amplification.

George Au-Yeung, Mathias Bressel, Yi-An Ko, John Andrews, Michelle L. Harrison, Yeh Chen Lee, Tarek Meniawy, Catherine M. Shannon, Ganessan Kichenadasse, Keri-Lee Geneser, Peter Fox, David Bowtell, Linda R. Mileschkin; Department of Medical Oncology and the Sir Peter MacCallum Department of Oncology, Peter MacCallum Cancer Centre and the University of Melbourne, Melbourne, VIC, Australia; Centre for Biostatistics and Clinical Trials, Peter MacCallum Cancer Centre; and Sir Peter MacCallum Department of Oncology, University of Melbourne, Melbourne, VIC, Australia; Centre for Biostatistics and Clinical Trials, Peter MacCallum Cancer Centre, Melbourne, VIC, Australia; ANZGOG, Camperdown, Australia; Chris O'Brien Lifehouse, Sydney, NSW, Australia; Prince of Wales and Royal Hospital for Women, Randwick, NSW, Australia; Sir Charles Gairdner Hospital, Nedlands, Western Australia, Australia; Mater Hospital Brisbane, South Brisbane, QLD, Australia; Flinders Medical Centre, Bedford Park, South Australia, Australia; Western Health, Medical Oncology - Sunshine Hospital, St. Albans, Australia; Orange Health Service, Orange, NSW, Australia; Peter MacCallum Cancer Center and Sir Peter MacCallum Department of Oncology, University of Melbourne, Melbourne, Australia; Department of Medical Oncology, Peter MacCallum Cancer Centre and; Sir Peter MacCallum Department of Oncology, the University of Melbourne, Melbourne, VIC, Australia

Background: Cyclin E1 (*CCNE1*) gene amplification and protein over-expression is a marker of platinum resistance in high grade serous ovarian, fallopian tube or primary peritoneal cancer (HGSC). Preclinical studies in breast and HGSC models have identified cyclin E1 amplification or over-expression as a potential predictive biomarker for improved sensitivity to ATR inhibition. We aimed to assess the efficacy of ceralasertib, an ATR inhibitor, in HGSC with cyclin E1 over-expression. **Methods:** IGNITE is a multicentre, Phase 2 trial enrolling women with recurrent platinum resistant HGSC. Tumors were assessed for Cyclin E1 protein expression by IHC and *CCNE1* copy number by FISH. Patients with evaluable disease by RECIST v1.1 or GCIG CA-125 criteria were included. Ceralasertib 160mg PO was given twice daily on days 1-14 of a 28-day cycle. The primary endpoint was investigator assessed overall response rate (ORR), defined as partial response (PR) or complete response (CR) at 16 weeks by RECIST v1.1 among patients with measurable disease, or by GCIG CA-125 criteria for patients with non-measurable disease. Here we present the 16-week response data for all patients treated with ceralasertib with a data cut-off of July 2025. **Results:** Between Feb-2024 and Apr-2025, 32 patients were accrued to IGNITE-Cerala. One patient was deemed ineligible after registration and was excluded. Median age was 64 years (range 40-76) and 74% had received ≥ 2 prior lines of chemotherapy. Median cyclin E1 IHC H-score was 190 (range 60 – 260). Twenty-seven patients (87%) had measurable disease by RECIST. Median number of cycles commenced was 3 (range 1-18). The ORR at 16 weeks was 10% (0 CR and 3 PR). The 6 month progression free survival estimate was 26% (range 12-42%). Treatment related adverse events (TRAE) were mostly grade 1-2 with the most common being gastrointestinal or hematologic. Six patients (19%) had Grade 3 TRAE, and one patient had Grade 4 TRAE. Six patients (19%) required a dose reduction, and no patients discontinued study drug due to toxicity. **Conclusions:** Ceralasertib was a well tolerated treatment, however responses did not appear to be enriched in a biomarker selected population and therefore future studies should consider rationale combinations with ceralasertib. Cyclin E1 over-expression and amplification remains an important biomarker in HGSC, with other strategies such as CDK2 or PK-MYT1 inhibitors under active investigation. Clinical trial information: ACTRN12619001185156. Research Sponsor: AstraZeneca.

Response at 16 weeks	Response evaluable patients (n=31)	RECIST measurable patients (n=27)
CR	0 (0%)	0 (0%)
PR	3 (10%)	3 (11%)
SD	7 (23%)	7 (26%)
No CA-125 response and no PD	1 (3%)	-
PD	20 (65%)	17 (63%)
ORR (CR/PR)	3 (10% [2, 26])	3 (11% [2, 9])

Budget impact analysis of heated intraperitoneal chemotherapy at interval cytoreductive surgery for stage III high grade serous carcinoma of tubo-ovarian origin.

Tal Milman, Charlotte Clayton, Lien Hoang, Shirley S.T. Yeung, Corinne Maurice-Dror, Janice S. Kwon; University of British Columbia, Vancouver General Hospital, Vancouver, BC, Canada; Faculty of Medicine, University of British Columbia, Vancouver, BC, Canada; Department of Anatomic Pathology, Vancouver General Hospital, Vancouver, BC, Canada; BC Cancer Pharmacy, BC Cancer Agency, Vancouver, BC, Canada; BC Cancer - Vancouver Cancer Centre, Vancouver, BC, Canada; University of British Columbia, Vancouver, BC, Canada

Background: Heated Intraperitoneal Chemotherapy (HIPEC) at interval cytoreductive surgery (ICS) for high grade serous carcinoma of tubo-ovarian origin (HGSOC) improves overall survival (OS) by 11.6 months and increases platinum sensitivity at recurrence. Our aim was to estimate the payer budget impact of adopting HIPEC in BRCA wild-type patients at a quaternary Canadian center. **Methods:** A retrospective review was conducted of patients undergoing surgery for metastatic HGSOC at Vancouver General Hospital, Vancouver, Canada between January 1 and December 31, 2024. A payer-perspective Markov model was constructed with monthly cycles and a five-year horizon. Six cycles of carboplatin and paclitaxel were costed in the initial episode. Health states were progression-free (PF), first platinum-sensitive recurrence (PS1), second platinum-sensitive recurrence (PS2), platinum-resistant recurrence (PR), and death. PF progression hazards were derived from median PFS reported in randomized clinical trials. Post-progression mortality hazards were calibrated to match OVHIPEC-1 median overall survival. Direct medical costs were estimated in 2025 Canadian dollars using publicly available provincial drug pricing data in British Columbia and institution-specific costs for surgery, HIPEC, and inpatient care. **Results:** Annual volume of ICS patients was 98, of whom 25 were eligible for HIPEC and wtBRCA. Over 5 years, with 25 new patients entering annually, total costs were \$9.05M without HIPEC versus \$11.07M with HIPEC, yielding an incremental budget impact of \$2.02M (\$16,186 per patient). Incremental cost was driven by the surgical episode (+\$1.90M), longer duration of maintenance niraparib (+\$0.26M), and treatment of platinum-sensitive recurrence (+\$0.15M) with carboplatin doublets. Incremental cost was partially offset by an estimated 11 fewer platinum-resistant recurrences within the 5-year horizon, resulting in cost savings of -\$0.28M from reduced platinum-resistant treatment. **Conclusions:** Adding HIPEC at ICS to patients with stage III wtBRCA HGSOC increases 5-year payer spending by \$2M for a 25 patient per year program. Additional cost is driven by provision of HIPEC surgery and postoperative care and is partially offset by near-term savings on platinum-resistant recurrence. Research Sponsor: None.

Treatment cost across a 5-year horizon for 25 patients treated annually (n = 125).

Category	No HIPEC	HIPEC	Incremental Cost	Incremental Cost Per Patient
Surgery +/- HIPEC	\$2,085,500	\$3,983,250	\$1,897,750	\$15,182
Initial chemotherapy	\$1,829,348	\$1,829,348	\$0.00	\$0.00
Niraparib	\$2,376,117	\$2,638,599	\$262,482	\$2,100
Maintenance				
Platinum Sensitive	\$1,243,222	\$1,389,325	\$146,103	\$1,169
Recurrence				
Platinum Resistant	\$1,515,639	\$1,232,611	-\$283,027	-\$2,264
Recurrence				
Total	\$9,049,824	\$11,073,132	\$2,023,308	\$16,186

Enhanced predictive value of KELIM for surgical resectability in HRD-positive high-grade serous ovarian cancer.

Mayerly Castrillón Sánchez, Gabriel Levin, Lawrie Shahbazian, Reitan Ribeiro, Xing Zeng, Laurence Bernard, Basile Tessier-Cloutier, Lucy Gilbert, Shuk On Annie Leung; McGill University Health Centre, Montréal, QC, Canada; RI-MUHC, Montréal, QC, Canada; McGill University Health Centre, Montreal, QC, Canada; Division of Gynecologic Oncology, Research Institute, McGill University Health Centre, Gerald Bronfman Department of Oncology, McGill University, Montreal, QC, Canada

Background: Neoadjuvant chemotherapy followed by interval debulking surgery is commonly used in the management of advanced ovarian cancer. However, there is currently no reliable tool to predict the likelihood of achieving complete cytoreduction after 3–4 cycles of chemotherapy. Surgical outcomes are classified as R0 (no residual disease), R1 (residual lesions <1 cm), or R2 (residual disease $\geq$ 1 cm). The KELIM index, calculated from CA-125 kinetics during chemotherapy, has emerged as a potential biomarker of tumor regression and chemosensitivity in advanced ovarian cancer. We aim to study the performance of KELIM score as predictor of complete cytoreduction. **Methods:** This single-center, retrospective study included 69 patients with advanced high-grade serous ovarian cancer (Stage III/IV) who underwent interval cytoreductive surgery following neoadjuvant chemotherapy between January 2020 and December 2025. Kelim index values were calculated using Biomarker-Kinetics and categorized as favorable ($\geq$ 1) or unfavorable (<1) as per literature. Further, ROC curve analysis was performed to identify the optimal KELIM cutoff for predicting complete cytoreduction. Correlations with degree of cytoreduction (R0, R1, R2) were analyzed using comparative statistics. Associations with molecular markers (BRCA, HRD) were also explored. **Results:** The median age of patients was 62 years [IQR 57–70]. The median KELIM score was 0.85 [IQR 0.69–1.00]. KELIM demonstrated statistically significant predictive performance for R0, with an area under the curve (AUC) of 0.69 (95% CI, 0.56–0.82; $p = 0.004$). The AUC optimal cutoff was KELIM = 0.995, yielding a sensitivity of 53.9% and specificity of 92.6%. Notably, this value closely aligns with the cutoff reported in the literature (KELIM = 1.0), which in our cohort corresponded to a sensitivity of 51.3% and specificity of 96.3% (Youden index = 0.47). Additional analyses were conducted using the literature-defined cutoff of KELIM = 1.0. Patients were categorized into two groups: Group A (22 patients) with favorable ($\geq$ 1) and Group B (47 patients) with unfavorable (<1) KELIM scores. Patients with a favorable KELIM were significantly more likely to achieve complete cytoreduction compared with those with an unfavorable KELIM (R0: 95.2% vs 41.3%, $p < 0.001$). The discriminative performance of KELIM was numerically higher in HRD-positive patients AUC 0.706 (95% CI, 0.28–1) compared with HRP patients AUC 0.563 (95% CI, 0–1). KELIM was associated with degree of cytoreduction: Median 1 [0.71–1.20] for R0, 0.79 [0.70–0.88] for R1, and 0.64 [0.48–0.70] for R2, $p=0.019$. **Conclusions:** KELIM is a good predictor of complete resectability in high grade serous ovarian cancer. The differential predictive performance among the HRD status should be further explored. Research Sponsor: None.

Impact of niraparib maintenance on progression-free survival and overall survival: An updated meta-analysis.

Roshan Mustafa Pathan, Jugraj Singh, Ponni Gayatri Twinkle Bade, Vamsi Krishna Kondepoti, Mukesh Ram Kumar Kommu; Government Siddhartha Medical College, Vijayawada, India; Midwestern University GME Consortium Program, Cottonwood, AZ; Konaseema Institute of Medical Sciences and Research Foundation, Amalapuram, India; Government Medical College Ongole, Ongole, India; Rangaraya Medical College, Kakinada, India

Background: Niraparib is an oral poly(ADP-ribose) polymerase (PARP) inhibitor used as maintenance therapy in advanced ovarian cancer after platinum response. Mature OS data were lacking, so we performed an updated meta-analysis. **Methods:** PubMed, Embase, and CENTRAL were searched from January 2023 to January 2026 for randomized controlled trials (RCTs) of niraparib maintenance in advanced ovarian cancer. Hazard ratios with 95% confidence intervals were pooled using random-effects models for TFST, OS, overall PFS, and subgroup PFS by BRCA, HRD status, and newly diagnosed patients. The study is registered in PROSPERO with ID CRD420261294461. **Results:** Four RCTs (PRIMA, NOVA, NORA, and PRIME) including 1935 patients were analysed, of whom 1,291 received niraparib, and 644 received placebo. Niraparib significantly prolonged the TFST (HR 0.54, 95% CI 0.42–0.69; $I^2=77.6\%$; $p<0.0001$). No statistically significant improvement in OS was observed (HR 0.94, 95% CI 0.82–1.08; $I^2=10.0\%$; $p=0.398$). Niraparib significantly improved overall PFS (HR 0.42, 95% CI 0.31–0.58; $I^2=83.8\%$). PFS in BRCA-mutated patients (HR 0.33, 95% CI 0.24–0.45; $I^2=46.0\%$), HRD-positive patients (HR 0.41, 95% CI 0.30–0.56; $I^2=58.6\%$) (all $p<0.0001$). HRD-negative patients (HR 0.56, 95% CI 0.35–0.89; $I^2=51.4\%$), and newly diagnosed (HR 0.55 95% CI 0.39–0.80, $I^2=79.1\%$) (all $p\leq 0.015$). **Conclusions:** Niraparib provides durable disease-control benefits across molecular subgroups and significantly delays the need for subsequent therapy, however, mature data does not demonstrate a corresponding overall survival advantage. These findings refine patient selection and highlight the need for strategies that translate PFS gains into survival benefit. Research Sponsor: None.

Updated meta-analysis of niraparib efficacy outcomes in advanced ovarian cancer.

Study	TFST (HR)	Overall Survival (HR)	Overall PFS (HR)	PFS in BRCA mutation (HR)	HRD+ PFS (HR)	HRD – PFS (HR)	Newly Diagnosed (HR)
PRIMA	0.74 (0.62–0.89) *	1.01 (0.84–1.23) *	0.66 (0.55–0.78) *	0.43 (0.31–0.59) *	0.51 (0.40–0.66) *	0.67 (0.50–0.89) *	0.66 (0.55–0.78) *
PRIME	0.45 (0.34–0.59)	0.63 (0.38–1.03) *	0.45 (0.34–0.60)	0.40 (0.23–0.68)	0.48 (0.34–0.68)	0.41 (0.22–0.75)	0.45 (0.34–0.60)
NOVA (gBRCA)	0.57 (0.41–0.78) *	0.85 (0.61–1.20) *	-	0.27 (0.17–0.41)	0.38 (0.24–0.60)	-	-
NOVA (non-gBRCA)	0.58 (0.45–0.74) *	1.06 (0.81–1.37) *	-	-	-	-	-
NORA	0.39 (0.29–0.52) *	0.86 (0.60–1.23) *	0.32 (0.23–0.45)	0.22 (0.12–0.40)	0.22 (0.12–0.40)	-	-
Total Result (95% CI)	0.54 (0.42–0.69)	0.94 (0.82–1.08)	0.42 (0.31–0.58)	0.33 (0.24–0.45)	0.41 (0.30–0.56)	0.56 (0.35–0.89)	0.55 (0.39–0.80)
I^2 (%)	77.6	10	83.8	46	58.6	51.4	79.1
p value	<0.0001	0.3979	<0.0001	<0.0001	<0.0001	0.0146	0.0014

*Indicate updated values.

TFST: time to first subsequent therapy; PFS: progression-free survival; HR: Hazard ratio; CI: confidence intervals.

Post-treatment ctDNA monitoring using a tumor-informed whole-genome sequencing-based assay in homologous recombination-proficient ovarian cancer.

Sophie Blakey-Cheung, Bhakti Dwivedi, Samuel Rivero-Hinojosa, Alison Parisian, Brandie Taylor, Carly Bess Scalise, Carcia Carson, Punashi Dutta, Ekaterina Kalashnikova, Gabrielle M. Heilek, Minetta C. Liu, Alexey Aleshin, Adam ElNaggar, Robert W. Holloway; AdventHealth Cancer Center, Orlando, FL; Natera, Inc., Austin, TX

Background: Ovarian cancer (OC) has high mortality due to advanced stage at diagnosis and frequent, incurable recurrences. Homologous recombination-proficient (HRP) disease comprises approximately half of high-grade serous OC and is associated with limited benefit from platinum chemotherapy and PARP inhibitors, leading to poorer outcomes. Circulating tumor DNA (ctDNA) is a validated biomarker for molecular residual disease and early relapse; this study evaluates its ability to stratify HRP patients (pts) into clinically meaningful risk groups.

Methods: We performed a retrospective analysis of clinically annotated residual samples from commercial ctDNA testing in pts diagnosed with OC. Signatera Genome assays (Natera, Inc.) were designed from the respective pts' matched tumor and normal whole genome sequencing (WGS) data to detect and quantify ctDNA in serially collected post-operative plasma. Adjuvant chemotherapy (ACT) decisions and cadence of testing were at the provider's discretion. HR status was determined using available clinical records and/or genomic data. Descriptive statistics were used to compare association of ctDNA across stages and at various timepoints post-surgery. Correlation between ctDNA status and progression-free survival (PFS) was assessed using Cox regression analysis. **Results:** Study cohort comprised 164 Stage I-IV OC pts, with 1,256 plasma samples for ctDNA testing (median: 7 tests/pt, range 1-24). The median age at diagnosis was 66 (range 19-89) years. A total of 157 cases were HRP; among these, clinical outcome data was available for 44 pts with corresponding ctDNA timepoints for analysis. ctDNA-positivity within two weeks post-debulking surgery (before starting ACT) was associated with significantly worse PFS compared to ctDNA-negativity (N=20; HR: 14.01, 95%CI: 0.6-308.16; p=0.01). Furthermore, ctDNA-positivity post-ACT was also associated with worse PFS (N=26; HR: 6.6, 95%CI: 1.7-25.3; p=0.002) compared to ctDNA-negativity. Among ctDNA-positive pts, 50% (5/10) had progression <6 months post-ACT, whereas no events were observed <12 months post-ACT in ctDNA-negative pts (N=12). Clinical follow-up and additional analyses are ongoing. **Conclusions:** Tumor-informed ctDNA monitoring identifies pts with HRP OC who are at high risk for recurrence post-surgery including treatment refractory/resistant cases. Post-operative and post-adjuvant ctDNA positivity was strongly associated with inferior PFS. These findings support the use of ctDNA as a clinically important biomarker to inform post-surgical/treatment risk stratification, and consideration of alternative or escalated therapeutic strategies in this high-risk population. These results showcase the utility of ctDNA to further risk stratify HRP OC pts, which supports its integration into prospective clinical trials and clinical care. Research Sponsor: None.

Spatial distribution and functional heterogeneity of CD56bright and CD56dim natural killer cells and the effects on the immune microenvironment in ovarian cancer.

Guo Huiming, Yuni Jin, Bao Chan, Li Tian, Hong Pan, Haohan Li; The First Affiliated Hospital of Kunming Medical University, Kunming, China

Background: Natural killer (NK) cells are key components of antitumor immunity, yet their functional heterogeneity and spatial distribution within the tumor microenvironment (TME) remain incompletely understood in ovarian cancer. CD56bright and CD56dim NK cell subsets exhibit distinct immunologic functions, but their relative infiltration patterns and associations with other immune cell populations have not been systematically characterized. **Methods:** A total of 157 ovarian cancer specimens were analyzed using multiplex immunofluorescence staining. NK cells were classified as CD56bright and CD56dim subsets, and their densities were quantified separately in tumor parenchyma and stroma. The associations between NK cell infiltration patterns and the densities of multiple immune cell populations. **Results:** Overall, ovarian cancer exhibited a CD56dim NK cell–dominant infiltration pattern. In tumor parenchyma, the mean density of CD56bright NK cells was 149 cells/mm², whereas CD56dim NK cells reached 406 cells/mm². In tumor stroma, CD56bright and CD56dim NK cell densities were 108 cells/mm² and 277 cells/mm², respectively. Patients with higher overall NK cell infiltration showed significantly increased densities of multiple immune cell populations in both tumor parenchyma and stroma, including CD8⁺ T cells ($P=0.0091$, 0.0167), M1 macrophages ($P=0.0002$, 0.0001), M2 macrophages ($P=0.0011$, 0.0008), PD-L1⁺ macrophages ($P=0.0164$, 0.0006), CD20⁺ B cells ($P=0.0001$, 0.0193), CD4⁺ T cells ($P=0.0001$, 0.0001), and CD4⁺FOXP3⁺ regulatory T cells ($P=0.0001$, 0.0001). When comparing NK cell subset dominance, patients with lower CD56dim than CD56bright NK cell infiltration in tumor parenchyma exhibited significantly higher M1 macrophage density (342 vs 180 cells/mm², $P=0.0344$) and lower stromal M2 macrophage infiltration ($P=0.0356$). In tumor stroma, lower CD56dim–dominant cases showed significantly increased infiltration of M1 macrophages (435 vs 242 cells/mm², $P=0.0336$), M2 macrophages (171 vs 48 cells/mm², $P=0.0053$), CD8⁺PD-1⁺ T cells (34 vs 10 cells/mm², $P=0.0299$), CD4⁺ T cells (140 vs 25 cells/mm², $P=0.0119$), and CD4⁺FOXP3⁺ T cells (73 vs 4 cells/mm², $P=0.0016$). **Conclusions:** Ovarian cancer is characterized by predominant infiltration of CD56dim NK cells; however, the balance between CD56bright and CD56dim NK cell subsets is closely associated with distinct immune microenvironment patterns. These findings highlight the functional heterogeneity of NK cell subsets and provide a potential mechanistic explanation for the variable prognostic and therapeutic relevance of NK cells across tumor types and immunotherapy contexts. Spatially resolved profiling of NK cell subsets may offer valuable insights for immunotherapy stratification in ovarian cancer. Research Sponsor: None.

Comprehensive profiling of antibody-drug conjugate target expression in epithelial ovarian cancer with pre- and post-ADC longitudinal assessment.

Yong jae Lee, Eun Kyung Kim, Junsik Park, Yoo Na Kim, Soyeon Kim, Sunghoon Kim, Jung-Yun Lee; Department of Obstetrics and Gynecology, Yonsei University College of Medicine, Seoul, South Korea; National Health Insurance Service Ilsan Hospital, Goyang-Si, South Korea; Department of Obstetrics and Gynecology, Soonchunhyang University Bucheon Hospital, Bucheon, South Korea; Yonsei Cancer Center and Severance Hospital, Yonsei University College of Medicine, Seoul, South Korea

Background: Antibody–drug conjugates (ADCs) are increasingly used in ovarian cancer, yet target expression may evolve over time and under treatment pressure. We characterized key ADC targets across disease timepoints and assessed paired changes after ADC exposure. **Methods:** We retrospectively analyzed epithelial ovarian cancer treated at Yonsei Cancer Center (n=158). Serial specimens obtained at diagnosis, interval debulking surgery, and relapse underwent immunohistochemistry for TROP2, HER2, FOLR1, CLDN6, B7H4, B7H3, and CDH6. Targets were scored 0/1+/2+/3+; overexpression was defined as 2+ or 3+. Longitudinal transitions were summarized using Sankey plots, including pre-/post-ADC comparisons. **Results:** We analyzed 158 epithelial ovarian cancer patients (HGSC n=120; non-HGSC n=38). In HGSC, the most frequent overexpressed targets (2+/3+) were TROP2 (100%) and FOLR1 (91.5%) at diagnosis, remaining high at relapse (TROP2 93.2%, FOLR1 82.2%), while HER2 overexpression was uncommon (20.3% at diagnosis; 6.9% at relapse). In non-HGSC subtypes, TROP2 was most frequently overexpressed in endometrioid (3+ in 100%) and clear cell tumors (2+/3+ in 100%), whereas mucinous tumors showed predominant HER2 overexpression (2+/3+ in 70%). In ADC-exposed paired pre-/post-ADC specimens, expression of the cognate ADC target generally decreased after exposure, including reduced FOLR1 after MIRV/MORAb-202, reduced HER2 after T-DXd, and reduced CDH6 after R-DXd. **Conclusions:** TROP2 and FOLR1 are broadly and consistently expressed across timepoints. Non-HGSC exhibits distinct histology-specific patterns, with particularly high HER2 expression in mucinous tumors. ADC treatment resulted in a reduced expression profile of its cognate target protein, which may contribute to the development of ADC resistance; however, further investigation is required to elucidate additional underlying mechanisms. Research Sponsor: None.

Primary analysis of pembrolizumab combined with chemotherapy in platinum-sensitive recurrent low-grade serous ovarian cancer: The NOGGO PERCEPTION phase II study.

Jacek P. Grabowski, Elena Ioana Braicu, Philipp Harter, Dario Zocholl, Fabian Schmeling, Florian Heitz, Tjadina Arndt, Julia Welz, Jalid Sehouli; North-Eastern German Society of Gynaecological Oncology (NOGGO) and Department of Gynecology with Center for Oncological Surgery, Charité-University Medicine of Berlin, Campus Virchow Klinikum, Berlin, Germany; Kliniken Essen-Mitte, Department of Gynecology and Gynecological Oncology, Essen, Germany; Charité - University Medicine of Berlin, corporate member of Free University of Berlin and Humboldt University of Berlin, Institute of Biometry and Clinical Epidemiology, Berlin, Germany; North-Eastern German Society of Gynaecological Oncology, Berlin, Germany

Background: Low-grade serous ovarian cancer (LGSOC), a rare ovarian malignancy, exhibits a very limited responsiveness to chemotherapy. There is a pressing need for new therapeutic combinations with modern agents to enhance response rates and prognosis in this patient subgroup. Immune checkpoint inhibitors offer a promising pathway, having shown effectiveness in various malignant diseases, including selected cases of ovarian cancer. If our trial should show pembrolizumab effectiveness in LGSOC, it would be a signal and impulse for future clinical studies in this rare disease. **Methods:** This multi-center, single-arm phase II study evaluates pembrolizumab in combination with platinum-based chemotherapy (carboplatin plus pegylated liposomal doxorubicin [PLD] or carboplatin plus gemcitabine) and as maintenance therapy in recurrent LGSOC. Eligible patients include those with disease progression or recurrence ≥ 6 months post prior platinum-based therapy and ECOG performance status 0-1. The primary endpoint is the 12-month progression-free survival (PFS) rate. Secondary endpoints include response rate (RR), PFS and ORR based on Ki67 expression. Using Simon's two-stage design, 33 patients were enrolled. Success is defined as ≥ 11 patients achieving 12-month PFS. Assuming a true PFS rate of 40%, the study has 5% type I error and 80% power. **Results:** Data from 33 patients were evaluated. At data cut-off, 12 patients were progression free at 12-months (median PFS 15.5 months) while 19 patients progressed or died within 12 months (median PFS 5.6 months). Overall PFS median was 8.4 months. Comparing the subgroups of pre-treatment Ki67 expression $< 3.6\%$ vs. $\geq 3.6\%$, the median PFS was 5.1 vs. 8.8 months. Four patients remain on pembrolizumab treatment; two of these have not yet reached the 12-month PFS endpoint. Median patient age was 52 years (range: 37-81), with ECOG performance status 0 in 30 patients (90.9%). Most patients had one prior chemotherapy line (61.1%; range: 1-5). Chemotherapy regimens included carboplatin + PLD (75.8%) and carboplatin + gemcitabine (24.2%). SAEs were reported in 22 patients (66.7%), with 11 (33.3%) considered treatment-related. **Conclusions:** The study achieved its primary objective in terms of the 12-months PFS and thus suggests efficacy of pembrolizumab in patients with platinum-sensitive recurrent LGSOC. Clinical trial information: 2023-508155-40-00. Research Sponsor: MSD Sharp & Dohme GmbH.

Update of the EORTC QLQ-Ovarian Cancer Module (EORTC-QLQ-OV28) phase I and II.

Vesna Bjelic-Radisic, Andy Nordin, Juan Ignacio Arraras, Ingvild Vistad, Ali Alkan, Anne Oberguggenberger, Karin Kuljanic, Pernille Tina Jensen, Shira Peleg Hasson, Muna AlKhaifi, Eleonora Van Dorst, Ligita Froding, Jennifer Steinmetz, Nora Nevries; Breast Unit, Helios University Clinic, University Witten-Herdecke, Wuppertal, Germany; East Kent Gynaecological Oncology Centre, Queen Elizabeth the Queen Mother Hospital, Margate, United Kingdom; IDISNA Pamplona, Pamplona, Spain; Department of Gynecology, Sørlandet Hospital Trust & Clinical Institute II, Medical Department, University of Bergen, Kristiansand, Kristiansand, Norway; Mugla Sitki Kocman University Faculty of Medicine, Mugla, Turkey; Medical University of Innsbruck, Innsbruck, Austria; University Hospital Centre Rijeka, Department of Obstetrics and Gynecology, Clinical Center Rijeka, Rijeka, Croatia; Aarhus University Hospital, Copenhagen, Denmark; Tel Aviv Sourasky Medical Center and Gray Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel; University of Toronto, Sunnybrook Health Sciences Centre, Toronto, ON, Canada; University Medical Center (UMC), Utrecht, Netherlands; Rigshospitalet, Copenhagen, Denmark; Helios University Hospital, Wuppertal, Germany

Background: Ovarian cancer is the eighth most common cancer in women worldwide. The 5-year survival rate is 90.0% for early-stage disease and 30.2% for advanced disease. The introduction of new treatment options, such as PARP inhibitors, immunotherapy and bevacizumab, has led to improved recurrence-free intervals and an increased number of long-term survivors. However, new therapies have also brought new side effects that are not sufficiently covered by the EORTC QLQ OV-28, which was developed in 1997. There is therefore a strong clinical and research need to update the questionnaire to reflect contemporary treatments and their impact on QoL. This work presents the results of Phases 1 and 2 of the EORTC module development study updating the EORTC QLQ-OV28. **Methods:** The EORTC QLQ-OV28 module was adapted in accordance with the EORTC QLG guidelines for methodology for updating modules focused on identifying QoL issues relevant to ovarian cancer patients. This involved a systematic literature search, a review of questionnaires, investigator brochures, focus groups, and research group meetings (Phase 1). An issue was added to the list if it had a patient and/or HCP relevance rating of at least 2 (on a scale of 1 to 4) and a priority rating of at least 30%. The relevant issues were then translated into items, resulting in a preliminary questionnaire (Phase 2). **Results:** The mixed methods approach identified 57 issues related to QoL in ovarian cancer patients. An issue list was created and used for interviews with 58 patients and 31 HCPs, who rated each issue according to its relevance using a four-point response format: 'not at all', 'a little', 'quite a bit', 'very much' and priority (yes/no). Of the initial 57 issues, 20 (as rated by patients) and 34 (as rated by HCPs) met both inclusion criteria. Sixteen of these were covered by the existing EORTC QLQ-OV28, and five new issues were identified: weight loss, numbness in the hands and feet, anxiety, concerns about acceptance of their condition, and impaired sexuality. Twelve issues from the existing questionnaire did not fulfil all the inclusion criteria. In Phase II, these issues were translated into items and used to create a preliminary 39-item questionnaire to assess QoL in ovarian cancer patients. **Conclusions:** The results of Phases I and II indicate that the current EORTC QLQ-OV28 module does not adequately address all the relevant QoL issues for patients with ovarian cancer. Five new issues are not addressed by the existing module, and twelve existing issues did not fulfil all the inclusion criteria. Therefore, the EORTC QLQ-OV28 module should be updated. A preliminary questionnaire will be tested in Phase III of the EORTC module development process. Note: This document represents preliminary findings of the module development and is subject to revision; subsequent modifications of the module in the next stages may reflect significant changes. Research Sponsor: EORTC QLQ.

Vididencel, an active immunotherapy in high-grade serous ovarian carcinoma patients: Analysis of tumor-directed immune responses post-primary treatment.

Annegé Vledder, Marco de Bruyn, Satwinder Kaur Singh, Koen Brummel, Anneke L. Eerkens, Nienke van Rooij, Annechien Plat, Tariq I. Mughal, Hans Nijman; University Medical Centre Groningen, Groningen, Netherlands; Mendus AB, Stockholm, Sweden; University Medical Center Groningen, Groningen, Netherlands

Background: Ovarian cancer (OC) remains the most common cause of mortality in gynecologic cancers, with advanced-stage high-grade serous carcinoma (HGSOC) accounting for most cases. PARP inhibitors have provided significant benefits and notable progression-free survival for patients with BRCAmut and HRD+, but survival benefits following primary treatment remains a major clinical challenge. We have conducted a phase 1 trial (NCT04739527) assessing the role of an active immunotherapy, vididencel, in patients with HGSOC post-primary treatment. Vididencel expresses multiple tumor-associated antigens (TAA), including WT1 and PRAME, which are frequently upregulated in HGSOC. **Methods:** Following primary treatment, patients received 8 doses of vididencel intradermally administered every 14 days, followed by 2 booster injections at week 14 and 18. Peripheral blood mononuclear cells (PBMC) were obtained at week 0, 4, 10, 14, 18 and 22. Disease status was evaluated at week 22 using clinical assessment and CA125 levels. Patients were followed for disease status for 2 years. IFN γ ELISpot was performed on PBMC for WT1, PRAME, MAGEA3/4 and NY-ESO1. Vididencel induced T-cell responses were calculated as ≥ 2 -fold increase of the mock-corrected baseline response. **Results:** All 17 patients completed treatment phase (up to week 22 or end of treatment). Patient demographics are outlined in table I. 11 out of 17 patients completed predefined 2-year follow-up. With median follow-up of 26.4 months 8 out of 11 patients remain alive. 12 out of 17 patients (71%) showed improved tumor-directed vididencel-induced immune responses (VIR) and are associated with improved progression-free survival. 5 of 12 patients (42%) with VIR still had stable disease, with 2 patients beyond 3.5 years of follow-up. **Conclusions:** Long-term follow-up of HGSOC patients treated with vididencel confirms safety, tolerability and feasibility resulting in strong T cell response against TAA. The improved tumor-directed responses were associated with better progression-free survival. These data confirm that vididencel is a safe immunotherapy and provides strong basis for novel combination treatments for ovarian cancer patients. Clinical trial information: NCT04739527. Research Sponsor: None.

Patient demographics.	
Demographics	
Total patients	17
Age(in years)	
Mean	61.6
Median	64
Range	43-75
Stage n(%)	
III	12(70.6)
IIV	5(29.4)
Primary treatment n(%)	
PDS	2(11.8)
IDS	15(88.2)
Surgery outcome n(%)	
Complete	15(88.2)
Optimal	2(11.8)
CA125 at screening	
Mean	21.8
Median	20
Range	7-55
Molecular subtype n(%)	
BRCAm	13(76.5)
BRCAwt	4(23.5)

PDS, primary debulking surgery IDS, interval debulking surgery; BRCAm, BRCA mutation; BRCAwt, BRCA wild type.

Association of AI-based quantitative B7-H3 evaluation in the tumor microenvironment with molecular subtypes in high-grade serous ovarian carcinoma.

Ryusuke Murakami, Takuma Kobayashi, Teppei Konishi, Kohei Hamada, Taito Miyamoto, Rin Mizuno, Mana Taki, Koji Yamanoi, Masaki Mandai; Department of Gynecology and Obstetrics, Graduate School of Medicine and Faculty of Medicine, Kyoto University, Kyoto, Japan; Biomy Inc., Tokyo, Japan

Background: High-grade serous ovarian carcinoma (HGSC) exhibits heterogeneous tumor microenvironments (TME) that correlate with clinical outcomes. We previously reported four molecular histopathological subtypes of HGSC based on gene expression profiles reflecting TME characteristics: Immune Reactive (IR), Mesenchymal (MT), Solid/Proliferative (SP), and Papillary/Glandular (PG). The IR subtype, characterized by tumor-infiltrating lymphocytes, demonstrates favorable prognosis (PMID:26993207, 30853361). We also identified lower B7-H3 expression in IR compared to non-IR subtypes (PMID:34799346). Here, we developed an AI-based B7-H3 IHC quantification method across TME compartments and investigated its association with molecular subtypes. **Methods:** Forty-five HGSC patients who underwent primary debulking surgery were enrolled. Molecular histopathological subtyping categorized cases into IR (n=16), MT (n=20), and Other (SP/PG, n=9). B7-H3 immunohistochemistry-stained whole slide images were analyzed using DeepPathFinder, an AI-based pathological image analysis tool that performs automated tissue segmentation and IHC marker quantification. B7-H3 expression was quantified across three tumor-associated compartments: tumor, peritumor (within 1000 μ m of the tumor border), and necrosis. An integrated B7-H3 score was calculated as the mean density across these compartments. Survival analyses were performed using the Kaplan-Meier method and Cox proportional hazards regression. **Results:** The integrated B7-H3 score showed a stepwise increase across subtypes: IR (0.148) < MT (0.219) < Other (0.252) (Kruskal-Wallis $p=0.091$), and was significantly lower in IR compared to non-IR subtypes (0.148 vs 0.229, $p=0.034$). B7-H3 expression was consistently lower in IR across all compartments: tumor (IR: 0.171, MT: 0.205, Other: 0.257), peritumor (IR: 0.100, MT: 0.154, Other: 0.164), and necrosis (IR: 0.171, MT: 0.298, Other: 0.336; $p=0.025$). Survival analysis revealed significant prognostic differences among subtypes. Compared to IR, MT showed significantly worse outcomes (PFS: HR=8.35, 95% CI 3.00–23.24, $p<0.0001$; OS: HR=15.35, 95% CI 3.50–67.31, $p=0.0003$). The Other subtype also demonstrated inferior OS (HR=6.38, 95% CI 1.17–34.95, $p=0.033$). Both MT and Other (SP/PG) subtypes, which exhibited higher B7-H3 expression, were associated with worse prognosis. **Conclusions:** AI-based quantitative B7-H3 evaluation revealed subtype-specific expression patterns in the HGSC tumor microenvironment. B7-H3 expression was lowest in IR and higher in non-IR subtypes across all tumor-associated compartments. These findings suggest that patients with higher B7-H3-expressing subtypes may benefit from B7-H3-targeted therapy. Research Sponsor: None.

Vaccine-induced immune responses, HLA genotyping, and molecular profiling in patients with metastatic ovarian cancer (the PESCO trial).

Ana Veneziani, Douglas G. Millar, Stephanie Lheureux, Ben Wang, Neesha C. Dhani, Ilaria Colombo, Ainhoa Madariaga, Swati Atale, Joshua Lee, Czin Czin Benito, Janelle Ramsahai, Judy Quintos, Paula Sliwo, Lisa Wang, Valerie Bowering, Pamela Ohashi, Amit M. Oza; Princess Margaret Cancer Centre, Toronto, ON, Canada; Tumor Immunotherapy Program, Princess Margaret Cancer Centre, University Health Network, Toronto, ON, Canada; Princess Margaret Cancer Centre, University Health Network, University of Toronto, Toronto, ON, Canada; Princess Margaret Cancer Centre, University Health Network, Toronto, ON, Canada; Instituto Oncologico Della Svizzera Italiana, Bellinzona, Switzerland; Hospital Universitario 12 de Octubre, Madrid, Spain; Drug Development Program, Princess Margaret Cancer Centre, Toronto, ON, Canada; Princess Margaret, University Health Network, Toronto, ON, Canada; Princess Margaret Cancer Centre, University Health Network & University of Toronto, Toronto, ON, Canada; Division of Medical Oncology and Hematology, Princess Margaret Hospital Cancer Centre, Toronto, ON, Canada

Background: PESCO, a phase 1/2 trial of Maveropepimut-S (MVP-S) in combination with Pembrolizumab and metronomic cyclophosphamide, showed safety and efficacy signals in metastatic ovarian cancer (OC). MVP-S uses the lipid-based DPX delivery platform to stimulate T cell immune response to survivin epitopes restricted by 5 HLA class I haplotypes (A1, A2, A3, A24, B7). Survivin is highly expressed in OC. We report exploratory correlative analysis including immune responses, HLA typing and molecular profiling. **Methods:** The study included a phase 1 dose escalation and expansion cohorts: A (platinum-sensitive high-grade serous [HGS]), B (platinum-resistant HGS), and C (rare OC histologies). Survivin-specific T-cell responses were assessed by flow cytometric detection of IFN γ following ex vivo PBMC re-stimulation with pooled survivin epitopes at on-treatment timepoints. A positive immune response was predefined as >0.1% IFN γ ⁺ CD8⁺ T cells. HLA genotyping was mapped to MVP-S-restricted alleles. Molecular profiling was performed using next-generation sequencing (NGS) and/or whole-genome transcriptomic sequencing (WGTS). **Results:** Across 44 patients (pts), 37 (84%) carried ≥ 1 vaccine-relevant HLA allele and 23 (52%) carried ≥ 2 . The most frequent alleles were A24 (16/44; 36%), A02 (15/44; 34%), A03 (12/44; 27%), B07 (11/44; 25%), and A01 (8/44; 18%). Survivin-specific immune responses were detected in 15/24 (62%) immune-evaluable pts and were strongly enriched among pts with clinical benefit: CR 1/1 (100%), PR 7/7 (100%), SD 6/10 (60%), versus PD 1/6 (16%); overall, 14/15 (93%) immune responders had clinical benefit. The longest survivin-specific response persisted for 195 weeks in a pt with MMR deficient tumor who had CR for 3 years. Exploratory HLA-outcome analysis suggested enrichment of A24 in pts with clinical benefit but absent in PD. NGS was performed in 44 pts and WGTS in 36. NGS identified at least one SNV/indel in 43/44 (97.7%) pts. In Phase 1 and Cohorts A/B (n=34, 68% HGS), TP53 was dominant (76.5%, 86% in HGS), followed by MYC (17.6%), NF1 (14.7%), and BRCA1/2 (each 8.8%). In Cohort C (n=10, 8 clear cell), ARID1A (70%) and PIK3CA (60%) were frequent. In platinum resistant pts (n=24), alterations included TP53 (67%), BRCA1/2 (21%), CCNE1(17%). Tumors with cell cycle/replication stress alterations were enriched among pts with PD (29% vs 8% in non-PD; P = 0.099) and immune non-responders (37.5% vs 6.7% in IFN responders; P = 0.103). Tumor mutation burden was low in all 26 pts tested. **Conclusions:** Survivin-specific immune responses were strongly enriched among pts with clinical benefit, supporting survivin as an active target in OC. HLA typing demonstrated broad coverage of MVP-S epitopes across pts. Molecular subtype may have influenced immune responses in this study. Our findings support biomarker-integrated studies to optimize immunotherapy combinations in OC. Clinical trial information: NCT03029403. Research Sponsor: None.

Addressing barriers to FR α -directed therapy integration in platinum-resistant ovarian cancer: A multi-phase, community-informed initiative.

Kia Jones, Tariqa Ackbarali, Barrett Lawson, Angeles Alvarez Secord, Kathleen N. Moore; Medlive - A PlatformQ Health Brand, Needham, MA; The University of Texas MD Anderson Cancer Center, Houston, TX; Duke Cancer Institute, Duke University School of Medicine, Durham, NC; Stephenson Cancer Center at the University of Oklahoma Medical Center, Oklahoma, OK

Background: Antibody–drug conjugates (ADCs) targeting folate receptor alpha (FR α) represent an important therapeutic advancement in ovarian cancer, introducing a new standard of care (SOC) for patients with FR α –positive platinum-resistant ovarian cancer (PROC). Despite this progress, real-world integration of FR α biomarker testing and FR α -directed therapies into clinical practice remains variable, particularly in community settings where most patients receive care. This multi-phase initiative was designed to assess real-world practice patterns and barriers related to FR α -directed care and to evaluate outcomes from an educational intervention addressing these gaps. **Methods:** Phase 1 formative research included a national claims data analysis, a community-based practice pattern analysis survey (n=100), and a clinician case crowdsourcing survey (n=100) examining biomarker testing practices, treatment sequencing, and perceived challenges in PROC care. Findings from Phase 1 informed development of a 60-minute, on-demand CME activity (Phase 2) targeting oncologists, gynecologic oncologists and pathologists, and APPs. Educational outcomes were assessed using pre-/post-activity knowledge and confidence measures, polling, and post-activity evaluations. Interim Phase 2 outcomes are reported. **Results:** Phase 1 analyses demonstrated variable use of FR α biomarker testing across the patient journey, with testing more frequently performed at initial diagnosis. Clinicians cited barriers including testing access and turnaround time, tissue adequacy, uncertainty around eligibility thresholds for FR α -directed therapy, and challenges in sequencing FR α -directed agents relative to other targeted options. Claims data showed continued predominance of cytotoxic regimens at first PROC progression. As of 2.5 months post-launch, over 5,100 clinicians have engaged with the education. Pre- to post-activity assessments demonstrated the largest gains in knowledge related to limitations of the current SOC in PROC and in understanding the role of FR α biomarker testing in informing treatment decisions. Confidence in appropriately incorporating FR α -directed therapies into treatment plans remained low at post-test. Intended practice changes included increased use of comprehensive biomarker testing (36%), reassessment of the role of PFI in treatment selection (41%), and routine FR α testing at recurrence (37%). **Conclusions:** This multi-phase initiative identified persistent gaps in FR α biomarker testing and therapeutic integration in PROC and demonstrated early educational gains in knowledge, with ongoing needs related to clinical application and confidence. These findings highlight the value of outcomes-driven education in addressing real-world barriers and supporting informed integration of FR α -directed therapies into PROC care. Research Sponsor: Genmab US, Inc.

Prognostic effect of neoadjuvant chemotherapy in gBRCA-mutated compared to gBRCA wild-type patients with advanced HGSOC treated with first-line PARP inhibitor maintenance: A large series propensity score-matching analysis.

Ilary Ruscito, Adriana Ionelia Apostol, Giorgia Russo, Serena Maria Boccia, Laura Vertechy, Matteo Bruno, Carolina Maria Sassu, Diana Giannarelli, Anna Fagotti, Claudia Marchetti; Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Italy; Fondazione Policlinico Universitario A. Gemelli, IRCCS, Rome, Italy

Background: Recent results from the TRUST trial (ENGOTov33/AGO-OVAR OP.7) have renewed interest in the prognostic role of primary debulking surgery (PDS) versus interval debulking surgery (IDS) in advanced high-grade serous ovarian cancer (HGSOC). This study evaluated the prognostic impact of neoadjuvant chemotherapy (NACT) according to germline BRCA (gBRCA) status in advanced HGSOC patients receiving first-line PARP inhibitor (PARPi) maintenance, and its influence on outcomes at recurrence. **Methods:** We retrospectively identified patients with advanced HGSOC, treated between 2019 and 2024 at our gynecologic oncology referral center, who underwent upfront surgery and platinum-based chemotherapy followed by PARPi monotherapy. gBRCA status, surgical approach (PDS vs NACT+IDS), and survival outcomes, were collected. Patients were stratified by gBRCA status (gBRCAmut vs gBRCAwt). Propensity score matching (PSM) was performed based on age, ECOG-PS, FIGO stage, tumor histotype, surgical approach, and residual disease after first cytoreduction. Progression-free survival (PFS), overall survival (OS), post-recurrence PFS (PFS2), and post-recurrence OS (OS2) were analyzed. **Results:** After PSM, 406 patients were included (203 gBRCAmut and 203 gBRCAwt). In the gBRCAmut cohort, 58.6% underwent PDS and 41.4% received NACT+IDS, while 42.9% and 57.1% of gBRCAwt underwent PDS and NACT+IDS, respectively. All gBRCAmut patients received olaparib maintenance; among gBRCAwt, those with somatic BRCA mutations received olaparib (45/203) and the remainder niraparib (158/203). Complete cytoreduction was achieved in 92.1% of cases, with no differences between groups. Among gBRCAwt patients, median PFS was 43 months with PDS versus 19 months with NACT+IDS ($p=0.008$). Among gBRCAmut, median PFS was not reached with PDS and was 28 months with NACT+IDS ($p<0.001$). Median OS was not reached in either surgical group for gBRCAwt patients, whereas in gBRCAmut patients median OS was not reached with PDS and was 60 months following NACT+IDS ($p<0.001$). At recurrence, PFS2 did not differ by upfront treatment. However, NACT+IDS was associated with inferior OS2 in both gBRCAwt ($p=0.019$) and gBRCAmut ($p=0.048$) patients, with shorter median OS2 observed in gBRCAmut (15 vs 18 months). **Conclusions:** NACT was associated with inferior survival outcomes in advanced HGSOC patients receiving first-line PARPi, with a more pronounced detrimental effect observed in gBRCAmut patients. This suggests that BRCA-mutated tumors, despite their intrinsic sensitivity to PARP inhibition, may be particularly vulnerable to the negative consequences of delayed cytoreduction, with potential implications for treatment sequencing and surgical decision-making. Research Sponsor: None.

Onsite serial monitoring of high grade serous ovarian cancer (HGSOC) mutations in circulating tumor DNA (ctDNA) via droplet digital PCR.

John Nakayama, Phillip Gallo, Patti Petrosko, Madeline Myers, Francisco Bizouarn, Patricia Schnepf, Eddy van Collenburg, Adam Corner, Emily Dalton, Thomas C. Krivak, David L. Bartlett, William LaFramboise; Allegheny Health Network, Pittsburgh, PA; Allegheny Health Network Cancer Institute, Pittsburgh, PA; Bio-Rad Laboratories, Hercules, CA; Illumina, Inc., San Diego, CA

Background: Comprehensive Genomic Profiling (CGP) of tumor and blood samples is increasingly employed for ovarian cancer diagnosis. We used diagnostic CGP sequencing results (523 genes) to identify mutations in HGSOC patients for surveillance of tumor treatment response by an onsite ddPCR assay (Bio-Rad, Hercules, CA). We compared ctDNA mutations to imaging (computed tomography & MRI) and CA125 values across a cohort of HGSOC patients undergoing surgery followed by platinum-based therapy with diverse outcomes. **Methods:** CGP mutations from matched index tumor, plasma and buffy coat cell samples (TSO-500, Illumina) were used to identify tumor- and patient-specific, coding mutations for interrogation of serial blood samples. Concordance was high for tumor and blood (MED = 97.1%, Q1: 93.3%, Q3: 98.8%) and 15 patients with inclusive longitudinal samples were selected for retrospective analysis of ctDNA samples versus CA-125, imaging and outcomes. Mutation variant allele frequency (VAF) suitable for primer construction ranged in variant allele frequency (VAF) from 0.5 to 24.4% (MED = 2.5%, Q1: 1.2; Q3: 3.8%) in cfDNA. A lower limit of detection (LLOD) of 1 to 2 copies/nanogram cell free DNA (cfDNA) was established using synthetic gene Block targets and FFPE tumor dilutions. **Results:** There was a significant correlation ($r^2 = 0.85$, $p < 0.0001$) of initial target cfDNA VAF and numbers of mutation copies detected per nanogram cfDNA. There was no significant correlation of mutation copies with index or serial CA125 values ($r^2 = 0.11$, $p = 0.38$) over the wide range of CA125 values across the patient cohort. However, all patients displayed parallel dynamic changes in multiplex ctDNA mutations and CA125 values with variations in disease status and outcome over 1-3 years. Platinum-sensitive patients with a sustained response to therapy ($n=3$) based on imaging and CA 125 values displayed rapid elimination of tumor mutations via ddPCR prior to stabilization of "normal" CA125 values. Absence of mutations was further validated by interrogating 5X concentrated patient cfDNA aliquots. Three patients (platinum-resistant) that initially responded to treatment by imaging and declining CA 125 values never achieved ctDNA mutation levels below the LLOD. These patients subsequently displayed tumor escalation with correlative increases in ctDNA mutation levels and CA125 values. **Conclusions:** Patient mutation monitoring via ddPCR of blood samples collected and processed onsite, provided rapid, iterative and quantitative results consistent with radiographic imaging and CA 125 assays. In addition, durable remission cases were characterized by rapid loss of mutations detected by ctDNA ddPCR assays prior to imaging and diminution of CA125 values. Low levels of ctDNA mutations above LLOD persisted in responders who otherwise achieved normal CA125 values but later developed disease progression. Research Sponsor: None.

The use of circulating tumor DNA to stratify the risk of recurrence after surgical debulking in epithelial ovarian cancer.

Muhammad Anees, Erin Grayhack, Ashten N. Omstead, Jenna Zimmerman, Grace Gorecki, Alyssa Wield, Christopher Morse, Sarah Crafton, Eirwen Miller, Britney G. Sadler, Greg J. Hogan, Sarah Ratzel, Jeff Jasper, Thomas C. Krivak, Ali Hussainy Zaidi, John Nakayama; Allegheny Health Network Cancer Institute, Allegheny Health Network, Pittsburgh, PA; Allegheny Health Network Cancer Institute, Pittsburgh, PA; Allegheny Health Network, Pittsburgh, PA; Myriad Genetics, Inc, Salt Lake City, UT; Myriad Genetics, Inc., Salt Lake City, UT

Background: Accurate risk stratification after debulking surgery in ovarian cancer remains challenging. Although surgical debulking status (SDS) and CA125 are standard prognostic markers, patients remain at high risk of recurrence despite optimal debulking and normalization of CA125. Circulating tumor DNA (ctDNA) has emerged as a sensitive biomarker for detecting molecular residual disease (MRD). We evaluated the prognostic value of post-surgical ctDNA compared with SDS and post-surgical CA125 in predicting recurrence. **Methods:** In a prospectively collected cohort of ovarian cancer patients undergoing standard-of-care treatment, we evaluated 37 patients with a reportable post-surgical MRD before initiation of adjuvant chemotherapy. Tumor-informed, patient-specific panels created from whole genome sequencing of matched tumors and normal samples were used to assess MRD (Precise MRD, Myriad Genetics). Postoperative CA-125 was stratified using a standard clinical cutoff of 35 U/mL. Median follow-up was 30 months (IQR 21.9). **Results:** Post-operative ctDNA was detected in 75.7% (28/37) of patients with 24.3% (9/37) detected at ultra-low levels ≤ 100 PPM. Among ctDNA-positive patients, 85.7% (24/28) recurred, compared with no recurrences among ctDNA-negative group (median PFS: 7.6 [3.0-23.2] months vs. not reached; $p < 0.001$). Post-operative CA125 showed a similar trend with elevated-CA125 patients having a shorter median PFS (7.5 [2.8-21.1] vs. 25.1 [9.7-58.0]; $p < 0.05$). Optimal SDS showed a trend toward longer median PFS (Optimal: 22.0 [4.1-58.0] vs. suboptimal: 10.8 [2.8-19.9], $p = 0.075$). Notably, all patients with suboptimal SDS and detectable ctDNA experienced recurrence (4/4). Among patients achieving no gross residual disease (NGR; $n = 25$), ctDNA strongly stratified outcomes: 82.4% (14/17) of ctDNA-positive patients recurred, whereas there were no recurrences in ctDNA-negative patients (median PFS: 4.6 [2.9-38.9] vs. not reached; $p < 0.001$). The median tumor fraction (TF) within this cohort for positive cases was 432.0 PPM (IQR: 49.4-2510.0), where 29.4% (5/17) were detected below 100 PPM. Similarly, within the NGR group, normal-CA125 patients demonstrated a trend toward improved PFS (38.9 [6.9-58.0] vs. 4.6 [2.7-23.2]; $p = 0.11$). Importantly, among patients with normal-CA125 ($n = 15$), ctDNA further discriminated risk: 90% (9/10) of ctDNA-positive patients recurred with a median PFS of 20.3 (4.1-38.9) months, while no recurrences occurred in ctDNA-negative patients ($p < 0.05$). Within this subgroup, the median TF was 235.0 PPM (IQR: 71.4-2640.0), where 26.7% (4/15) were below 100 PPM. **Conclusions:** Postoperative ctDNA after surgical debulking predicts early recurrence in ovarian cancer, including patients with NGR, supporting its role as a biomarker of MRD and postoperative risk stratification along with CA125. Research Sponsor: Myriad Genetics.

Precision histopathologic classification of epithelial ovarian cancer subtypes using a computationally efficient multilayer perceptron framework with global validation.

Elangovan Krishnan, Sophia Ahmed, Gowrishankar Palaniswamy, Kavin Elangovan, Ramya Elangovan, Jansi Rani Sethuraj, Hammad Khan, Mustafa Abrar Zaman; AIM DOCTOR, Thiruverkadu, India; Allama Iqbal Medical College, Lahore, Pakistan; Ayub Medical College, Abbottabad, Pakistan; AIM DOCTOR, Dhaka, Bangladesh

Background: Epithelial ovarian cancer is the leading cause of gynecologic cancer mortality, with treatment and prognosis strongly dependent on accurate histopathologic subtype classification. The five major epithelial subtypes—high-grade serous, low-grade serous, endometrioid, mucinous, and clear cell carcinoma—exhibit distinct clinical behaviors, yet conventional interpretation is limited by subjectivity and interobserver variability. Although deep learning has advanced digital pathology, most high-performing models require substantial computational resources, limiting clinical scalability. We evaluated whether a lightweight multilayer perceptron (MLP) combined with structured dimensionality reduction could enable accurate and globally deployable ovarian cancer subtyping. **Methods:** We analyzed 9,521 anonymized histopathology image patches representing five epithelial ovarian cancer subtypes from publicly available datasets with expert pathologist consensus ground truth. Images underwent Gaussian random projection followed by principal component analysis to preserve discriminative morphologic features. A feedforward MLP (2,048→1,024→512→5 neurons) with batch normalization and dropout ($p=0.3$) was trained using AdamW optimization with cosine annealing over 50 epochs on 80% of the data. External validation was performed on independent datasets. Performance metrics included accuracy, sensitivity, specificity, F1 score, and AUROC. The model was deployed on a cross-platform digital pathology system and evaluated by pathologists across six continents. **Results:** The MLP achieved 97.4% test accuracy with balanced subtype performance. Sensitivity ranged from 94.2% to 99.3%, with a macro-averaged F1 score of 0.993 and AUROC >0.99 for all classes. External validation accuracy ranged from 91% to 93% across heterogeneous staining protocols. Sensitivity for low-grade serous carcinoma (92.1%) exceeded reported interobserver agreement (52–73%). Inference time averaged 0.33 seconds per image on standard CPU hardware. Pathologists rated the system clinically useful in >90% of evaluations. The model contained 2.8 million parameters, representing an 89% reduction compared with conventional convolutional architectures. **Conclusions:** A computationally efficient MLP enables accurate and reproducible epithelial ovarian cancer subtype classification while substantially reducing computational complexity. This approach mitigates interobserver variability and supports scalable AI-assisted pathology deployment. Prospective multicenter studies are warranted to assess integration into routine diagnostic workflows and impact on treatment stratification. Research Sponsor: None.

High-dimensional multiplex immunofluorescence to reveal immune microenvironment remodeling in matched primary and recurrent serous ovarian cancer.

Yookyung Lee, Hayeon Shin, Jae-Hoon Kim; Gangnam Severance Hospital, Yonsei University College of Medicine, Seoul, South Korea

Background: Recurrent serous ovarian cancer is associated with treatment resistance and poor prognosis, and changes in the tumor immune microenvironment (TIME) during recurrence have been suggested to contribute to these clinical features. However, spatial studies that quantitatively compare immune cell composition between primary and recurrent tumors at the single-cell level within the same patients remain limited. This study aimed to compare the TIME of primary and recurrent serous ovarian cancer using high-dimensional multiplex immunofluorescence. **Methods:** Tissue microarray (TMA) were constructed from formalin-fixed, paraffin-embedded (FFPE) tumor samples obtained from patients with primary and recurrent serous ovarian cancer. High-dimensional multiplex immunofluorescence staining was performed using the Akoya IO60 panel. Single-cell image analysis was conducted to segment cells and classify them into 19 distinct cell types. Differences in cell proportions were evaluated using unpaired analyses across all cores and paired analyses using matched primary-recurrent samples from the same patients (n=35). For paired analyses, cell proportions were compared using paired t-tests. **Results:** The 19 cell types included tumor epithelial cells, immune cell populations, and stromal cell populations. In unpaired analyses, recurrent tumors showed differences in immune cell composition compared with primary tumors, with relatively higher proportions of T cell-macrophage-associated populations and B cells. In paired analyses of matched samples (n=35), the proportion of T cell-macrophage-associated populations was significantly increased in recurrent tumors compared with primary tumors ($p=0.0042$). The proportion of B cells was also higher in recurrent tumors ($p=0.0463$). No statistically significant differences were observed in other cell types. **Conclusions:** Using high-dimensional multiplex immunofluorescence-based spatial analysis, we compared the tumor immune microenvironment of primary and recurrent serous ovarian cancer at the patient-matched level. Paired analyses demonstrated increased proportions of T cell-macrophage-associated populations and B cells in recurrent tumors, suggesting selective remodeling of the immune microenvironment during disease recurrence. Research Sponsor: None.

Bevacizumab rechallenge in platinum-resistant ovarian cancer: Evidence from a propensity score–matched analysis.

Celso Silva Sousa Filho, Lurick Rodrigues Soares, Débora Guilherme de Albuquerque e Rodrigues de Sousa, Artur Lício Júnior, Luanna Martins de Sa Oliveira, Louise De Brot Andrade, Andrea Gadelha, Glaucio Baiocchi, Elizabeth Santos, Alexandre André Balieiro Anastácio da Costa; A.C. Camargo Cancer Center, São Paulo, Brazil; Hospital AC Camargo (AC Camargo Cancer Center), São Paulo, Brazil; Department of Gynecologic Oncology, A.C. Camargo Cancer Center, São Paulo, Brazil

Background: Bevacizumab is approved for the treatment of ovarian carcinoma across multiple disease settings, from first-line therapy to late platinum-resistant recurrences (PROC). The greatest relative benefit of bevacizumab has been observed in the platinum-resistant setting. While evidence supports bevacizumab rechallenge in the first platinum-sensitive recurrence, no randomized trial has demonstrated a benefit of bevacizumab rechallenge in PROC. **Methods:** We conducted a retrospective cohort study including patients with PROC treated with chemotherapy with or without bevacizumab. Patients were matched using propensity score matching based on histology (HGSC vs others), chemotherapy backbone, line of platinum-resistant treatment, age, BRCA pathogenic variant status, and prior bevacizumab exposure. Nearest-neighbor matching with a 1:2 ratio (bevacizumab:non-bevacizumab) and a caliper of 0.2 was applied. Balance between groups was assessed using standardized mean differences. Progression-free survival (PFS) and overall survival (OS) were estimated using Kaplan–Meier methods and compared using log-rank tests. Hazard ratios (HRs) were estimated using Cox proportional hazards models with robust variance accounting for matching. Subgroup analyses were performed according to prior bevacizumab exposure, and treatment–exposure interaction was formally tested. **Results:** A total of 149 patients with PROC were included. Baseline clinicopathologic characteristics were well balanced between treatment groups. In the overall matched cohort, bevacizumab use was associated with significantly improved PFS compared with chemotherapy alone (median PFS 7.79 vs 4.37 months; HR 0.49, 95% CI 0.36–0.68; $p<0.001$), as well as improved OS (median OS 23.06 vs 10.45 months; HR 0.47, 95% CI 0.34–0.66; $p<0.001$). In bevacizumab-naïve patients, bevacizumab remained significantly associated with longer PFS (median 7.79 vs 4.04 months; HR 0.47, 95% CI 0.33–0.68; $p<0.001$) and OS (median 23.06 vs 10.05 months; HR 0.46, 95% CI 0.32–0.67; $p<0.001$). Among patients previously exposed to bevacizumab, re-exposure was associated with numerically longer PFS (median 8.49 vs 4.89 months; HR 0.61, 95% CI 0.31–1.20; $p=0.15$) and OS (median 21.29 vs 10.45 months; HR 0.54, 95% CI 0.26–1.11; $p=0.09$), although these differences did not reach statistical significance. There was no statistically significant interaction between prior bevacizumab exposure and treatment effect for PFS (p for interaction = 0.60). **Conclusions:** The addition of bevacizumab to chemotherapy is associated with significant benefit in bevacizumab-naïve patients with PROC. In patients previously exposed to bevacizumab, re-exposure was not associated with a statistically significant improvement in outcomes, underscoring ongoing uncertainty regarding the role of bevacizumab rechallenge in this setting. Research Sponsor: Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP); 2024/13952-4.

AI-driven multi-scale histopathologic classification of epithelial ovarian cancer to support precision oncology.

Yashwanth Kancharla, Elangovan Krishnan, Jansi Rani Sethuraj, Kavin Elangovan, Ramya Elangovan, Gowrishankar Palaniswamy, Rithish Nimmagadda, Sophia Ahmed, Nayanika Chowdary Tummala, Sravani Bhavanam, Ali Ataur Rehman, Hammad Khan, Shankar Biswas, Jeimy Castallanos; Harnett Health GME, Dunn, NC; University of Louisville, Louisville, KY; AIM DOCTOR, Thiruverkadu, India; Medical University of South Carolina, Lancaster, SC; One Brooklyn Health - Interfaith Medical Center, New York, NY; Allama Iqbal Medical College, Lahore, Pakistan; NYMC at St. Mary's General Hospital and Saint Clare's Health, Denville, NJ; Brookdale University Hospital and Medical Center, New York, NY; Liaquat College of Medicine and Dentistry, Karachi, Pakistan; Ayub Medical College, Abbottabad, Pakistan; Ivano-Frankivsk National Medical University, Ivano-Frankivsk, Ukraine; Brooklyn Health, New York, NY

Background: Epithelial ovarian cancer (EOC) comprises five histologically distinct subtypes associated with divergent molecular profiles, therapeutic responsiveness, and prognostic outcomes. Accurate histologic classification is essential for precision oncology but remains limited by morphologic overlap and interobserver variability. Deep learning architectures capable of multi-scale spatial feature extraction may enable objective and reproducible subtype discrimination. We evaluated the performance of a multi-scale factorized convolutional neural network (InceptionV3) for automated EOC subtype classification. **Methods:** Digitized hematoxylin-eosin-stained histopathology images were obtained from the University of British Columbia Ovarian Cancer Subtype Classification and Outlier Detection (UBC-OCEAN) dataset, including high-grade serous, low-grade serous, endometrioid, clear cell, and mucinous carcinomas. An ImageNet-pretrained InceptionV3 architecture was fine-tuned using a five-class classification head. The model leverages parallel convolutional branches with factorized asymmetric kernels to simultaneously capture fine cellular features and global tissue architecture. Images were normalized and augmented. Training was performed using 299×299 inputs, Adam optimizer (learning rate 1×10^{-4}), cross-entropy loss, and six epochs. Performance was assessed using accuracy, precision, recall, F1-score, and macro-averaged AUROC. External clinical validation was conducted by 57 board-certified gynecologic pathologists and oncologists across 14 geographic regions. **Results:** The model achieved an overall accuracy of 95.0% (491/517 test images). Subtype-specific F1-scores were 0.96 for high-grade serous carcinoma, 0.94 for endometrioid, 0.93 for clear cell, 0.92 for mucinous, and 0.88 for low-grade serous carcinoma. Macro-averaged AUROC was 0.957 (95% CI, 0.948–0.966). Computational efficiency was preserved with 23.9 million parameters and 11.6 billion FLOPs. Independent clinician validation demonstrated strong concordance with AI predictions, with mean inter-rater agreement of 95.3% ($\kappa=0.936$; 95% CI, 0.923–0.949), consistent across institutional practice settings. **Conclusions:** Multi-scale factorized convolutional modeling enables near-expert performance for automated EOC subtype classification by integrating cellular- and tissue-level morphologic features. High inter-rater concordance with an international specialist cohort supports translational reliability. This framework represents a scalable decision-support tool with potential to improve diagnostic standardization and precision therapeutic stratification. Prospective multi-center validation is warranted. Research Sponsor: None.

The role of combined T cell and NK cell activity in immune checkpoint inhibitor (ICI) therapy in endometrial cancer (EC).

Danielle Greenberg, Patrick Penalosa, Wen Gu, Sharon Wu, Matthew James Oberley, Michael Toboni, Britt Kristina Erickson, Krishnansu Sujata Tewari; UC Irvine Division of Gynecologic Oncology, Department of Obstetrics and Gynecology, Orange, CA; UC San Diego Department of Obstetrics and Gynecology, La Jolla, CA; CARIS Life Sciences, Phoenix, AZ; Caris Life Sciences, Phoenix, AZ; Comprehensive Cancer Center, University of Alabama at Birmingham, Birmingham, AL; University of Minnesota, Masonic Cancer Center, Minneapolis, MN; GOG Foundation and University of California Irvine Medical Center, Irvine, CA

Background: The efficacy of ICI in EC has largely been attributed to high microsatellite instability (MSI-H) causing increased tumor mutational burden (TMB) and T-cell mediated immunity. However, a subset of patients with microsatellite-stable (MSS) tumors also derive clinical benefit, indicating that MSI status alone is insufficient for patient selection and contributing to the 2024 Food and Drug Administration approval of chemotherapy plus ICI for all patients with EC. We evaluated established biomarkers of a T-cell-inflamed tumor microenvironment alongside alternative immune pathways, notably natural killer (NK) cell activity, to define determinants of overall survival (OS) benefit in EC patients treated with ICI. **Methods:** Patients with EC treated with pembrolizumab or dostarlimab were identified from the Caris Life Sciences database with paired whole exome and transcriptome sequencing (WES/WTS). OS was defined from ICI initiation to death or last contact via insurance claims. Patients were grouped as long vs short survivors (LS/SS) by median post-ICI OS (mOS). Associations between OS and expression of pre-annotated T- and NK-cell-related genes were analyzed with Kaplan–Meier and multivariable Cox models adjusting for clinicopathologic factors. **Results:** Of 6,354 patients, 25% were MSI-H and 71% MSS. Immune deconvolution of WTS showed higher levels of CD8⁺ T cells ($p=0.034$) and regulatory T cells ($p=0.026$) in LS vs SS. In multivariable analyses of the MSS subset, 63 T- and NK-cell-related genes were associated with improved OS, including FASLG (mOS 19.7 months vs 14.7 months in LS vs SS, HR=0.77, CI 0.70–0.85), IFNG (mOS 18.9 months vs 15.5 months in LS vs SS, HR=0.78, CI 0.71–0.86) and SIRPG (mOS 18.8 months vs 15.6 months in LS vs SS, HR=0.79, CI 0.71–0.87) (all $p<0.0001$). The IFN Tumor Inflammation Signature (TIS) was not associated with OS in MSS EC, whereas T-cell, NK-cell, and combined T/NK gene signatures were (Table 1). **Conclusions:** Improved OS after ICI in MSS EC is associated with both T-cell and NK-cell activity. NK-cell-related and combined T/NK signatures were associated with improved survival, suggesting NK-cell activation contributes to ICI efficacy. These findings warrant validation in independent cohorts prior to use as a potential biomarker for ICI use in MSS EC. Research Sponsor: None.

T/NK signature scores are associated with improved OS in MSS EC.		
Label	HR (95% CI)	P value
Gene set		
NK (high vs low)	0.82 (0.74–0.90)	<0.001
T + NK (high vs low)	0.84 (0.77–0.93)	0.001
T (high vs low)	0.84 (0.77–0.93)	0.001
Covariate		
p53: mutant vs wildtype	1.54 (1.38–1.73)	<0.001
TMB: high vs low	0.66 (0.49–0.90)	0.008
Chemotherapy: yes vs no	1.13 (0.98–1.31)	0.101
Biopsy site: metastasis vs primary	0.92 (0.83–1.02)	0.124
Lenvatinib: yes vs no	0.95 (0.86–1.05)	0.293

Multivariable Cox models adjusted for p53 status, TMB, site, chemotherapy and lenvatinib use.

Sequencing of fallopian tube p53 signature found concurrently with p53 mutant uterine cancers and their somatic mutation profiles.

Erika Joelle Lampert, Mackenzy Radolec, Danyang Li, Macy Hale, Jamie Lee Lesnock, Lan Gardner Coffman; UPMC Magee, Pittsburgh, PA; University of Pittsburgh Medical Center (UPMC), Pittsburgh, PA; University of Pittsburgh, Pittsburgh, PA; Magee-Women's Hospital of UPMC, Pittsburgh, PA; Magee-Womens Research Institute, Pittsburgh, PA

Background: The tumor protein 53 gene (p53) encodes a protein that suppresses replication of DNA-damaged cells. Mutations resulting in protein dysfunction are common in many cancers. A p53 signature is an aberrant immunohistochemical expression in 12 or more consecutive epithelial cells in the fallopian tube (FT) and is thought to be an early precursor lesion in a spectrum to high grade serous ovarian carcinoma (HGSOC). P53 mutations have also been described in endometrial cancer (EC), specifically high grade histologies such as uterine papillary serous carcinoma (UPSC). NextGen Sequencing of UPSC tumors and concurrent FT lesions has identified overlapping p53 mutations, raising the possibility that these could represent a precursor lesion. The objective of this study was to delineate the clonal relationship between p53-mutation harboring epithelial lesions in the FT and other histologic subtypes of EC, which could have implications for risk stratification, counseling, and treatment. **Methods:** We identified 7 patients with EC and a concurrent p53 FT signature. DNA extraction (Qiagen) from FFPE samples was performed and sent for whole genome sequencing (Novogene) on the paired FT and endometrial tissues to identify the specific p53 mutations. Using a position-wise comparison, we evaluated the clonal relationship between the specific p53 mutations identified in each pair. **Results:** In this cohort, 4 patients had endometrioid adenocarcinoma, 1 had mixed endometrioid and carcinosarcoma, 1 had high grade endometrial stromal sarcoma (ESS), and 1 had UPSC. All 7 patients had a p53 signature identified in the FT. Four patients had p53 overexpression while 3 had heterogenous p53 expression in the endometrium on IHC. Among the 7 patients, sequencing revealed 5 pairs with at least 1 shared somatic mutation identified in both the endometrium and FT. A shared mutation was identified in patients with carcinosarcoma, high grade ESS, UPSC, and two endometrioid adenocarcinomas. As of 9/2025 or last follow-up, no patients had developed a primary peritoneal malignancy, but 2 patients had disease recurrence. Both patients who had disease recurrence were among those with a shared somatic mutation identified. **Conclusions:** To our knowledge, this is the first study evaluating the relationship between concurrent FT p53 signatures and uterine cancer beyond serous. We identified 5 patients with at least 1 shared somatic p53 mutation. While these specific mutations have not been described as known pathogenic driver mutations in the literature to date, further exploration into these alleles is needed. A clonal relationship between FT lesions and endometrial cancer could have important implications on clinical counseling and management, thus further research into the specific p53 mutations identified and validation within a larger cohort is warranted. Research Sponsor: None.

Ultra-sensitive circulating tumor DNA (ctDNA) detection as predictor of survival outcomes in endometrial cancer patients undergoing frontline treatment.

Jeffrey Andrew How, Morgan Bou Zerdan, Melissa Pham, Xun Xu, Kathleen Keough, Charles Abbott, Yi Chen, Sean Michael Boyle, Richard Chen, Natalie Celestino, Shannon Neville Westin, Amir A. Jazaeri, Pamela T. Soliman; The University of Texas MD Anderson Cancer Center, Houston, TX; Personalis, Inc., Menlo Park, CA; Personalis, Inc., Fremont, CA

Background: For endometrial cancer (EC), clinicopathologic and molecular characterization add to the risk stratification complexity, but remain limited to predict risk of recurrence. Precise biomarkers are needed to guide treatment. This study seeks to investigate the value of circulating tumor DNA (ctDNA) in EC patients. **Methods:** In an ongoing, single-institution prospective study of EC patients undergoing primary surgical management, serial plasma samples were collected at multiple timepoints: pre-(pre-op)/post-operatively (post-op), post-definitive treatment (dTx), and surveillance. If patients did not have adjuvant therapy, the post-op time point was considered the dTx timepoint. ctDNA analysis was performed on banked samples at the non-surveillance timepoints using NeXT Personal, a personalized whole genome sequencing-based tumor-informed assay tracking up to 1800 mutations, (Personalis, Fremont, CA). Primary endpoint was ctDNA detection rate. Secondary endpoints included correlation with survival outcomes (recurrence free survival [RFS] and overall survival [OS]). Multivariable analysis was performed for RFS adjusting for dTx ctDNA detection, stage, and TP53 mutation status. Given the limited number of deaths, multivariable analysis was not performed for OS. **Results:** 99 patients and 254 samples were included for ctDNA analysis. Median age at surgery was 65.1 (range 42–85) years. After a median follow-up of 24.1 (range 3.4 – 67) months, there were 25 recurrences and 10 deaths. Majority had stage I (68.7%), grade 3 (73.7%) tumors, non-endometrioid histologic tumor components (63.7%), and received adjuvant therapy (79.8%; therapy declined in 4 [4%] patients). Adjuvant radiation and chemotherapy was given in 67 (67.7%) and 53 (53.5%) patients, respectively. ctDNA was detected in 83.3% (75/90) of pre-op, 19.5% (17/87) of post-op, and 14.1% (9/64) of dTx samples. Although pre-op ctDNA was not associated with survival, post-op ctDNA detection was associated with worse RFS (HR 6.3, 95% CI 2.6–15.5; $p < 0.001$) and OS (HR 24.6, 95% CI 3–205; $p = 0.003$). Post-op detection in the ultrasensitive range (< 100 PPM) were also significantly prognostic of worse RFS (HR: 5.1, 95% CI 1.3–19.5, $P = 0.02$). Similarly, dTx detection was associated with worse RFS (HR 27.7, 95% CI 8.9–86.6; $p < 0.001$) and OS (HR 7.5, 95% CI 1.7–33.7; $p = 0.01$). On multivariable analysis, dTx detection was independently associated with worse RFS (HR 27.7, 95% CI: 8.9–86.6; $p < 0.001$). **Conclusions:** In a predominantly early-stage, high-risk cohort of EC patients, post-op and dTx ctDNA detection is associated with inferior survival. ctDNA detection in the ultrasensitive range may hold promise to identify EC patients at risk for recurrence which may not be identified in conventional assays. These results support ctDNA as a promising biomarker for clinical decision-making in EC. Research Sponsor: None.

Pembrolizumab–lenvatinib beyond immunotherapy progression in endometrial cancer: A real-world analysis.

Alberto Farolfi, Chiara Casadei, Emanuela Scarpi, Eleonora Paoletti, Francesca Rusconi, Simone Sabbioni, Caterina Gianni, Michela Palleschi, Daniela Montanari, Andrea Carlini, Giulia Miserocchi, Nicola Gentili, Olga Serra, Giandomenico Di Menna, Alice Andalò, Filippo Merloni, Marianna Sirico, Lorenzo Cecconetto, Samanta Sarti, Antonino Musolino; IRCCS Istituto Romagnolo per lo Studio dei Tumori (IRST) "Dino Amadori", Meldola, Italy; TriNetX Europe, Milan, Italy; IRCCS Istituto Romagnolo per lo Studio dei Tumori (IRST) "Dino Amadori", Meldola, Italy; Alma Mater Studiorum - Università di Bologna, Bologna, Italy; Data Unit, IRCCS Istituto Romagnolo per lo Studio dei Tumori (IRST) "Dino Amadori", Meldola, Italy; IRCCS - Istituto Romagnolo per lo Studio dei Tumori (IRST) Dino Amadori, Meldola, Italy; Medical Oncology, Breast & GYN Unit, IRCCS Istituto Romagnolo per lo Studio dei Tumori "Dino Amadori" - IRST, Meldola, Italy

Background: The integration of immune checkpoint inhibitors (ICIs) into frontline therapy for advanced or recurrent endometrial cancer (aEC) has transformed treatment paradigms. However, the management of patients who experience disease progression after ICI-based therapy remains challenging. In the absence of prospective guidance, ICI rechallenge and ICI-based combinations beyond progression are already being used in clinical practice. In this real-world study, we aimed to evaluate the effectiveness of pembrolizumab–lenvatinib (PL) beyond ICI progression in patients with aEC. **Methods:** A retrospective study was conducted using the TriNetX database, defining two cohorts of aEC patients: 527 patients who received PL and 2,582 patients who did not receive PL but were treated with either paclitaxel or doxorubicin (chemotherapy, CHT cohort). Both cohorts had received an ICI-based regimen within the previous three years. Patients with any other malignancy were excluded. Propensity score matching (PSM) was used to balance cohorts for age, race, body mass index (BMI), major comorbidities, mismatch repair (MMR) status and prior olaparib exposure. The primary endpoint was overall survival (OS); secondary endpoints were treatment-related toxicities, including hypothyroidism and heart failure. OS was estimated using Kaplan–Meier methods, with hazard ratio (HR) used to compare OS and odds ratio (OR) used to compare toxicities. **Results:** After PSM, 521 matched pairs of patients (mean age $\pm$ standard deviation: 66,4 $\pm$ 9,6 years) were included in the PL and CHT cohorts, respectively, with well-balanced baseline characteristics. Asian patients were similarly represented in the two groups (7.3% vs 7.4%), most patients were obese (BMI ≥ 30 : 59,3% vs 57,8%), only a small proportion had known MMR-deficient disease (2.1% and 1.9%), and just few of them were previously treated with olaparib (1.9%). After a median follow-up of 8.6 months (interquartile range, IQR 14.3) in the PL cohort and 11.5 months (IQR 16.7) in the CHT cohort; median OS was 27,4 months with PL and was not reached with CHT (HR = 2.25, 95% CI 1.76–2.89; $p < 0.001$). **Conclusions:** The rise of ICIs in frontline therapy for aEC marks a paradigm shift and raises the question on how to manage patients who progress after prior immunotherapy. This is the first large, real-world cohort analysis to evaluate PL beyond immunotherapy progression in aEC. In this study, PL did not improve OS compared with CHT in patients previously exposed to ICIs. These findings suggest that PL may not be the optimal choice in this setting, and further work is needed to clarify the best post-ICI sequencing strategies and to develop approaches to overcome resistance. Research Sponsor: None.

Circulating tumor DNA (ctDNA) from a phase II study of adjuvant dostarlimab with pelvic radiation in locally advanced, mismatch repair–deficient (MMR-D) endometrial cancer (D-RT study).

Gabriela Sotolongo, David N. Brown, Maria M. Rubinstein, Robin Guo, Qin Zhou, Alexia Iasonos, Seth M. Cohen, William P. Tew, Sminu Bose, Alison M. Schram, Vicky Makker, M. Herman Chui, Marisa Kollmeier, Nadeem Abu-Rustum, Roisin Eilish O'Cearbhaill, Dmitriy Zamarin, Carol Aghajanian, Kaled M. Alektiar, Britta Weigelt, Ying L. Liu; Gynecologic Oncology Service, New York, NY; Memorial Sloan Kettering Cancer Center, New York, NY; Gynecologic Medical Oncology Service, Memorial Sloan Kettering Cancer Center, New York, NY; Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, NY; Icahn School of Medicine at Mount Sinai, New York, NY; Gynecologic Medical Oncology, Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, NY; Gynecologic Medical Oncology Service, Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, NY

Background: Although ctDNA is a promising, non-invasive tool for cancer evaluation and monitoring, its use in endometrial cancer (EC) is currently limited. We sought to evaluate ctDNA dynamics and associations with clinical outcomes as part of a novel study of adjuvant immune checkpoint blockade (ICB) with radiation (RT) in locally advanced MMR-D EC. **Methods:** The D-RT study was an investigator-initiated, single-arm, phase II trial evaluating the safety and efficacy of 5 cycles of dostarlimab given concurrently with standard pelvic intensity modulated RT (IMRT), NCT04774419. The study included patients with newly diagnosed clinical stage III/IVA MMR-D EC. Primary endpoint was progression-free survival (PFS) at 2 years defined by RECIST V1.1 compared with historical control. All patients consented to MSK-IMPACT tumor-normal genetic testing. We performed MSK-ACCESS targeted ctDNA sequencing in a subset of patients with at least 3 timepoints (baseline post-surgery, on-treatment, post-treatment/follow-up) and correlated with baseline tumor genomics and clinical outcomes. **Results:** We previously reported the primary endpoint in 31 evaluable patients with 2-year PFS of 80.6% (95% 1-sided CI 65.3–100%), meeting pre-specified threshold for a positive study (data cutoff 8/1/2025). Here, we report ctDNA results from a subset of 15 patients with 58 total samples. Median age was 62 years (range 51–89 years) with 1 stage IB (i+), 3 stage IIIA, 9 stage IIIC1, and 2 stage IIIC2 MMR-D ECs (FIGO 2009). Histology included 8 endometrioid grade I/II, 5 endometrioid grade III, and 2 dedifferentiated carcinomas. Six patients (40%) had detectable baseline ctDNA post-surgery, with 5/6 (84%) having visible/residual disease at baseline. Of these, 3/6 (50%) had eventual disease recurrence post adjuvant treatment. In 8 patients with visible disease post-surgery, only 2 did not have detectable baseline ctDNA. ctDNA cleared post-treatment in all but 2 patients who had aggressive, dedifferentiated carcinomas. Among the 5 patients with recurrence (4 distant, 1 local), ctDNA detection preceded or coincided with radiographic detection of disease in the 4 patients (80%) with distant disease. One patient had a biopsy-proven, vaginal cuff recurrence only and never had detectable ctDNA. In the 10 patients without disease recurrence, none had detectable ctDNA post-treatment. **Conclusions:** In patients with locally advanced MMR-D EC, ctDNA detection after surgery correlated with visible disease. ctDNA levels declined during dostarlimab and RT treatment for most patients, and ctDNA detection was correlated with disease recurrence in distant but not local disease, suggesting its potential as a non-invasive marker of disease. Future studies should explore the utility of ctDNA as a disease monitoring tool to guide therapy decisions. Clinical trial information: NCT04774419. Research Sponsor: Federal; GSK.

Forecasting global disparities in cervix and corpus uteri cancers: GLOBOCAN 2022–2040 projections.

Sonia Babu, Berkha Rani, Ahmad Abed, Sai Abhishek Narra, Hira Jawed, Vidushi Reddy Gillela, Saqib Rangoonwala, Abul Hasan Shadali Abdul Khader, Elizaveta Bodrova, Rajesh Thirumaran, Manzoor Rather; Mercy Catholic Medical Center, Darby, PA; The University of Southwestern Medical Center, Dallas, TX; Mercy Catholic Medical Center, Philadelphia, PA

Background: Uterine cancers, including cervix uteri (C53) and corpus uteri (C54), are a major burden on global healthcare with marked geographic and socioeconomic disparities. Key risk factors including persistent high-risk HPV infection for cervical cancers), limited screening access, and modifiable factors like obesity and exogenous hormone exposure (e.g., oral contraceptive use), which vary across settings and could influence future burden. Predicting epidemiological trends is essential to guide prevention, screening, and treatment modalities. This study compares predicted changes in incidence and mortality for C53 and C54 across countries, WHO regions, income groups, and HDI categories from 2022 to 2040. **Methods:** Incidence and mortality data for 2022 and predictions for 2040 were extracted from GLOBOCAN database for 185 countries. Countries were classified by WHO region, World Bank income level, and HDI categories. Percentage changes in incidence and mortality were calculated for both cancer types across all categories. **Results:** Globally, C53 incidence is forecasted to rise from 1.32 million to 5.94 million cases (+348.4%), with mortality increasing from 697,418 to 3.41 million deaths (+389.5%). C54 shows a modest increase in incidence (840,256 to 899,224; +7.0%) but substantial increase in mortality (195,310 to 899,224; +360.5%). Across WHO regions, the largest increases in C53 incidence and mortality occur in AFRO and EMRO (+1043%, +1066% and +918%, +1029%, respectively). C54 incidence advances most in AFRO (+279%) and EMRO (+254%) and least in EURO (+97.8%). Mortality growth is highest in EMRO (+1205%) and AFRO (+1106%). Income-level patterns show increasing disparities: low-income countries have the highest increases for C53 incidence (+1062%) and mortality (+1073%), with high-income regions showing the lowest (+693%, +781%). Similar trends are observed for C54, with incidence rising most in low-income settings (+302%) and least in high-income regions (+139%), while mortality increases range from +1096% (low-income) to +872% (high-income). HDI patterns are similar to income trends: Low-HDI countries reveal the highest increases for C53 (+1062% incidence, +1073% mortality) and C54 (+302%, +1096%), while Very-High-HDI regions show the lowest rises for both cancers. **Conclusions:** Burden of uterine cancer is predicted to rise steeply by 2040, with greatest increases in low-income, low-HDI, AFRO, and EMRO regions. The disproportionate escalation in mortality (especially for corpus uteri cancers) highlight the importance of prevention, screening, early detection, and equal access to treatment to prevent expanding global disparities, including improved availability of HPV vaccination, targeted public education efforts, and engagement of primary care physicians and OB/GYNs to ensure that patients are vaccinated and screened appropriately. Research Sponsor: None.

A phase II trial of lenvatinib plus pembrolizumab in patients (pts) with endometrial or ovarian carcinosarcoma.

Sminu Bose, Corbyn Mbock Nchako, Qin Zhou, Alexia Iasonos, Ashley Rodriguez, Mauline Onsombi, Kara Pierro, Korri Sagoes, Natalie Solberg, Viktoriya Paroder, Maria M. Rubinstein, Seth M. Cohen, Martee Leigh Hensley, Chrisann Kyi, William P. Tew, Ying L. Liu, Alison M. Schram, Britta Weigelt, Carol Aghajanian, Vicky Makker; Memorial Sloan Kettering Cancer Center, New York, NY; MSKCC, New York, NY; MSKCC Memorial Hospital Clinical, New York, NY; Gynecologic Medical Oncology, Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, NY; Gynecologic Medical Oncology Service, Memorial Sloan Kettering Cancer Center, New York, NY

Background: Carcinosarcoma is a rare and aggressive histology of gynecologic carcinomas that has limited treatment options and is often excluded from larger therapeutic clinical trials. In KN775, treatment with multikinase inhibitor lenvatinib plus PD-1 inhibitor pembrolizumab led to significantly longer progression-free survival (PFS) and overall survival (OS) than chemotherapy among patients with previously treated advanced non-carcinosarcoma endometrial carcinomas. We report results from a phase 2 trial of lenvatinib + pembrolizumab in pts with endometrial or ovarian carcinosarcoma. **Methods:** In this open label, single institution, investigator initiated, phase 2 study, pts had confirmed recurrent/persistent endometrial or ovarian carcinosarcoma with progression after at least 1 prior platinum chemotherapy but no more than 3 prior lines, measurable disease, and ECOG performance status ≤ 1 . Pts received oral lenvatinib 20 mg/day plus pembrolizumab 200 mg intravenously every 3 weeks. The primary endpoints were objective response rate (ORR) per RECIST v1.1 and PFS rate at 27 weeks (PFR27). Secondary endpoints included median duration of response (mDOR), clinical-benefit rate (CBR: complete response (CR) + partial response (PR) + stable disease (SD) at 27 weeks), median overall survival (mOS), and safety. Next generation sequencing, MSK-IMPACT, was performed on tumors from all 27 patients for exploratory analysis. **Results:** As of data cutoff on 12/15/2025, 27 pts enrolled; median age was 63 years (range: 51–79); and at least 26.4% pts were non-white. Primary tumor site was 63% (17/27) endometrial and 37% (10/27) ovarian; tumors were 19% (5/27) dMMR and 81% (22/27) pMMR. Confirmed ORR was 18.5% (5/27; 0 CRs, 3 PRs in endometrial, 2 PRs in ovarian), meeting the interim analysis primary endpoint. Of the 5 confirmed responses, 4 occurred in pts with pMMR tumors, and 1 in a pt with dMMR tumor. There are 2 additional unconfirmed PRs. Responses in pts with ovarian tumors included 1 platinum-sensitive and 1 platinum-resistant. PFR27 was 35.7% (90% CI: 24 – 100), mDOR was 26.5 months (80% CI: 3.8 – NE), CBR was 37% (80% CI: 24.4 – 51.2), and mOS was 15.3 months (95% CI: 7.1 – 24.4). Two pts remain on treatment and were censored for time to event analyses. All pts had at least one treatment-emergent adverse event (TEAE). The most common TEAEs were fatigue (74%), hypertension (56%), diarrhea (52%), anorexia (48%), and weight loss (48%). Grade 3 and 4 TEAEs occurred in 44% and 7.4% patients, respectively. There were no grade 5 TEAEs. 5 Pts (19%) discontinued study treatment due to TEAEs. Further genomic analyses are underway. **Conclusions:** Encouraging efficacy and durable responses were observed in endometrial and ovarian carcinosarcoma pts treated with lenvatinib + pembrolizumab, regardless of MMR status or primary site. The study met its predefined interim analysis endpoint. No new safety signals were identified. Clinical trial information: NCT02501096. Research Sponsor: None.

Antibody-drug conjugate (ADC) biomarker targets in endometrial cancer (EC): Molecular characterization and implications for therapeutic decision-making.

Britt Kristina Erickson, Michael Toboni, Sharon Wu, Mary M. Mullen, Kathleen N. Moore, Ramez Nassef Eskander, Theodore Nicolaides, Rebecca Christian Arend, Joyce F. Liu, Shaina Bruce, Beryl Manning-Geist, Robert Louis Coleman, Thomas J. Herzog; University of Minnesota, Masonic Cancer Center, Minneapolis, MN; Comprehensive Cancer Center, University of Alabama at Birmingham, Birmingham, AL; Caris Life Sciences, Phoenix, AZ; Washington University in St. Louis Department of Genetics, St. Louis, MO; Fred and Pamela Buffett Cancer Center at the University of Nebraska Medical Center, Omaha, NE; UC San Diego Moores Cancer Center, La Jolla, CA; Caris Life Sciences, Irving, TX; The University of Alabama at Birmingham, Birmingham, AL; Dana-Farber Cancer Institute, Boston, MA; Penn State Health, Hershey, PA; Emory University School of Medicine, Atlanta, GA; Texas Oncology, US Oncology Research, The Woodlands, TX; GOG Foundation and University of Cincinnati Cancer Center, Cincinnati, OH

Background: Given the evolving landscape of ADCs, we evaluated expression of emerging ADC targets in EC and compared expression patterns across molecular subgroups (POLE mutated [POLEm], MSI-high [MSI-H], TP53-mutated [TP53m] or No Specific Molecular Profile [NSMP]) defined by the Proactive Molecular Risk Classifier for Endometrial Cancer. **Methods:** Tumors were analyzed by DNA and RNA sequencing and immunohistochemistry (IHC) for select proteins (Caris Life Sciences, Phx, AZ). ER+ defined as % staining $\geq 1\%$. Statistics were calculated by Mann-Whitney U test and adjusted for multiple comparisons ($q < 0.05$). Expression was split into top quartile (^H) and bottom quartile (^L). Overall survival (OS) was obtained from insurance claims data and calculated from first treatment to last contact. Hazard ratios (HR) were calculated by Cox proportional hazards with p-values by log-rank tests. **Results:** Of 13,731 EC samples, 2.4% (n=335) were POLEm, 21.6% (n=2,961) MSI-H, 46.8% (n=6,420) TP53m and 29.2% (n=4,015) NSMP. HER2+ by IHC was highest in TP53m tumors compared to POLEm, MSI-H, and NSMP (15.9% vs 1.2% vs 0.8% vs 4.0%; $p < 0.05$). TP53m tumors had the highest RNA expression of CDH6, B7-H4, CLDN6, ERBB3, ERBB2, FOLR1, NECTIN2, NECTIN3, and TF; NSMP tumors had the highest expression of TROP2 and NECTIN4 relative to other subtypes (Table 1). Compared to all solid tumors, TP53m EC had the highest median RNA expression of B7-H4 and second highest of CLDN6 and FOLR1. Assessing the prognostic effect of ADC targets by subtype, POLEm CLDN6^H tumors had improved OS compared to CLDN6^L (HR 0.39, $p = 0.003$). In MSI-H tumors, TROP2^H, CDH6^H, B7-H4^H, CLDN6^H, ERBB3^H, ERBB2^H, FOLR1^H and NECTIN2-4^H was associated with improved OS (HR 0.57-0.84, $p < 0.05$). In TP53m tumors, TROP2^H, B7-H4^H, FOLR1^H, HER3^H, and NECTIN4^H was associated with improved OS (HR: 0.75-0.80, $p < 0.05$) and NECTIN1^H and B7-H3^H with worse OS (HR: 1.26, $p < 0.001$). In ER- NSMP tumors (n=804), B7-H4^H, ERBB3^H, ERBB2^H and NECTIN4^H had improved OS (HR: 0.62-0.74, $p < 0.05$) and B7-H3^H and NECTIN1^H had worse OS (HR: 1.40, $p = 0.01$). In ER+ NSMP tumors (n=2,896), TROP2^H and TF^H had improved OS (HR: 0.73-0.82, $p < 0.05$) and ERBB2^H and CDH6^H had worse OS (HR: 1.24-1.29, $p < 0.05$). **Conclusions:** Expression of ADC targets differs by molecular subtype with varying associations with OS in EC patients. Focusing future clinical trials on EC subsets with high biomarker expression will be critical to efficiently developing novel targeted therapeutics. Research Sponsor: None.

RNA expression by subtype (transcripts per million).													
Subtype	B7-H3	B7-H4	CD276	CLDN6	ERBB2	ERBB3	FOLR α	NECTIN1	NECTIN2	NECTIN3	NECTIN4	TF	TROP2
POLEm	10.0	10.0	24.9	0.38	25.6	52.7	7.6	7.2	14.9	15.0	5.6	0.70	58.2
MSI-H	5.8	12.0	23.2	0.32	23.3	58.9	8.6	7.8	14.7	13.6	9.7	0.84	61.1
TP53m	21.5	15.8	22.0	2.90	32.8	62.4	20.7	6.0	18.6	18.6	7.1	0.98	54.8
NSMP	7.5	14.0	22.3	0.35	25.1	56.2	10.3	6.6	14.9	11.5	10.5	0.78	81.8

Accumulation of cholesterol, cortisol, and glutathione in mitochondria as a marker of metabolic adaptation in serous and clear cell endometrial carcinoma.

Anna Petrovna Menshenina, Valeria Bandovkina, Elena M. Frantsiyants, Tatiana I. Moiseenko, Mark A. Rogozin, Ekaterina I. Surikova, Irina Valerevna Neskubina, Elena A. Ozerkova, Valeria A. Menshenina, Elena V. Shalashnaya, Natalya Chugunova, Ekaterina V. Verenikina, Sofya A. Kornienko, Meri Adamyan, Alla A. Adamyan, Zlata V. Verenikina, Larisa N. Vashchenko, Iuliana S. Shatova, Arthur Andryasovich Antonyan, Oleg Ivanovich Kit; National Medical Research Centre for Oncology, Rostov-on-Don, Russian Federation; Rostov State Medical University, Rostov-on-Don, Russian Federation

Background: Aggressive endometrial carcinoma subtypes, such as serous (USC) and clear cell (CCC) carcinomas, are characterized by distinct cellular metabolism and dysregulation. Altered homeostasis of metabolites and hormones within mitochondria serves as a molecular driver of metabolic reprogramming in cancer cells. Excess mitochondrial cholesterol can induce oxidative stress, whereas glutathione provides antioxidant defense. Cortisol levels are capable of modulating organelle function. The aim of this study was to evaluate the levels of cholesterol, cortisol, and glutathione in mitochondria isolated from serous and clear cell endometrial carcinomas to characterize the metabolic profile of tumor cells. **Methods:** The study was conducted on mitochondria isolated from tumor tissue of 41 patients with USC (n=21) and CCC (n=20), stage III–IV, histological grade G3; the mean patient age was 59.6 ± 6.7 years. Mitochondria isolated from normal endometrium (n=20) obtained during hysterectomies for uterine leiomyoma (mean age 57.8 ± 8.2 years) served as controls. Cortisol, cholesterol, and glutathione concentrations in the mitochondrial fraction were determined by enzyme-linked immunosorbent assay (ELISA). Statistical analysis was performed using parametric and non-parametric tests with adjustments for multiple comparisons. **Results:** A significant increase in cholesterol levels was observed in mitochondria from these rare endometrial carcinoma subtypes: 2.1-fold in USC and 1.9-fold in CCC compared with normal endometrium. Cortisol content was elevated by 2.1- and 2.5-fold, respectively. Mitochondrial glutathione concentration was also increased: 2.4-fold in USC and 1.9-fold in CCC. **Conclusions:** The data reveal a universal mechanism of metabolic adaptation in serous and clear cell endometrial carcinomas, characterized by a unified mitochondrial metabolic profile featuring co-accumulation of cholesterol, cortisol, and glutathione. Elevated cholesterol generates a pro-apoptotic signal, which is counterbalanced by increased glutathione levels to maintain redox homeostasis. The concurrent rise in cortisol indicates the engagement of mitochondrial stress-response pathways. This constellation of alterations reflects fundamental reprogramming of cellular homeostasis in aggressive endometrial cancers and may be considered a potential target for mitochondrial-directed therapy. Research Sponsor: None.

p53 R248Q upregulation of VTCN1 via dual mechanisms as a driver of immune evasion and adaptive resistance to CDK4/6 inhibitors: Rationale for combination immunotherapy in endometrial cancer.

Yan Ding, Bilan Li; Tongji University, Shanghai, China

Background: TP53-mutated endometrial cancer (EC) is a heterogeneous disease with variable responses to immunotherapy. While generic p53 mutation status is a standard biomarker, the distinct clinical impact of specific hotspot mutants remains underappreciated. Our bioinformatics analysis of TCGA data suggested that the R248Q hotspot—but not others—is specifically linked to an "immune-desert" phenotype. We aimed to mechanistically define this subtype and validate its diagnostic value as a predictor for immune exclusion and CDK4/6 inhibitor sensitivity. **Methods:** We performed a comprehensive bioinformatic analysis of the TCGA-UCEC cohort to correlate specific p53 hotspot mutations with immune landscapes. To elucidate the underlying mechanism, we engineered a panel of isogenic EC cell lines (p53-null, R248Q, R175H, R248W, R273H/C) and assessed VTCN1 (B7-H4) regulation via biochemical assays. To validate these findings clinically, we established an independent cohort of 254 EC patients with tissue microarrays (TMA); whole-exome sequencing (WES) is currently underway to pinpoint hotspot mutations and correlate them with VTCN1 expression and immune infiltration. **Results:** Discovery of Diagnostic Target: In the TCGA cohort, stratifying p53 mutants revealed that R248Q carriers exhibited the most profound "cold" tumor microenvironment compared to other hotspots, suggesting it as a potential negative predictive biomarker. Mechanistic Validation: Using our isogenic models, we observed that R248Q specifically drives high VTCN1 expression. Mechanistically, R248Q appears to promote VTCN1 via a dual pathway: transcriptional upregulation and, uniquely, protein stabilization by inhibiting proteasomal degradation. This indicates VTCN1 as a potential surrogate marker for the R248Q subtype. Therapeutic Implications: In preclinical models, abemaciclib treatment paradoxically upregulated VTCN1 in R248Q cells, suggesting adaptive resistance. However, this induced vulnerability was associated with enhanced sensitivity to combined CDK4/6 inhibition and immunotherapy (anti-VTCN1), which elicited superior tumor regression compared to monotherapy. **Conclusions:** Our study suggests the potential value of refining p53 diagnostics from binary (mutant/WT) to hotspot-specific resolution. Current data indicate that p53 R248Q may function as a distinct driver that contributes to an immunosuppressive "cold" TME in EC, likely through synergistic transcriptional and post-translational upregulation of VTCN1. Furthermore, abemaciclib-induced VTCN1 elevation points to a possible mechanism of monotherapy resistance. These findings provide a strong preclinical rationale to explore combining CDK4/6 inhibitors with immunotherapy, specifically for patients with the high-risk p53 R248Q subtype. Research Sponsor: Funding Agency: National Natural Science Foundation of China (NSFC), Grant No: 82172714.

Preoperative endocrine treatment response in primary postmenopausal endometrial cancer.

Fabian Trillsch, Sven Mahner, Angelina Vlaski, Mara Franzl, Tanja Paul, Doris Mayr, Christina Victoria Isabella Tauber, Susanne Beyer, Bastian Czogalla, Alexander Burges, Mirjana Kessler, Nadia Harbeck, Anca Chelariu-Raicu; LMU University Hospital, LMU Munich, Munich, Germany; LMU University Hospital, Department of Obstetrics and Gynecology, Munich, Germany; Institute of Pathology, Faculty of Medicine, University Hospital, LMU Munich, Munich, Germany; Breast Center, Department of Obstetrics and Gynecology, LMU University Hospital Munich, Munich, Germany

Background: While preoperative endocrine therapy with letrozole has become an established approach for treatment decisions in estrogen receptor (ER) positive breast cancer, this concept has not been transferred to endometrial cancer so far. We hypothesized that preoperative endocrine treatment response to letrozole, assessed by changes in Ki67 expression between baseline and surgery as a marker for cellular proliferation, can be evaluated in primary endometrial cancer as a predictive, patient-specific biomarker. **Methods:** Postmenopausal patients with first diagnosis of endometrial cancer planned to undergo definitive surgical management with hysterectomy were prospectively included in this single-arm biomarker analysis. Letrozole was administered orally at a daily dose of 2.5mg for a period of 2 to 4 weeks until surgery. Eligibility criteria included all molecular subtypes and histologies and no prior treatment for endometrial cancer was allowed. Ki67 expression was assessed immunohistochemically by two independent pathologists as the percentage of positive tumour nuclei. Relative change in Ki67 (%) from pre-treatment biopsy to post-treatment specimen was assessed using the Wilcoxon signed-rank test, substantial response was defined as relative reduction of Ki67 expression $\geq 50\%$. **Results:** A total of 23 patients were prospectively enrolled with median age of 70 years (range 52–88) and median BMI of 32 kg/m² (range 20–48). 22 patients had endometrioid histology (22/23, 95.7%), of those 86.4% (19/22) low-grade and three high-grade (13.6%). One patient had a high-grade serous tumor. 17 of the 23 patients (73.9%) were classified as NSMP (no specific molecular profile), 14 of them ER positive (82.3%). 5 of 23 patients were classified as dMMR (mismatch repair deficient, 21.7%) and one as p53mut (p53 mutant). Median pre-treatment Ki67 expression was 50% (range 10–85) compared to 15% (range 1–80) post-treatment ($p < 0.0002$). Following preoperative letrozole treatment, 16 of 23 patients (69.6%) had a relative reduction of more than 50% in Ki67 expression, 13 of these (81.3%) were of NSMP, three (18.8%) of dMMR molecular subtype. Regarding ER expression in these responders, all dMMR and 11/13 NSMP tumors (84.6%) were ER positive. Two NSMP tumors (14.5%) showed a response to endocrine treatment despite being ER negative. **Conclusions:** Short-term preoperative letrozole treatment enables identification of patients with substantial endocrine treatment response in primary endometrial cancer. Using this preoperative window-of opportunity, dynamic Ki67 evaluation might serve as an easily accessible predictive biomarker to tailor patient-specific treatment decisions. Research Sponsor: None.

Racial disparities in endometrial cancer (EC) survival after molecular classification (MC).

Jill Roberts, Sharon Wu, Michael Toboni, Britt Kristina Erickson, Ninad Kulkarni, Matthew James Oberley, Navya Nair, Wafa Khadraoui, Abdulrahman Sinno; Sylvester Comprehensive Cancer Center/University of Miami, Miami, FL; Caris Life Sciences, Phoenix, AZ; Comprehensive Cancer Center, University of Alabama at Birmingham, Birmingham, AL; University of Minnesota, Masonic Cancer Center, Minneapolis, MN

Background: Black (BAA) patients with EC have double the mortality rate compared to White patients. It is unclear if these survival differences persist after MC. Here, we examine racial disparities in this context and seek to identify molecular differences by race. **Methods:** EC samples (n = 10,162: BAA n=2,410, White n=7,752) were analyzed by NGS (NextSeq/NovaSeq) and RNA (NovaSeq) (Caris Life Sciences, Phx, AZ). Four well-described EC groups were created: POLE ultramutated (POLE-mt), MSI-H, TP53-mt, or No Specific Molecular Profile (NSMP; TP53-wt). Overall survival (OS) was obtained from insurance claims and calculated from tissue collection to last contact for MC cohorts. Hazard ratio (HR) was calculated by Cox proportional hazards, with p-value calculated by log-rank test. Race was self-reported. **Results:** There was a higher prevalence of BAA patients in the TP53-mt subtype (69.1% vs. 43%), compared with POLE-mt (1% vs. 2.26%) and NSMP (16.4% vs. 31%) (p<0.001). Across EC, BAA patients had shorter OS (29.8 vs 39.7 months (m); HR: 1.30 (1.22-1.39), p<0.001). BAA patients had worse OS in the NSMP cohort (36.8 vs 49.5m; HR 1.35 (1.15-1.59), p<0.001) and TP53-mt cohort (26.1 vs 29.6 m; HR 1.13 (1.05-1.22), p=0.002). Race was not associated with differences in OS in POLE-mt (NR vs was 51.4 m) and MSI-H (44.4 vs 45.9 m). There were molecular differences between race when stratified by MC (q<0.05) (Table 1). Gene set enrichment analysis showed down-regulation of immune-related pathways in BAA. In NSMP tumors, BAA patients had lower IFN γ signature (0.72-fc) and worse post-pembrolizumab survival (16.9 vs 24.6 m; HR 1.46 (1.09-1.95), p=0.011). **Conclusions:** Previous studies demonstrated that racial disparities in endometrial cancer persist even when controlling for histology. This study demonstrates that these disparities persist even after controlling for MC, as defined by the ProMisE classification. BAA patients were more likely to develop TP53-mt tumors, but the survival disparity was largest in the NSMP group. Furthermore, Black and White patients exhibit differential expression of known prognostic mutations even within the same MC group. Research Sponsor: None.

Molecular differences by race and subtype.

Biomarker	TP53-mt		NSMP	
	BAA %	White %	BAA %	White %
<i>ARID1A</i> -mt	4.47	10.3	32.8	48.9
<i>CTNNB1</i> -mt	NS	NS	31.1	40.2
<i>FGFR2</i> -mt	0.60	2.94	3.29	11.3
<i>PIK3CA</i> -mt	23.1	36.6	NS	NS
<i>PIK3R1</i> -mt	9.58	15.4	17.9	35.0
<i>PTEN</i> -mt	6.83	15.7	40.4	66.9
<i>PPP2R1A</i> -mt	15.5	23.8	NS	NS
<i>CDKN2A</i> -del	NS	NS	22.0	13.7
<i>CDKN2B</i> -del	NS	NS	13.7	5.45
<i>MTAP</i> -del	NS	NS	18.8	8.92
ER+	NS	NS	62.6	76.0
PR+	NS	NS	53.1	67.4

NS=not significant.

Aspirin use and survival outcomes in endometrial cancer.

Zachary Gentry, Quinn Kistenfeger, Lauren Wegner, Aidan Coon, Reed O'Connor, Casey Cosgrove, Laura Chambers; The Ohio State University, Columbus, OH

Background: Given the worsening survival trends of endometrial cancer in the United States, further improvement in adjuvant treatment of this cancer is needed. Aspirin use has been shown to reduce cancer risk in multiple cancer types. A randomized controlled trial recently showed that aspirin therapy significantly improved overall survival in patients with colorectal cancer with PIK3CA mutations, a mutation that is seen in up to 50% of endometrial cancers. We therefore hypothesized that aspirin use may similarly improve survival in patients with endometrial cancer. **Methods:** We conducted a retrospective review of all patients with endometrial cancer treated at a single academic institution between 2014–2017. Demographics, clinicopathologic data, surgical and adjuvant treatment, and aspirin use were collected from the medical record. Proportional variables were compared using Fisher's exact and Chi-square tests. Continuous variables were compared using t-tests and Mann-Whitney U-tests. Disease-specific survival (DSS, time from diagnosis to death due to cancer) was estimated using Kaplan-Meier plots, with log-rank and Cox proportional hazards analysis used to compare groups. **Results:** A total of 765 patients were included in the study. Most patients were white (92%), had Stage I disease (79.9%), had endometrioid histology (87.1%), and were mismatch repair (MMR) proficient (74.6%). Of the 765 patients, 243 (31.8%) were taking ASA at the time of their endometrial cancer diagnosis, while 522 (68.2%) were not. Patients taking aspirin at the time of diagnosis were significantly older than those who were not (66.2 vs 59.8, $p < 0.0001$). Otherwise, there was no significant difference in BMI, stage, grade, histology, MMR status, or adjuvant treatment between the two groups. On multivariate analysis, aspirin use at diagnosis was significantly associated with improved DSS (HR 0.27 [0.10–0.64], $p = 0.0020$) after adjusting for age, stage, grade, histology, MMR status, and adjuvant treatment. **Conclusions:** Aspirin use at the time of endometrial cancer diagnosis was associated with a significant improvement in DSS in our cohort. While retrospective, this data is promising as a potential improvement in therapy for patients with endometrial cancer. Additionally, this intervention would be inexpensive and easily accessible for all patients. Prospective data is needed to further evaluate the effect of aspirin on endometrial cancer outcomes. Research Sponsor: None.

MicroRNAs as surrogate biomarkers of future endometrial malignancy in women with endometrial hyperplasia without atypia and an open-label randomized trial of metformin, weight control, and exercise intervention.

Chyong-Huey Lai, Wei-Yang Chang, Chiao-Yun Lin, Shih-Ming Jung, Chin-Jung Wang, Huei-Jean Huang, Hsiu-Jung Tung, Yun-Hsin Tang, Angel Chao; Gynecologic Cancer Research Center, Taoyuan City, Taiwan; Linkou Chang Gung Memorial Hospital of Linkou, Taoyuan, Taiwan; Gynecologic Cancer Research Center, Chang Gung Memorial Hospital, Taoyuan, Taiwan; Department of Pathology, Chang Gung Memorial Hospital and Chang Gung University college of Medicine, Taiwan; Gynecologic Cancer Research Center, Chang Gung Memorial Hospital, Taoyuan, Taiwan; Department of Obstetrics and Gynecology, Chang Gung Memorial Hospital, Linkou Branch and Chang Gung University, Taoyuan City, Taiwan; Gynecologic Cancer Research Center, Taoyuan City, Taiwan, Taiwan; Department of Obstetrics and Gynecology, Chang Gung Memorial Hospital, Taoyuan City, Taiwan; Gynecologic Cancer Research Center, Chang Gung Memorial Hospital, Linkou Branch, Taoyuan, Taiwan

Background: Endometrial hyperplasia (EH) is regarded as an endometrial cancer (EC) precursor. The severity of atypia reflects risk of future EC. According to Kurman et al., the risk of progression to EC was < 1% in simple hyperplasia (SH) and 3% in complex hyperplasia (CH) without atypia (non-A). Our group previously identified 4 MicroRNAs (MiRs) and PTEN by immunohistochemistry stain are significant risk biomarkers of future endometrial malignancy.

Methods: This prospective open-label randomized controlled study enrolled a total of 60 patients SH/CH non-A. All participants were randomized 1:1 to with or without metformin intervention and received education for exercise and weight control. A stratification of body mass index was performed, but not for HbA1C. PTEN immunohistochemistry stain and MiR profiles of the endometrial tissue were analyzed. **Results:** 57 participants were eligible for analysis. After all the participants had been followed up for 3 years, an analysis was performed in which 3 with progression to atypical hyperplasia and 6 with recurrent SH/CH non-A were observed. Exercise intensity was inversely correlated with use of metformin or not ($p = 0.028$). The predicting progression/recurrence by any of the 4 miRs (miR30a-3p, miR141, miR-200a, and miR200b) were all significant ($p < 0.05$). PTEN expression, metformin, exercise, or body weight control intervention did not alter the risk of EH recurrence/EC progression. Metformin group has a trend of decreased risk of progression/recurrence yet not significant ($p = 0.291$). The decreased impact of metformin may be partly related to their lower intensity of exercise as compared to no-metformin group. Impact of interventions may need longer observation.

Conclusions: Presence of any of the 4 miRs (miR30a-3p, miR141, miR-200a, and miR200b) seem related to risk of recurrence/progression of SH/CH non-A, while PTEN expression, metformin, exercise, and weight control are not, in our prospective cohort. Clinical trial information: NCT05292573. Research Sponsor: National Science and Technology Council, Taiwan; 2018-2021 MOST-107-2314-B-182-040 -MY3.

Whole-genome sequencing–based ctDNA testing for post-surgical monitoring and early detection of recurrence or progression in uterine cancer.

Abigail Barger, Brandie Taylor, Alison Parisian, Bhakti Dwivedi, Samuel Rivero-Hinojosa, Carly Bess Scalise, Carcia Carson, Punashi Dutta, Ekaterina Kalashnikova, Gabrielle M. Heilek, Minetta C. Liu, Alexey Aleshin, Adam ElNaggar, Ashley Graul; St. Luke's University Health Network, Bethlehem, PA; Natera, Inc., Austin, TX

Background: Reliance on clinicopathologic risk factors to guide adjuvant therapy in early-stage uterine cancer (UC) has not improved survival, underscoring the need for biomarkers for post-treatment monitoring. In this study, we evaluate ctDNA as a prognostic biomarker using a whole-genome sequencing (WGS)–based assay in the post-surgical UC setting. **Methods:** We performed a retrospective analysis of clinically annotated residual samples from commercial ctDNA testing in 118 patients diagnosed with UC. Signatera Genome assays (Natera, Inc.) were designed from the WGS data of matched tumor tissue and normal blood samples to detect and quantify ctDNA in serially collected post-operative plasma. Descriptive statistics were used to compare association of ctDNA across stages and timepoints. **Results:** Among 118 UC patients, 20/118 were metastatic and excluded from analysis. Of the remaining 98 patients, 77 had stage I and 21 had stage II–III disease. Median clinical follow-up was 11.2 months (range: 0.8–33.2) with 13% (13/98) of patients having recurrence/progression within a median of 8.5 (range: 3.9–25.1) months from surgery. ctDNA analysis was performed across 1004 total tests with a median of 8 tests per patient (range: 2–16) and a median testing cadence of 2.9 (range: 0–12.7) months. Post-surgical ctDNA assessment (2–8 weeks post-operatively) was available for 35 stage I patients with a ctDNA detection rate of 9% (3/35). Focusing on the 32 patients with >12 months of postoperative clinical follow-up, one patient was ctDNA-positive postoperatively and recurred 7.2 months after surgery. Among the ctDNA-negative patients (N=31), 84% (26/31) remained serially negative with no evidence of recurrence at a median clinical follow-up of 26.3 (range: 13.5–38.7) months post-surgery. The remaining ctDNA-negative patients (N=5) converted to positive during longitudinal monitoring, all subsequently experiencing recurrence/death. Longitudinal ctDNA detection rate during surveillance was 32.1% (25/78) in stage I and 47.6% (10/21) in stage II–III. Of the stage I patients with recurrence (N=8), 100% were ctDNA-positive prior to or at the time of the clinical finding, with a median lead time of 5.2 (range: 1.2–15.8) months. Similarly, in stage II–III patients with recurrence/progression (N=5), 100% were ctDNA-positive prior to the clinical finding with a median lead-time of 6.07 (range: 4.1–23.7) months. **Conclusions:** ctDNA positivity postoperatively identifies UC patients at increased risk of recurrence/progression, often preceding clinical relapse by several months. Serial ctDNA negativity using a tumor-informed, WGS-based ctDNA assay correlated with absence of recurrence. Postoperative longitudinal ctDNA monitoring shows promise as a clinically actionable biomarker to guide adjuvant treatment decisions and improve post-operative surveillance. Research Sponsor: None.

Development of an endometrial cancer test from a vaginal swab.

Bridget Z. Gagrut, Jamie Nadine Bakkum-Gamez, Martin Krockenberger, Mark Camardo, John B. Kisiel, Seth Slettedahl, Maureen Lemens, William R. Taylor, Shariska Harrington, Julia Zella, Elle Kielar-Grevstad, Tomasz M. Beer, Marilyn Olson; Exact Sciences Corporation, Madison, WI; Department of Obstetrics and Gynecology, Mayo Clinic, Rochester, MN; Division of Gastroenterology and Hepatology, Mayo Clinic Rochester, Rochester, MN; Department of Quantitative Health Sciences, Mayo Clinic Rochester, Rochester, MN; Gastroenterology, Molecular Cancer Diagnostic Laboratory, Mayo Clinic Rochester, Rochester, MN

Background: Endometrial cancer (EC) is the most common gynecologic cancer and abnormal uterine bleeding (AUB) is the predominant presenting symptom. While <10% of AUB represents underlying EC, endometrial sampling is currently required to rule out EC. To develop an alternative, non-invasive rule-out strategy, we aimed to refine a previously reported EC-associated methylated DNA marker (MDM) panel in vaginal swabs. **Methods:** Patients ≥ 18 years old with AUB who met ACOG recommendations for endometrial sampling and those undergoing a hysterectomy for biopsy-proven EC or atypical hyperplasia (AH) were prospectively enrolled in a multicenter cohort study. A vaginal fluid specimen was collected via swab by a provider during a speculum exam. DNA was extracted from samples and bisulfite treated, followed by a target and signal amplification method to detect 8 previously identified MDMs. The cross-validated EC classification model used the mean of standardized MDMs. Clinical classification of benign endometrium (BE), EC, and AH was based on central pathology review. EC diagnoses were based on hysterectomy specimens. Endometrioid and mucinous constituted type 1 EC; serous, carcinosarcoma, clear cell, and mixed histology ECs were collectively analyzed as type 2. **Results:** Of 693 participants enrolled, 670 were evaluable with valid results: 524 in the AUB cohort and 146 in the suspected EC cohort. Within the AUB cohort, 16 had EC or AH. The final analysis cohort included 508 BE, 156 EC, and 6 AH. Of the evaluable participants 20% identified as Black, 3% Asian or Pacific Islander, 75% White, and 3% Other; 7% reported Hispanic ethnicity. Median age was 66 and 50 years for EC and BE AUB, respectively; 80% of those with EC and 43% with benign AUB reported being postmenopausal. Among participants with EC, 102 (65%), 17 (11%), 30 (19%), 6 (4%) were stage I, II, III, and IV, respectively; one EC was unstaged. Type 2 EC accounted for 42 (27%) of all EC cases. A 4-MDM panel yielded an AUC of 0.97 (0.96–0.99, 95% CI) for EC; models with 5–8 MDMs gave identical performance. All-stage EC sensitivity was 97, 97, 96, 95, and 92% at specificities ranging from 75, 80, 85, 90, and 95%, respectively. At the 85% (82–88%) specificity threshold, sensitivities across EC stage, type, and age were consistently high (Table). Sensitivity for AH was 33% (10–70%). **Conclusions:** An MDM panel demonstrated high sensitivity for EC across stage and EC type, supporting the potential for a non-invasive vaginal swab-based test to rule out EC. Future studies are necessary to finalize the panel and algorithm, prior to validating the test. Clinical trial information: NCT06294886. Research Sponsor: Exact Sciences Corporation.

EC	Sensitivity (%; 95% CI) at 85% Specificity
All Stages (n=156)*	96 (92-98)
Stage I (n=102)	94 (88 - 97)
II (n=17)	100 (82 - 100)
III (n=30)	100 (89 - 100)
IV (n=6)	100 (61 - 100)
Type 1 (n=114)	95 (89 - 98)
2 (n=42)	100 (92 - 100)
Age ≤ 66 yrs (n=86)	95 (89 - 98)
> 66 (n=70)	97 (90 - 99)

*n=1 EC was un-staged.

GLP-1 receptor expression in a molecularly characterized cohort of endometrial carcinoma: Results from the GEICO 163-T/SPECTRUM study.

Carlos González-Merino, Alfonso Cortes-Salgado, Esther Moreno, Irene Carretero-Barrio, Eva Guerra, Marta Rosas, Cristina Saavedra, Mónica García-Cosío, María Gion, Tamara Caniego-Casas, María Fernández-Abad, Ignacio Ruz-Caracuel, Elena López-Miranda, Silvia González-Martínez, Noelia Martínez-Jañez, Elena Vida-Navas, Patricia Guerrero-Serrano, Coral García de Quevedo, José Palacios, Belén Pérez; Medical Oncology Department, Hospital Universitario Ramón y Cajal, Madrid, Spain; Pathology Department, Ramón y Cajal University Hospital, IRYCIS, Madrid, Spain; Pathology Department, Ramón y Cajal University Hospital, IRYCIS, CIBERONC, Madrid, Spain; Pathology Department, Hospital Universitario Ramón y Cajal, IRYCIS, CIBERONC, Faculty of Medicine, Universidad de Alcalá, Madrid, Spain; Pathology Department, Hospital Universitario Ramón y Cajal, IRYCIS, Madrid, Spain; Pathology Department, Hospital Universitario Ramón y Cajal, IRYCIS, CIBERONC, Madrid, Spain; IRYCIS, CIBERONC. "Contigo Contra el Cáncer de la Mujer" Foundation, Madrid, Spain; Pathology Department, Hospital Universitario Ramon y Cajal, IRYCIS, CIBERONC, Faculty of Medicine, Universidad de Alcalá, Madrid, Spain; Pathology Department, Hospital Universitario de Ramon y Cajal, IRYCIS, CIBERONC, Faculty of Medicine, Universidad de Alcalá, Madrid, Spain

Background: The glucagon-like peptide-1 receptor (GLP-1R) plays a central role in metabolic, and hormonal signaling and has gained increasing clinical relevance due to the widespread use of GLP-1R agonists. Given the strong link between obesity and endometrial carcinoma (EC), data on GLP-1R expression in EC are of clinical interest. We aimed to evaluate GLP-1R expression in a large, molecularly classified EC cohort and analyze its association with clinico-pathological and molecular features. **Methods:** GLP-1R immunohistochemistry was performed on tissue microarrays from 192 ECs included in the SPECTRUM cohort. This cohort included 111 low grade endometrioid and 81 high grade ECs. 187 tumors were successfully classified according to WHO 2020 criteria, including 3% POLE-mutated (POLEmut), 25% mismatch repair-deficient (dMMR), 43% no specific molecular profile (NSMP), and 29% p53 abnormal (p53abn) carcinomas. Additionally, *CTNNB1* mutation status was available in 168 tumors (16% mutated). GLP-1R expression was evaluated using the Allred scoring system (range 0–8). GLP-1R positivity was defined as Allred ≥ 6 according to previously published criteria (Kanda et al. 2018). Associations were evaluated using univariable analyses and multivariable logistic regression, reporting ORs with 95% confidence intervals; $p < 0.05$ was considered statistically significant. **Results:** GLP-1R expression was evaluated in 172 EC. GLP-1R positivity was observed in 32.0% of the overall cohort and differed across molecular subtypes: 41.9% in NSMP, 40.0% in POLEmut, 28.9% in p53abn and 20.5% in dMMR tumors ($p = 0.099$). Progesterone receptor (PR) levels were significantly higher in GLP-1R-positive compared with GLP-1R-negative tumors (median 55% vs 20%, $p = 0.015$), whereas a non-significant trend toward higher estrogen receptor (ER) expression was observed (median 50% vs 25%, $p = 0.18$). GLP-1R positivity was more frequent in *CTNNB1* mutated tumors (50.0% vs 28.9%; $p = 0.041$). In multivariable logistic regression including PR (continuous), *CTNNB1* mutation status and molecular classification, only PR levels remained independently associated with GLP-1R positivity (OR per 10% increase 1.15, 95% CI 1.02–1.30; $p = 0.019$). **Conclusions:** GLP-1R is frequently expressed in EC, particularly in PR positive tumors and within the NSMP molecular subtype, suggesting that the underlying pathway of carcinogenesis may influence GLP-1R expression. These findings may inform the design of future translational and clinical studies exploring GLP-1R-targeted strategies in endometrial carcinoma. Research Sponsor: None.

Examining the relationship between social support and inflammatory markers among patients with gynecologic cancer.

Oluwafemifola Oyediji, Lina Reyes-Fontalvo, Courtney Riedinger, Jill Maples, Emily Olatt, Larry Clinton Kilgore, Patricia N.E. Roberson, Laura A. Gilliam, Caroline E.R. Souleyrette, Kristopher J. Kimball; North Knoxville Medical Center, Powell, TN; University of Tennessee Health Science Center College of Medicine Knoxville, Knoxville, TN; The University of Tennessee Medical Center, Knoxville, TN; University of Tennessee Medical Center, Knoxville, TN; University of Tennessee College of Nursing, Knoxville, TN; Halloran Consulting Group, Inc., Boston, MA

Background: Social support has been associated with improved health outcomes. Little research on the association between social support and inflammatory markers has been done among patients with gynecological cancer. The aim of this study is to examine whether there is an association between social support and inflammatory markers in patients currently receiving treatment for gynecologic cancer. **Methods:** These data were collected from a prospective cohort study designed to investigate the potential associations between cardiometabolic health and cancer treatment among women with gynecological cancer. As a secondary outcome, social support was assessed using the social provision scale (SPS), with higher scores indicating greater perceived social support. Fasting venous blood was collected for inflammatory marker analysis (Interleukin-6: IL-6, Tumor Necrosis Factor- α : TNF- α , C-reactive protein: CRP). Descriptive statistics included means for continuous variables and frequencies for categorical variables. Correlation analyses were used to assess the degree of relationship between variables. Partial correlations were used to adjust for potential confounders. Study protocol was approved by IRB at the University of Tennessee Graduate School of Medicine. **Results:** A total of 43 women with gynecological cancer (primary site: uterus = 16, ovary = 24, cervix = 1, vulva/vagina = 2) completed study measures. The mean age was 63.5 years (SD=10.5). Regarding participants characteristics, 91% identified as White, 99% identified as non-Hispanic, 35% reported being high school graduate or GED, 45% were unemployed, 66% were married, 51.2% had newly diagnosed cancer, 49% had metastatic disease, 74% received chemotherapy only, 14% immunotherapy, 12% combination of both immunotherapy and chemotherapy. SPS scores were negatively correlated with IL-6 ($\rho = -0.362$, $p = 0.038$), indicating that higher perceived social support was associated with lower IL-6 levels. SPS scores were not significantly correlated with CRP ($\rho = -0.09$, $p = 0.62$) and TNF- α ($\rho = -0.295$, $p = 0.096$). After adjusting for BMI, SPS score showed significant associations with IL-6 ($\rho = -0.406$, $p = 0.021$) and TNF- α ($\rho = -0.360$, $p = 0.043$), but its relationship with CRP ($\rho = -0.029$, $p = 0.874$) remained non-significant. **Conclusions:** The results of this study suggest a negative association between social support and inflammation among patients with gynecologic cancer. Future research may consider exploring the pathways to explain this relationship and identify possible interventions focused on social support to decrease inflammatory processes among patients with gynecologic cancer. Research Sponsor: University of Tennessee Medical Center Cancer Institute.

A phase 2 study evaluating SSGJ-707 (PF-08634404), a PD-1/VEGF bispecific antibody, + chemotherapy (chemo) in patients (pts) with first-line (1L) advanced/recurrent endometrial cancer (EC).

Qi Zhou, Xingtao Long, Dong Wang, Li Li, Ke Wang, Yumei Wu, Guixiang Weng, Tao Wu, Yang Sun, Qingshui Li, Ying Yang, Guiling Li, Weifeng Song, Matko Kalac, Jing Lou; Cancer Hospital Affiliated to Chongqing University, Chongqing, China; Cancer Hospital Affiliated To Guangxi Medical University, Nanning, China; Tianjin Medical University Cancer Institute & Hospital, Tianjin, China; The Capital Medical University Affiliated Beijing Obstetrics and Gynecology Hospital, Beijing, China; Linyi People's Hospital, Linyi, China; The First People's Hospital of Changde, Changde, China; Fujian Cancer Hospital, Fuzhou, China; Shandong First Medical University Affiliated Tumor Hospital, Jinan, China; Yantai Yuhuangding Hospital, Yantai, China; Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China; Shenyang Sunshine Pharmaceuticals Co. Ltd., Shenyang, China; Pfizer Inc., Los Angeles, CA

Background: SSGJ-707 is a fully human immunoglobulin G4 bispecific antibody targeting programmed death 1 (PD-1) and vascular endothelial growth factor (VEGF). SSGJ-707 has demonstrated promising efficacy and manageable safety alone and in combination with chemo in phase 2 studies in solid tumors. We report results from the phase 2 SSGJ-707-ST-II-02 study (NCT06522828) of 1L SSGJ-707 + chemo in advanced/recurrent EC. **Methods:** Pts with newly diagnosed stage III/IV or recurrent EC with low potential for cure by radiation therapy (tx) or surgery and systemic tx-naïve were enrolled. Pts received SSGJ-707 5 mg/kg or 10 mg/kg Q3W + chemo (carboplatin AUC 5 + paclitaxel 175 mg/m²) Q3W for 6 cycles, followed by SSGJ-707 maintenance tx until loss of clinical benefit or intolerable toxicity for up to 2 years. Primary endpoints were safety and ORR (RECIST 1.1). Secondary endpoints include duration of response (DOR), PFS, OS, PK, and biomarkers. **Results:** At data cutoff (Nov 28, 2025), 32 pts with EC (26 mismatch repair proficient [pMMR], 6 MMR deficient [dMMR]) received 5 mg/kg (n=16) or 10 mg/kg (n=16) SSGJ-707 + chemo. Median SSGJ-707 tx duration was 5.6 mo (range, 0.2-13.6); 8 pts (25.0%) discontinued tx. In the evaluable population, confirmed ORR was 85.7% (12/14 pts) for the 5 mg/kg dose and 80.0% (12/15) for the 10 mg/kg dose. Results for pMMR and dMMR groups are in the Table. Median PFS, OS, and DOR were not reached for either dose. Any-grade tx-related adverse events (TRAEs) were reported in 30/32 pts (93.8%) and grade ≥3 TRAEs in 22/32 pts (68.8%). The most common TRAEs (≥40%) included neutrophil count decreased (59.4%), white blood cell count decreased (59.4%), anemia (56.3%), and platelet count decreased (56.3%). No TRAEs led to death. TRAEs led to discontinuation of SSGJ-707 in 2 pts (6.3%). Immune-related AEs occurred in 6 pts (18.8%): hypothyroidism (n=4), hyperthyroidism (n=3), and rash (n=2). VEGF-related AEs occurred in 13 pts (40.6%): blood pressure elevation (n=6), proteinuria (n=6), hemorrhage (urinary occult blood positive; n=2), perforation and fistula (n=2), and venous thrombosis (n=1). **Conclusions:** SSGJ-707 + chemo demonstrated promising efficacy with a manageable safety profile in pts with tx-naïve advanced/recurrent EC, supporting further investigation of SSGJ-707 in these pts. Clinical trial information: NCT06522828. Research Sponsor: This study was originally sponsored by 3SBio; SSGJ-707 was licensed to Pfizer in July 2025. Medical writing support was provided by Akshaya Srinivasan, PhD, and Eleanor Porteous, MSc, of Nucleus Global, an Inizio Company, and was funded by Pfizer.

	5 mg/kg Q3W (n=14) pMMR (n=12)	dMMR (n=2)	10 mg/kg Q3W (n=15) pMMR (n=11)	dMMR (n=4)
Confirmed ORR, n (%) [95% CI]	10 (83.3) [51.6, 97.9]	2 (100) [15.8, 100.0]	9 (81.8) [48.2, 97.7]	3 (75.0) [19.4, 99.4]
Complete response	0	0	1 (9.1)	0
Partial response	10 (83.3)	2 (100)	8 (72.7)	3 (75.0)
Stable disease	2 (16.7)	0	2 (18.2)	1 (25.0)
Progressive disease	0	0	0	0
CR/PR pending	—	—	1 ^a	1
Unconfirmed ORR, n (%) [95% CI]	10 (83.3) [51.6, 97.9]	2 (100) [15.8, 100.0]	10 (90.9) [58.7, 99.8]	4 (100) [39.8, 100.0]

^aOne additional pt in the 10 mg/kg group confirmed in Dec.

TroFuse-036/GOG-3123/ENGOT-cx22: A 2-part, phase 3, randomized study of sacituzumab tirumotecan (sac-TMT) + pembrolizumab (pembro) ± bevacizumab (bev) vs standard of care (SoC) as first-line maintenance therapy for PD-L1-positive cervical cancer.

Brian M. Slomovitz, Bradley J. Monk, Krishnansu Sujata Tewari, Noelle Cloven, Alberto Farolfi, Annamaria Ferrero, David Cibula, Coraline Dubot, Lisa Barraclough, Lorena Fariñas-Madrid, Ignacio Casarini, Andreia Cristina de Melo, Fernando Contreras Mejia, Sudeep Gupta, Jung-Yun Lee, Kosei Hasegawa, Zhou Yu, Cumhur Tekin, Ved Desai, Toon Van Gorp; GOG Foundation and Mount Sinai Medical Center, Miami Beach, FL; GOG Foundation and Florida Cancer Specialists and Research Institute, West Palm Beach, FL; GOG Foundation and University of California Irvine Medical Center, Irvine, CA; Texas Oncology, Fort Worth, TX; Istituto Romagnolo per lo Studio dei Tumori Dino Amadori, IRCCS, Meldola, Italy; Department of Surgical Sciences University of Torino and Academic Division Gynaecology and Obstetrics Mauriziano Hospital, Torino, TO, Italy; CEEGOG and General University Hospital in Prague, First Faculty of Medicine, Charles University, Prague, Czech Republic; Centre François Baclesse and GINECO, Caen, France; Christie NHS Foundation Trust, Clinical Oncology, Manchester, United Kingdom; Vall d'Hebron Institute of Oncology (VHIO), Hospital Universitari Vall d'Hebron, Barcelona, Spain; Hospital Bernardo Houssay and Faculty of Medicine, Universidad Nacional de Mar del Plata, Mar Del Plata, Buenos Aires, Argentina; Division of Clinical Research and Technological Development, Brazilian National Cancer Institute (INCA), Rio De Janeiro, Brazil; National Cancer Institute of Colombia, Bogotá, Colombia; Tata Memorial Centre and Homi Bhabha National Institute, Mumbai, India; Yonsei Cancer Center and Severance Hospital, Yonsei University College of Medicine, Seoul, South Korea; Saitama Medical University International Medical Center, Hidaka, Saitama, Japan; Merck & Co., Inc., Rahway, NJ; Merck & Co, Inc., Rahway, NJ; BGOG and University Hospital Leuven, Leuven Cancer Institute, Leuven, Belgium

Background: First-line pembro + platinum-doublet chemo ± bev is the preferred SoC for PD-L1-positive stage IVB, persistent, or recurrent cervical cancer. However, ~50% of patients experience progressive disease (PD) within 1 y, highlighting the need for first-line maintenance therapies that can extend clinical benefit. Sac-TMT is a TROP2-directed antibody-drug conjugate with a unique, bifunctional linker that maximizes payload delivery to tumor cells. In a prior phase 2 basket study, sac-TMT + pembro demonstrated promising antitumor activity (ORR, 58% [22/38]) with a manageable safety profile in participants (pts) with recurrent or metastatic cervical cancer that progressed on or after platinum-doublet chemo. TroFuse-036/GOG-3123/ENGOT-cx22 (NCT07216703) is evaluating first-line maintenance therapy with sac-TMT + pembro ± bev vs SoC in pts with cervical cancer. **Methods:** This 2-part, phase 3, randomized, open-label study is enrolling pts aged ≥18 y with persistent, recurrent, or newly diagnosed stage IVB squamous cell carcinoma, adenosquamous carcinoma, or adenocarcinoma of the cervix that is not amenable to curative treatment (surgery/radiation), ECOG PS of 0 or 1, and PD-L1 combined positive score ≥1. In part 1 (safety run-in), ~20 eligible pts who complete 6 cycles of induction therapy with pembro 200 mg Q3W + paclitaxel 175 mg/m² Q3W + cisplatin 50 mg/m² (or carboplatin AUC 5 mg/mL/min Q3W) + bev 15 mg/kg Q3W without PD per investigator will receive maintenance therapy with sac-TMT 4 mg/kg Q2W + pembro 400 mg Q6W for ≤14 6-wk cycles + bev 15 mg/kg Q3W until treatment discontinuation criteria are met. Enrollment in part 2 will start after enrollment in part 1 is complete. In part 2, ~1003 eligible pts will receive 6 cycles of induction therapy (same doses as in part 1) with pembro + platinum-doublet chemo ± bev at investigator discretion. For randomization to maintenance therapy, pts must complete induction therapy and have CR, PR, or SD per RECIST v1.1 by investigator as assessed by an evaluable tumor scan at week 18; evaluable TROP2 expression; and resolution of any AEs to grade ≤1. After part 1 safety data review is complete, ~802 eligible pts in part 2 maintenance part will be randomized 1:1 to receive sac-TMT 4 mg/kg Q2W + pembro 400 mg Q6W for ≤14 6-wk cycles ± bev 15 mg/kg Q3W or SoC with pembro 400 mg Q6W for ≤14 6-wk cycles ± bev 15 mg/kg Q3W; bev use is at investigator discretion and continues until treatment discontinuation criteria are met. The primary endpoint is safety in part 1 and PFS per RECIST v1.1 by blinded independent central review and OS with maintenance therapy in part 2. Secondary endpoints associated with maintenance therapy in part 2 are PFS2 per investigator, safety, and patient-reported outcomes. Enrollment began in Dec 2025. Clinical trial information: NCT07216703. Research Sponsor: Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA.

Iparomlimab and tuvonralimab combined with paclitaxel and cisplatin as neoadjuvant therapy for cervical cancer: A phase II umbrella trial.

Junjun Qiu Sr., Xinqu Qu, Xingyu Chang, Xiaoyan Tang, Keqin Hua; Obstetrics and Gynecology Hospital of Fudan University, Shanghai, China

Background: There is an urgent need to improve neoadjuvant therapy for locally advanced cervical cancer (LACC) and fertility-preserving neoadjuvant therapy for early-stage cervical cancer patients. However, there is no study evaluating the efficacy and safety of PD-1 and CTLA-4 dual blockade-based therapy for above clinical scenarios. The present study aims to assess QL1706 combined with paclitaxel and cisplatin as neoadjuvant therapy for LACC and early-stage cervical cancer patients for fertility-preservation respectively. **Methods:** Trial design: For Arm 1 (LACC), patients aged 18-75 years, with FIGO 2018 stages IB3, IIA2, IIB, or IIICr (lesion ≥ 4 cm, confirmed by MRI), histologically confirmed as cervical squamous cell carcinoma, cervical adenocarcinoma, or cervical adenosquamous carcinoma will be included. For Arm 2 (fertility preservation), patients aged 18-45 years old, who have a strong desire to preserve fertility, with FIGO 2018 stages IB2, IB3 (lesion ≤ 6 cm), IIA1, or IIA2 (lesion ≤ 6 cm) and histologically confirmed as cervical squamous cell carcinoma, cervical adenocarcinoma, or cervical adenosquamous carcinoma, will be included. All participants will be given 3 cycles of neoadjuvant treatment with QL1706 (5 mg/kg), paclitaxel (135-175 mg/m²) and cisplatin (75-80 mg/m²) per 21 days. Patients in Arm 1 (LACC) who achieve CR/PR will undergo radical hysterectomy plus lymphadenectomy after 3 cycles of neoadjuvant therapy whereas patients in Arm 2 (fertility preservation) who achieve CR/PR will undergo fertility-preserving surgery. For IB1/IB2 patients, conization or simple trachelectomy plus lymphadenectomy will be performed. For IIA1/IIA2 patients, radical trachelectomy plus lymphadenectomy will be performed. Patients achieve PD/SD will be given standard treatment according to the current NCCN guideline. The primary endpoints consist of objective response rate (ORR), pathological complete response (pCR) and changes in tumor-related biomarkers (ctDNA, etc). Secondary endpoints include 2-year overall survival (OS), 2-year disease-free survival (DFS) and adverse events. Other endpoints are 2-year pregnancy rate and infant survival rate for Arm 2. Sample size is 20 for Arm 1 and 15 for Arm 2. Clinical trial identification: NCT06878222. Clinical trial information: NCT06878222. Research Sponsor: Qilu Pharmaceutical Co., Ltd.

A phase II trial of a FAK inhibitor combined with albumin-bound paclitaxel and an anti-PD-1/CTLA-4 bispecific antibody for metastatic, recurrent, or persistent gastric-type endocervical adenocarcinoma (GIFT Study).

Yingchao Zhao, Ting Peng, Peng Wu; Hubei Key Laboratory of Precision Radiation Oncology, Wuhan, Hubei, China; National Clinical Research Center for Gynecology and Obstetrics, Cancer Biology Research Center (Key Laboratory of the Ministry of Education), Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, Hubei, China

Background: Gastric-type endocervical adenocarcinoma (GAC) is a rare, HPV-independent subtype of cervical cancer with an aggressive clinical course and an exceptionally poor prognosis. Current clinical guidelines offer largely non-specific treatment recommendations, and conventional chemotherapy-based regimens, even when combined with immunotherapy, frequently demonstrate limited efficacy and early resistance in patients with advanced, recurrent, or metastatic disease. Preclinical studies demonstrate that FAK inhibition can remodel the tumor microenvironment and enhance sensitivity to both cytotoxic chemotherapy and immunotherapy. This study aims to evaluate the efficacy and safety of the FAK inhibitor IN10018 in combination with immunotherapy and chemotherapy in patients with GAC.

Methods: The GIFT study is a multicenter, open-label, single-arm, prospective phase II trial designed to evaluate the combination of the FAK inhibitor IN10018 with nab-paclitaxel and cadonilimab (a PD-1/CTLA-4 bispecific antibody) in patients with metastatic, recurrent, or persistent gastric-type endocervical adenocarcinoma. A total of 25 eligible patients will receive oral IN10018 (100 mg once daily) in combination with intravenous nab-paclitaxel (260 mg/m²) and cadonilimab (10 mg/kg) on day 1 of each 21-day cycle. Tumor response will be assessed every 6 weeks by imaging according to RECIST v1.1. Patients will receive up to six cycles of combination chemotherapy, followed by maintenance therapy with IN10018 and cadonilimab until disease progression or unacceptable toxicity. The primary endpoint is objective response rate. Secondary endpoints include progression-free survival, disease control rate, and safety. An additional exploratory objective is to longitudinally evaluate alterations in peripheral circulating cell-free DNA and the tumor microenvironment and to examine their association with therapeutic response. The study is currently active and enrolling patients. As of the data cutoff, 14 of the planned 25 patients have been enrolled. The trial is registered at ClinicalTrials.gov (NCT06654011). Clinical trial information: NCT06654011. Research Sponsor: Noncommunicable Chronic Diseases-National Science and Technology Major Project; 2025ZD0544103; National Natural Science Foundation of China; 82372929.

Neoadjuvant chemoimmunotherapy before chemoradiation vs chemoradiation alone for stage IIB-IIIC1 carcinoma of the cervix: A phase II open-label randomized controlled trial (NeoCHIMERA).

Praveen Kumar Marimuthu, Neenu Oliver John, Vinitha Tony, Aisha Lakhani, Deepa Susan Philip, Anjana Joel, Ajoy Oommen John, Josh Thomas Georgy, Sharief Sidhique, Rohan Samuel Thomas, Anitha Thomas, Vinotha Thomas, Dhanya Susan Thomas, Anuradha Chandramohan, Sheenu Sara Varghese, Sherin Daniel, Kovilapu Harikrishna, Reka Karuppusami, Thomas Samuel Ram, Ashish Singh; Christian Medical College, Vellore, Tamil Nadu, India; Christian Medical College, Vellore, India

Background: Locally advanced cervical cancer (FIGO 2018 stages IIB–IIIC1) remains a major cause of cancer-related mortality in low- and middle-income countries. Concurrent chemo-radiation (CCRT) with brachytherapy is the current standard of care; however, rates of persistent disease and distant failure remain substantial, particularly in patients with bulky tumors or nodal involvement. Although advances in radiotherapy have improved outcomes, survival in resource-constrained settings continues to lag behind that in high-income countries. Recent randomised trials have demonstrated improved outcomes with two distinct strategies: delivery of dose-dense induction chemotherapy followed by timely initiation of chemoradiation, and the addition of immunotherapy with pembrolizumab to concurrent chemoradiation followed by maintenance therapy for up to one year. Despite these advances, concerns about radiotherapy dose and technique in induction chemotherapy trials, and the feasibility of prolonged maintenance immunotherapy in resource-limited settings, have limited widespread adoption. The optimal dose, timing, and duration of immunotherapy in locally advanced cervical cancer remain undefined. This study was designed to evaluate whether short-course neoadjuvant chemo-immunotherapy administered prior to standard CCRT can improve early tumor response with an acceptable safety profile while preserving treatment feasibility across diverse healthcare settings. **Methods:** The NeoCHIMERA trial is a multicenter, open-label, randomized phase II study designed to evaluate this hypothesis. Eligible patients include those with biopsy-proven FIGO 2018 stage IIB–IIIC1 cervical carcinoma (squamous, adeno, or adenosquamous histology) who are treatment-naïve and suitable for CCRT. Participants will be randomized 1:1 to the experimental or control arm, stratified based on stage and histology. The experimental arm will receive six weeks of neoadjuvant carboplatin (AUC 2) and paclitaxel (60 mg/m²) weekly, combined with low-dose nivolumab (40 mg IV every three weeks for two cycles), followed by standard CCRT (cisplatin 40 mg/m² weekly with external beam radiation and brachytherapy). The control arm will receive CCRT alone. The primary endpoint is complete clinical response at 3 months after completion of chemoradiation. Secondary endpoints include safety, treatment completion rates, event-free survival, quality of life, and cost-effectiveness from a societal perspective. A total of 154 patients (77 per arm) will be accrued. One interim safety analysis is planned after 40 patients with predefined stopping rules for excess toxicity. Thirty-three of the planned 154 participants have been recruited. This study is registered with the Clinical Trials Registry of India (CTRI/2025/04/085540). Clinical trial information: CTRI/2025/04/085540. Research Sponsor: Christian Medical College, Vellore.

NRG-GY037: A phase III randomized trial of induction chemotherapy and pembrolizumab followed by chemoradiation and pembrolizumab maintenance versus standard chemoradiation and pembrolizumab maintenance in high-risk locally advanced cervical cancer.

Jyoti Mayadev, Wei Deng, Heather A. Lankes, Hayeon Kim, Jayanthi Sivasothy Lea, Ying Xiao, Huaizhi Geng, Tashanna K. N. Myers, Allison Elizabeth Garda, Diandra Norelle Ayala-Peacock, Martin Ma, Ursula A. Matulonis, Theresa Kuhn, Erica Huelsmann, Robert S. Mannel, Thomas J. Herzog, Carol Aghajanian, Charles A. Leath III, Dmitriy Zamarin; University of California, San Diego Medical Center, La Jolla, CA; NRG Oncology, Clinical Trial Development Division, Biostatistics & Bioinformatics, Roswell Park Comprehensive Cancer Center, Buffalo, NY; The GOG Foundation, Inc., Edgewater, MD; Magee-Womens Hospital and UPMC Hillman Cancer Center, Pittsburgh, PA; UT Southwestern Medical Center, Dallas, TX; Department of Radiation Oncology, University of Pennsylvania, Philadelphia, PA; University of Pennsylvania, Department of Radiation Oncology, Philadelphia, PA; Baystate Medical Center, Springfield, MA; Mayo Clinic Rochester, Rochester, MN; Duke Cancer Institute, Raleigh, NC; Department of Radiation Oncology, University of Washington, Fred Hutchinson Cancer Center, Seattle, WA; Dana-Farber Cancer Institute, Boston, MA; Lehigh Valley Hospital, Allentown, PA; Fox Chase Cancer Center, Philadelphia, PA; University of Oklahoma Health Sciences Center, Oklahoma City, OK; GOG Foundation and University of Cincinnati Cancer Center, Cincinnati, OH; Gynecologic Medical Oncology, Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, NY; University of Alabama at Birmingham, Birmingham, AL; Icahn School of Medicine at Mount Sinai, New York, NY

Background: Concurrent chemoradiation therapy (CCRT) is the standard of care for locally advanced cervical cancer (LACC); however, outcomes remain suboptimal in patients with high-risk disease. Recent studies suggest that integration of immunotherapy (IO) with definitive chemoradiation, or induction chemotherapy prior to CCRT improves outcomes. Whether treatment intensification with induction systemic therapy and IO prior to CCRT and IO further improves disease control remains unknown. Induction chemotherapy may reduce tumor burden, eradicate micrometastatic disease, and improve tumor immunogenicity prior to definitive CCRT. Preclinical and clinical data support synergy between systemic therapy or radiotherapy and immune checkpoint blockade, providing the rationale for evaluating an induction strategy incorporating chemotherapy and immunotherapy before standard CCRT with immunotherapy, followed by maintenance immunotherapy. Optional tumor tissue and blood samples will be collected for exploratory correlative analyses, including immune and molecular biomarkers associated with response, resistance, and patterns of failure. **Methods:** NRG-GY037 is a prospective, multi-institutional phase III randomized trial conducted through NRG Oncology. A total of 336 patients will be enrolled (168 per arm). Patients will be stratified by FIGO stage (III vs. IVA) and presence or absence of para-aortic lymph nodes (N2). The primary endpoint is progression free survival (PFS). The study has 90% power to detect PFS hazard ratio of 0.65 in the experimental arm. Treatment: Patients with previously untreated, high-risk LACC are randomized to receive either induction chemotherapy with pembrolizumab for 6 weeks followed by CCRT with pembrolizumab and pembrolizumab maintenance, or standard CCRT with pembrolizumab followed by pembrolizumab maintenance. Major Eligibility Criteria: Eligible patients have histologically confirmed cervical carcinoma (squamous, adenocarcinoma, or adenosquamous), TNM T3 and T4 disease, No-2, ECOG performance status 0-1, and no prior definitive therapy for cervical cancer. Current Enrollment Status: The trial is actively accruing patients. No efficacy or safety data are available at the time of submission. Clinical Trial Registration: ClinicalTrials.gov identifier: NCT07061977. Clinical trial information: NCT07061977. Research Sponsor: National Cancer Institute.

A single-arm, phase 2 study of neoadjuvant mirvetuximab soravtansine and carboplatin for FR α -expressing advanced-stage serous epithelial ovarian, fallopian tube, or primary peritoneal cancer (M25-231; NCT06890338; GOG-3115).

Rebecca Arend, Christine M. Lee, Charles K. Anderson, Krista Pfaendler, Peter Lim, Sonali Pandya, Mingwei Fei, Erin Saks; University of Alabama at Birmingham, O'Neal Comprehensive Cancer Center, Birmingham, AL; Texas Oncology - The Woodlands, The Woodlands, TX; Willamette Valley Cancer Institute and Research Center, Eugene, OR; West Virginia University, WVU Cancer Institute Mary Babb Randolph Cancer Center, Morgantown, WV; Center of Hope, Reno, NV; AbbVie, North Chicago, IL; Carilion Clinic, Roanoke, VA

Background: Folate receptor alpha (FR α) has limited expression on normal tissues but is highly expressed in most high-grade serous epithelial ovarian cancers (EOC), making it an attractive therapeutic target. Mirvetuximab soravtansine (MIRV), an antibody-drug conjugate targeting FR α , has demonstrated efficacy and manageable safety in recurrent, FR α -expressing EOC when used as monotherapy. Additionally, a phase 1b/2 study (IMGN853-0402) of MIRV + carboplatin showed promising clinical activity in patients with platinum-sensitive ovarian cancer who had tumor recurrence after platinum-based chemotherapy. The safety and efficacy of neoadjuvant MIRV + carboplatin in newly diagnosed, advanced-stage FR α -expressing high-grade serous ovarian cancer (HGSOC) remains unknown. **Methods:** This single-arm phase 2 trial will evaluate the safety and efficacy of MIRV + carboplatin in newly diagnosed patients with advanced-stage (Stage III/IV), FR α -expressing ($\geq 75\%$ tumor cells with $\geq 2+$ membrane intensity per the VENTANA FOLR1 (FOLR1-2.1) Rx Dx Assay [Roche Diagnostics]) HGSOC. Approximately 140 patients (aged ≥ 18 years) will be enrolled; 5 patients were enrolled as of January 23, 2026. Patients will receive ≤ 6 cycles of MIRV (6 mg/kg adjusted ideal body weight) and carboplatin (AUC 5) intravenously every three weeks before interval debulking surgery (IDS), with a total of ≤ 9 cycles pre- and post-IDS. IDS suitability will be evaluated radiologically, and all eligible patients, including those with progressive disease (PD), will undergo IDS after Cycle 3 Day 1. IDS-ineligible patients may receive ≤ 3 additional cycles and undergo repeat imaging to assess IDS suitability. Patients with complete response (CR), partial response (PR), or stable disease will resume MIRV + carboplatin 3–6 weeks post-IDS following radiologic assessment. At the treating physician's discretion, bevacizumab may be added post-IDS and standard-of-care maintenance therapy may begin ≥ 21 days after MIRV + carboplatin $\pm$ bevacizumab completion. Imaging will occur every 9 weeks after IDS (for those who undergo IDS) or last radiologic tumor assessment (for those who do not) until 1 year from the first dose of study treatment and then every 12 weeks until PD, death, or withdrawal of consent. The primary endpoint is objective response (OR), defined as best overall response of radiographic CR or PR assessed by Independent Central Review (ICR) per Response Evaluation Criteria in Solid Tumors v1.1 prior to initiation of subsequent anticancer therapy (including IDS). Secondary endpoints include OR by investigator (INV), disease control by ICR and INV, IDS, extent of cytoreduction at the time of IDS, cancer antigen 125 response, progression-free survival by INV, and patient-reported outcomes (NFOSI-18). Clinical trial information: NCT06890338. Research Sponsor: AbbVie Inc.

NRG-GY036: A phase III trial of one vs. two years of maintenance olaparib, with or without bevacizumab, in patients with *BRCA1/2*-mutated or homologous recombination deficient (HRD+) ovarian cancer following response to first line platinum-based chemotherapy.

Ying L. Liu, Austin Miller, Kathleen N. Moore, Joyce F. Liu, Heather A. Lankes, Roisin Eilish O'Cearbhaill, Leslie Siriya Bradford, David Bender, Aliza L. Leiser, Marilyn Huang, Ursula A. Matulonis, Mitchell Ira Edelson, Haider Mahdi, Elizabeth M. Swisher, Paul Disilvestro, Elise C. Kohn, Carol Aghajanian; Memorial Sloan Kettering Cancer Center, New York, NY; Roswell Park Comprehensive Cancer Center, Buffalo, NY; Stephenson Cancer Center at the University of Oklahoma Medical Center, Oklahoma, OK; Dana-Farber Cancer Institute, Boston, MA; The GOG Foundation, Inc., Edgewater, MD; Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, NY; Maine Medical Partners MaineHealth, Scarborough, ME; University of Iowa Hospitals and Clinics, Iowa City, IA; Rutgers Cancer Institute of New Jersey, Rutgers Robert Wood Johnson Medical School, New Brunswick, NJ; UVA Health, Charlottesville, VA; Hanjani Institute for Gynecologic Oncology, Jefferson Abington Hospital, Willow Grove, PA; University of Pittsburgh Medical Center (UPMC), Pittsburgh, PA; University of Washington, Seattle, WA; Program in Women's Oncology, Department of Obstetrics and Gynecology, Women and Infants Hospital, Brown University, Providence, RI; National Cancer Institute, National Institutes of Health, Rockville, MD; Gynecologic Medical Oncology, Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, NY

Background: The profound progression-free survival (PFS) benefit shown in the SOLO-1 and PAOLA-1 randomized clinical trials set the standard of 2 years of PARP inhibitor (PARPi) maintenance with olaparib, with or without bevacizumab, in patients with *BRCA1/2*-mutated and homologous recombination deficient (HRD+) ovarian carcinoma after response to frontline platinum-based chemotherapy, and this was approved by the FDA in December 2018. However, newer studies have elucidated the long-term toxicity risk of prolonged PARPi use, specifically treatment-related myeloid neoplasms (TMN), along with detrimental effects on subsequent platinum-based chemotherapy and overall survival. Given this, we seek to test de-escalation of PARPi maintenance therapy, evaluating if 1 year is non-inferior to 2 years, using a pragmatic and streamlined study design. **Methods:** NRG GY036 is a phase III, randomized, non-inferiority study of 1 versus 2 years of olaparib maintenance, with or without bevacizumab, in those with *BRCA1/2*-associated and HRD+ ovarian cancer, after response to frontline platinum-based chemotherapy (NCT06580314). Key eligibility criteria include a deleterious *BRCA1/2* mutation, germline or somatic, or HRD+ tumor using any CLIA-certified test. Patients must have undergone cytoreductive surgery and had a clinical response after a minimum of 4 cycles of platinum-based chemotherapy. The primary endpoint is investigator assessed PFS using RECIST v1.1 criteria for 1 vs. 2 years in a modified intention to treat (mITT) population, where time at risk starts 360 days after randomization to account for the time where both arms receive the same treatment. Secondary endpoints include overall survival (OS), PFS2, PFS in the ITT and as-treated populations, and toxicity including rates of TMN. The statistical design is based on a hazard ratio non-inferiority margin of 1.36 (1-sided alpha 0.05, power 0.9). The null hypothesis will be rejected if $HR < 1.15$, giving 90% certainty that the true median PFS loss is not more than 10 months based on historical controls from SOLO1 and the HRD+ subgroup of PAOLA-1. We anticipate enrolling 880 patients to have at least 735 patients in the mITT population. This IND-exempt study pragmatically mimics real-world clinical practice by using commercially available drug, implementing broad eligibility criteria, allowing physician's choice bevacizumab, and incorporating individual physician and institution's standard practices. It also employs a streamlined approach with minimal data collection forms and abbreviated adverse event reporting. NRG GY036 was activated on 1/16/2025. The first patient enrolled on 3/12/2025. As of 1/16/2026, there are 676 participating sites and 152/880 (17%) patients enrolled. Clinical trial information: NCT06580314. Research Sponsor: NRG Oncology and NIH/NCI/CTEP.

A phase I, open-label, dose-finding, safety, tolerability, and exploratory trial of intraperitoneal THEO-260 in patients with high-grade serous or endometrioid ovarian cancer.

Helen D. Clark, Anne Knisely, Alexandra Villanueva, Kathryn Lito, Miriam Bazan-Peregrino, Harris Owen, Robert Nutbrown, Helen Bridger, Matilde Saggese, David Apelian, Margaret Duffy, Amir A. Jazaeri; The University of Texas MD Anderson Cancer Center, Houston, TX; Theolytics, Oxford, United Kingdom

Background: Ovarian cancers are immunologically cold at baseline and typically characterized by a rich stromal component with a high proportion of cancer-associated fibroblasts (CAF). These features limit efficacy of immunotherapy and virotherapy due to the immunosuppressive effects of abundant CAFs. THEO-260 is an oncolytic adenovirus that exhibits selective replication, lysis, and killing of cancer cells and CAFs. This unique mechanism-of-action positions THEO-260 as a potential efficacious treatment option for patients with platinum-resistant ovarian cancer. Intraperitoneal (IP) delivery may further enhance efficacy by enabling high locoregional dose with lower systemic exposure. **Methods:** This phase I, open-label, single-institution study (NCT07211659) evaluates IP THEO-260 in patients with platinum-resistant or refractory high grade serous (HGS) or endometrioid ovarian, peritoneal, or fallopian tube cancer. The primary objectives are to evaluate the safety and tolerability of THEO-260 when administered intraperitoneally and to establish the recommended phase 2 dose (RP2D) using a Bayesian Optimal Interval design with 4 dose levels in cohorts of 3. Patients receive up to 6 doses of THEO-260 over 15 days: 2 desensitization doses followed by 4 target-dose administrations. Secondary objectives include PK, viral shedding, systemic cytokine release, and preliminary efficacy assessment. Response assessments will be conducted every 8 weeks starting on day 29 through week 52 and thereafter every 12 weeks until progression, death, or end of trial. Eligibility includes histologically confirmed, platinum-resistant or refractory HGS, endometrioid cancer of the ovary, peritoneum, or fallopian tube, measurable peritoneal disease per RECIST v1.1, ECOG 0-1, adequate organ function, life expectancy of ≥ 6 months, and feasibility of intraperitoneal catheter placement. Prior treatments must include optimal surgical debulking, bevacizumab, or PARP inhibitor therapy as indicated. Key exclusions include serosal disease > 3 cm, bowel obstruction history or symptoms, uncontrolled pleural or pericardial effusions, and prior pneumonitis or interstitial lung disease. Enrollment began in November 2025. Clinical trial information: NCT07211659. Research Sponsor: Theolytics.

TroFuse-022/ENGOT-ov84/GOG-3103 part 2: A phase 3 study of maintenance therapy with sacituzumab tirumotecan $\pm$ bevacizumab vs standard of care following second-line platinum-based doublet chemotherapy for platinum-sensitive recurrent ovarian cancer.

Antonio Gonzalez Martin, Thomas J. Herzog, Kosei Hasegawa, Coriolan Lebreton, David M. O'Malley, Stephanie Lheureux, Jung-Yun Lee, David Cibula, Mariana Ribeiro Monteiro, Joo Ern Ang, Valeria Cáceres, Charlotte Aaqvist Haslund, Toon Van Gorp, Jacob Korach, Karin Sayuri Yamada, Chenxiang Li, Matthew Horn, Katherine Cynthia Fuh; GEICO and Cancer Center Clínica Universidad de Navarra, Madrid, Spain; GOG Foundation and University of Cincinnati Cancer Center, Cincinnati, OH; Saitama Medical University International Medical Center, Hidaka, Saitama, Japan; GINECO and Institut Bergonié, Bordeaux, France; GOG Foundation and The Ohio State University and The James Comprehensive Cancer Center, Columbus, OH; Princess Margaret Cancer Centre, Toronto, ON, Canada; Yonsei Cancer Center and Severance Hospital, Yonsei University College of Medicine, Seoul, South Korea; CEEGOG and General University Hospital in Prague, First Faculty of Medicine, Charles University, Prague, Czech Republic; Instituto Américas, São Paulo, Brazil; GTG-UK and Addenbrooke's Hospital, Cambridge University Hospitals NHS Foundation Trust, Cambridge, United Kingdom; Instituto de Oncología Ángel H. Roffo, Buenos Aires, Argentina; NSGO-CTU and Aalborg University Hospital, Aalborg, Denmark; BGOG and University Hospital Leuven, Leuven Cancer Institute, Leuven, Belgium; ISGO and Sheba Medical Center, Tel Aviv University, Tel Aviv, Israel; Merck & Co., Inc., Rahway, NJ; Merck & Co., Inc., Rahway, NJ; GOG Foundation and University of California San Francisco, San Francisco, CA

Background: There is an unmet clinical need for novel therapies for patients with platinum-sensitive recurrent ovarian cancer (PSROC). Trophoblast cell-surface antigen 2 (TROP2) is highly expressed in multiple tumor types, including ovarian cancer. Sacituzumab tirumotecan (sac-TMT) is a TROP2-directed antibody-drug conjugate with a unique, bifunctional linker that maximizes delivery of a belotecan-derived topoisomerase 1 inhibitor payload to tumor cells. The current TroFuse-022/ENGOT-ov84/GOG-3103 study (NCT06824467) is evaluating maintenance therapy with sac-TMT $\pm$ bevacizumab (bev) vs standard of care (SoC) following second-line (2L) platinum-based doublet chemotherapy (chemo) in participants (pts) with PSROC. The study includes a safety run-in part (part 1) and a phase 3 part (part 2). We present the trial design for part 2 of this study. **Methods:** Part 2 is enrolling ~750 pts aged ≥ 18 y with histologically confirmed epithelial ovarian, fallopian tube, or primary peritoneal carcinoma with PSROC (radiographic evidence of PD >180 d after the last dose of first-line [1L] platinum-based doublet chemo $\pm$ bev); pts with BRCA mutation or homologous recombination deficiency-positive status with no evidence of disease (NED), CR, or PR after 1L chemo must have received a PARP inhibitor as 1L maintenance therapy. All pts must have received 6 cycles of 2L carboplatin-based doublet chemo $\pm$ bev and achieved NED, CR, PR, or SD per investigator assessment; pts with SD must have received bev in combination with 2L chemo and be eligible to continue treatment with bev. Other inclusion criteria are an ECOG PS of 0 or 1 and an available tumor sample for central testing of TROP2 and BRCA status. Candidates for curative-intent surgery or radiotherapy at enrollment are not eligible. Pts are randomized 1:1 to receive maintenance therapy with sac-TMT 4 mg/kg IV Q2W $\pm$ bev 15 mg/kg IV Q3W (arm 1) or SoC treatment with observation $\pm$ bev 15 mg/kg IV Q3W (arm 2). Use of bev is at the investigator's discretion and can only be given to eligible pts who received ≥ 2 doses of bev 15 mg/kg Q3W or equivalent dose (with no dose reductions) in combination with 2L chemo; pts with SD after 2L chemo must receive bev (pts with SD not receiving bev are ineligible). Treatment with sac-TMT (arm 1) and bev (if elected, arms 1 and 2) continues until PD, unacceptable toxicity, or other protocol-defined reason for discontinuation. Pts in arm 2 are not permitted to cross over to arm 1. The primary endpoint is PFS per RECIST version 1.1 as assessed by blinded independent central review. Secondary endpoints include OS, safety and tolerability, and patient-reported outcomes. PFS and OS will be assessed in pts with medium/high TROP2 expression tumors and all pts. The study is ongoing, and enrollment in part 2 is open. Clinical trial information: NCT06824467; EU CT, 2023-508015-23; UTN, U1111-1297-4489. Research Sponsor: Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA.

REJOICE-Ovarian01: Phase 3 part of a phase 2/3 study evaluating raludotatug deruxtecan (R-DXd) versus treatment of physician's choice in patients with platinum-resistant ovarian cancer.

Debra L. Richardson, Kathleen N. Moore, Kosei Hasegawa, Petar Jelinic, Connor Mailley, Sandra Re, Wanying Ma, Tsvetomir Mitov, Isabelle Laure Ray-Coquard; Stephenson Cancer Center, University of Oklahoma Health Campus, Oklahoma City, OK; Fred and Pamela Buffett Cancer Center at the University of Nebraska Medical Center, Omaha, NE; Saitama Medical University International Medical Center, Hidaka, Saitama, Japan; Merck & Co., Inc., Rahway, NJ; Daiichi Sankyo, Inc., Basking Ridge, NJ; Oncology Clinical Development, Daiichi Sankyo, Inc., Basking Ridge, NJ; Daiichi Sankyo UK Ltd., Uxbridge, United Kingdom; Centre Léon Bérard, Centre Régional de Lutte Contre Le Cancer de Lyon, Lyon, France

Background: Platinum-resistant ovarian cancer (PROC) is associated with poor outcomes. Standard-of-care single-agent non-platinum therapies, with or without bevacizumab, have demonstrated only modest activity in PROC, while targeted therapies remain limited to specific biomarker-defined patient populations. Cadherin-6 (CDH6), a mediator of cell-cell adhesion, is aberrantly expressed in up to 94% of epithelial ovarian cancer tumors. R-DXd is an antibody-drug conjugate comprising a humanized CDH6 antibody covalently linked to a topoisomerase I inhibitor payload (DXd) via a tumor-selective cleavable linker. REJOICE-Ovarian01 is a Phase 2/3 study of R-DXd monotherapy in patients with PROC. Among patients who had completed ≥ 18 weeks of follow-up or discontinued treatment in the Phase 2 dose-optimization part, the objective response rate (ORR) by blinded independent central review (BICR) was 44.4% (16/36) at 4.8 mg/kg, 50.0% (18/36) at 5.6 mg/kg, and 57.1% (20/35) at 6.4 mg/kg, including three complete responses overall. Clinically meaningful tumor responses were observed irrespective of tumor CDH6 expression, and the safety profile of R-DXd was manageable. R-DXd 5.6 mg/kg was identified as the optimal dose for further evaluation in the Phase 3 part of REJOICE-Ovarian01, which is described here. **Methods:** The Phase 3 part of REJOICE-Ovarian01 (NCT06161025) is a global, randomized, open-label study of R-DXd in patients with platinum-resistant, high-grade serous or high-grade endometrioid ovarian, primary peritoneal, or fallopian tube cancer. Patients must have received 1–4 prior lines of therapy (LOT), including bevacizumab (unless ineligible) and mirvetuximab soravtansine for folate receptor α -positive disease (unless not available locally). Patients are not selected based on tumor CDH6 expression. Approximately 600 patients will be randomized 1:1 to receive either R-DXd 5.6 mg/kg intravenously every 3 weeks until disease progression per Response Evaluation Criteria in Solid Tumours version 1.1 (RECIST 1.1), lost to follow-up, death, or other reason per protocol, or treatment of physician's choice (TPC; weekly paclitaxel, pegylated liposomal doxorubicin, or topotecan) per local guidelines. Randomization will be stratified by number of prior LOT, tumor CDH6 expression, and by TPC. The primary endpoint is progression-free survival (PFS) by BICR per RECIST 1.1. Key secondary endpoints include overall survival (OS) and quality of life. Stratified log-rank tests will be used to compare PFS and OS between treatment groups. Stratified Cox regression models will be fitted to estimate the hazard ratios for PFS and OS. Enrollment in Phase 3 began in December 2025. Clinical trial information: NCT06161025. Research Sponsor: Daiichi Sankyo, Inc.; Merck.

A phase 1/2 study of ubamatamab (REGN4018), a MUC16×CD3 bispecific antibody, administered alone or in combination with cemiplimab in a low-grade serous ovarian cancer cohort: Trial in progress.

Els Van Nieuwenhuysen, Judith Michels, Hee Seung Kim, Victor Moreno, Nicoletta Colombo, P. B. Ottevanger, Roisin Eilish O'Cearbhaill, Ruth Perets, An K.L. Reyners, Suk-Young Yoo, Bin Wang, Jurriaan Brouwer, Mihaela C. Cristea, Nicole Costigan, Mary Jane Peterman, Brigid Barnes, Israel Lowy, Elizabeth Miller, Gloria S. Huang, Thomas S. Uldrick; Leuven Kankerinstituut, Leuven, Belgium; Institute of Cancer Gustave Roussy, Villejuif, France; Seoul National University College of Medicine, Seoul, South Korea; Clinical Research Early Phase Trials Unit, START Madrid-Fundación Jiménez Díaz (FJD), Hospital FJD, Madrid, Spain; Department of Medicine and Surgery, Università degli Studi di Milano-Bicocca, Istituto Europeo di Oncologia, IRCCS, Milan, Italy; Radboud University Medical Center, Medical BioSciences, Nijmegen, Netherlands; Department of Medicine, Memorial Sloan Kettering Cancer Center and Weill Cornell Medical College, New York, NY; Division of Oncology, Rambam Medical Center, Haifa, Israel; University Medical Center Groningen, University of Groningen, Groningen, Netherlands; Regeneron Pharmaceuticals, Inc., Tarrytown, NY

Background: Low grade serous ovarian cancer (LGSOC) typically has a poor response to chemotherapy, presenting an unmet need for efficacious novel therapies that remain tolerable. Mucin 16 (MUC16) is a cell surface glycoprotein that is highly expressed in ovarian cancers, including LGSOC, and has been identified as a potential therapeutic target. Ubamatamab, a MUC16 × cluster of differentiation 3 bispecific antibody, bridges MUC16+ tumor cells and T cells through a major histocompatibility complex-independent mechanism, promoting cytotoxicity. In a first-in-human study (NCT03564340), ubamatamab demonstrated an acceptable safety profile and durable clinical activity in recurrent ovarian cancer, including LGSOC, which has particularly high MUC16 expression on tumor cells. Here, we describe an LGSOC-specific expansion cohort. **Methods:** In the LGSOC-specific cohort, patients who have received prior platinum-containing therapy (no maximum number of prior therapies) and whose disease has relapsed or progressed after the most recent line of therapy will receive ubamatamab 800 mg intravenously (IV) once every 3 weeks (Q3W). Prior to Q3W dosing of ubamatamab, patients will receive once-weekly step-up dosing to mitigate the risk of cytokine release syndrome, as well as sarilumab 350 mg IV prophylaxis on Day 1. Utilizing a Simon two-stage design, 20 patients will initially be enrolled in this cohort, expanding to 50 if there are ≥ 3 objective responses. The cohort may be further expanded to 100 patients if ≥ 14 objective responses (28%) are observed in the first 50 patients. The primary endpoint is objective response rate per Response Evaluation Criteria in Solid Tumors version 1.1. Secondary endpoints include safety, pharmacokinetics, patient-reported outcomes and further efficacy assessments. As of January 5, 2026, 6 patients with LGSOC have initiated ubamatamab treatment. Findings from this study will clarify the therapeutic potential of targeting MUC16 in LGSOC. Clinical trial information: NCT03564340. Research Sponsor: Regeneron Pharmaceuticals, Inc.

A phase 1/2 study of REGN5668, a MUC16×CD28 costimulatory bispecific antibody, in combination with other targeted therapies, in patients with recurrent ovarian or endometrial cancer: Trial in progress update.

Roisin Eilish O'Cearbhaill, John W. Moroney, Lainie P. Martin, Jill Tseng, Els Van Nieuwenhuysen, Sara Boubherhan, Ira Seth Winer, John L. Hays, Kalyan Banda, Dario R. Roque, Victor Moreno, Mihae Song, Maria-Pilar Barretina-Ginesta, Luis Manso, Suk-Young Yoo, Tahmineh Tabrizian, Mary Jane Peterman, Thomas S. Uldrick, Gloria S. Huang, Elizabeth Miller; Department of Medicine, Memorial Sloan Kettering Cancer Center and Weill Cornell Medical College, New York, NY; Department of Obstetrics and Gynecology, The University of Chicago, Chicago, IL; Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA; Department of Gynecologic Oncology, UC Irvine Medical Center, Orange, CA; Leuven Kankerinstituut, Leuven, Belgium; Division of Hematology/Oncology, Massachusetts General Hospital, Boston, MA; Division of Gynecologic Oncology, Department of Oncology, Wayne State University and Karmanos Cancer Center, Detroit, MI; Department of Obstetrics and Gynecology, Division of Gynecologic Oncology, The Ohio State University, Columbus, OH; Clinical Research Division, Fred Hutchinson Cancer Center, Seattle, WA; Division of Gynecologic Oncology, Department of Obstetrics and Gynecology, Feinberg School of Medicine, Northwestern University, Chicago, IL; START-Madrid-FJD Early Phase Clinical Trials Unit, Hospital Universitario Fundación Jiménez Díaz, Madrid, Spain; Division of Gynecologic Oncology, Duarte Cancer Center, City of Hope National Medical Center, Duarte, CA; Grupo Español de Investigación en Cáncer de Ovario (GEICO) and Medical Oncology Department, Institut Català d'Oncologia (ICO), Girona, Spain; Medical Oncology Division, Hospital Universitario 12 de Octubre, Madrid, Spain; Regeneron Pharmaceuticals, Inc., Tarrytown, NY

Background: REGN5668 and ubamatamab are immunoglobulin G4-based bispecific antibodies that bridge mucin 16 (MUC16)+ tumor cells to T-cell-expressed cluster of differentiation (CD) 28 and CD3, respectively, to stimulate T-cell cytotoxicity. Cemiplimab (anti-programmed cell death-1 [PD-1]) and fianlimab (anti-lymphocyte activation gene 3 [LAG-3]) are monoclonal antibodies that target inhibitory T-cell immune checkpoints. This first-in-human, multicenter, Phase 1/2 trial (NCT04590326) will assess safety, tolerability, pharmacokinetics (PK), and antitumor activity of REGN5668 + cemiplimab ± fianlimab (Module 1) or ubamatamab (Module 2) in patients with platinum-resistant recurrent ovarian cancer (OC) or endometrial cancer (EC). In Module 1, REGN5668 dose escalation is complete (n=58), demonstrating early clinical activity and only 1 dose-limiting toxicity, a treatment delay of >7 days due to Grade 1 dry eye. Here we present details of additional dose escalation and expansion modules currently enrolling patients. **Methods:** Module 1 dose expansion will evaluate REGN5668 + cemiplimab ± fianlimab in OC and EC cohorts. In the OC cohort, patients will receive REGN5668 + cemiplimab + fianlimab, with an initial 12-patient safety lead-in. In the EC cohort, patients will receive REGN5668 + cemiplimab; an additional EC cohort may be added to evaluate REGN5668 + cemiplimab + fianlimab. Each cohort will follow a Simon two-stage design. In stage 1, 20 patients will be enrolled; if there are ≥3 objective responses, stage 2 will proceed with enrollment of ≤50 patients. In Module 2, dose escalation will evaluate patients with OC receiving escalating doses of REGN5668 + ubamatamab using a Bayesian optimal interval design. Patients may also receive sarilumab to mitigate the risk of cytokine release syndrome. Key OC cohort eligibility criteria include histologically confirmed diagnosis of advanced epithelial OC (except carcinosarcoma), ≥1 prior line of platinum-based systemic therapy, and disease relapse or progression during most recent therapy. Key EC cohort eligibility criteria include histologically confirmed diagnosis of EC with disease recurrence or progression after anti-PD-1 therapy and platinum-based chemotherapy, ≤4 prior lines of systemic therapy, ≥30 days since anti-PD-1 therapy administration, and ≥25% of tumor cells that are MUC16+. Primary endpoints are safety and PK in dose escalation, and objective response rate (ORR) in dose expansion. Secondary endpoints include ORR (Module 2 dose escalation), safety and PK (Module 1 dose expansion), further efficacy outcomes, and immunogenicity (all cohorts). Module 1 dose expansion has opened, with the first two patients enrolled. In Module 2, dose escalation of REGN5668 has progressed through multiple dose levels; enrollment is ongoing. Clinical trial information: NCT04590326. Research Sponsor: Regeneron Pharmaceuticals, Inc.

RegeNovar: A phase I/II study of ubamatamab plus carboplatin, paclitaxel, and bevacizumab as salvage therapy in ovarian cancer with poor response to first-line chemotherapy.

Benoit You, Coriolan Lebreton, Fabien Subtil, Aurore Carrot, Jean-Sebastien Frenel, Leila Bengrine-Lefevre, Lauriane Eberst, Brunhilde Hanvic, Renaud Sabatier, Coraline Dubot, Stanislas Quesada, Alexandra Leary; Centre Hospitalier Lyon Sud, and GINECO, Pierre-Benite, France; GINECO and Institut Bergonié, Bordeaux, France; Service de Biostatistique Bioinformatique – Hospices Civils de Lyon, Lyon, France; Institut de Cancérologie de l'Ouest, Saint Herblain, France; Georges-François Leclerc Cancer Center, Dijon, France; Hôpitaux Universitaires de Strasbourg and GINECO, Strasbourg, France; Department of Medical Oncology, Centre Léon Bérard and GINECO, Lyon, France; Institut Paoli Calmettes, Marseille, and GINECO, Paris, France; Centre François Baclesse and GINECO, Caen, France; Department of Medical Oncology, Montpellier Cancer Institute (ICM), GINEGEPS and GINECO, Montpellier, France; Gustave-Roussy Cancer Campus, Villejuif, and GINECO, Paris, France

Background: Patients with advanced epithelial ovarian cancer (EOC) treated with neoadjuvant platinum-based chemotherapy who are not amenable to complete interval cytoreductive surgery (ICS) due to poor chemosensitivity—defined by a CA-125 KELIM score <1.0 —have a particularly poor prognosis, with approximately 20% 5-year overall survival. Ubamatamab is a human IgG4-based bispecific antibody targeting MUC16 (CA-125-expressing ovarian cancer cells) and CD3+ T cells and has demonstrated clinical activity in platinum-resistant recurrent ovarian cancer (Lee et al, Proc ESMO 2025). We hypothesize that adding ubamatamab to standard carboplatin–paclitaxel–bevacizumab may enhance tumor response and improve surgical resectability in patients with advanced high-grade EOC with poor chemosensitivity and disease not amenable to complete ICS after initial neoadjuvant chemotherapy. **Methods:** RegeNovar (EuCT 2025-524232-20-00) is an academic, multicenter phase I–II trial enrolling patients with stage III–IV high-grade EOC who, after 3–4 cycles of standard neoadjuvant carboplatin–paclitaxel administered every 3 weeks, present two poor prognostic features: (1) unfavorable standardized KELIM score <1.0 , and (2) disease considered not amenable to complete ICS. The trial includes two sequential parts: (i) a phase I safety run-in to evaluate the safety of ubamatamab in combination with carboplatin–paclitaxel–bevacizumab and confirm the recommended phase II dose (RP2D); and (ii) a phase II efficacy part assessing the antitumor activity of this combination. Patients receive carboplatin AUC5 ; paclitaxel 175 mg/m²; and bevacizumab 15 mg/kg Q3 weeks for three cycles. Ubamatamab is administered with weekly step-up dosing during cycle 1, followed by a fixed dose of 800 mg Q3 weeks during cycles 2 and 3. Feasibility of complete late cytoreductive surgery is evaluated after three cycles of the study regimen. Subsequent maintenance treatment consists of olaparib plus bevacizumab for patients with BRCA-mutated or HRD-positive tumors, or ubamatamab plus bevacizumab for up to 15 months in patients with HRD-negative tumors. The primary endpoint of phase I is safety, including treatment-related adverse events (NCI CTCAE v6.0), DLT within the first 4 weeks, and RP2D determination using a BOIN design targeting a DLT probability $\leq 28\%$. The primary endpoint of phase II is the objective response rate (ORR) after three cycles per RECIST 1.1 (H_0 5%, H_1 30%, one-sided $\alpha=5\%$, power=80%). Total 31 to 43 patients are required, depending on potential need for dose de-escalation. Secondary endpoints include ORR, duration of response, disease control rate, rate of late cytoreductive surgery, PFS, OS, and progression-free survival during subsequent therapy. The trial is sponsored by ARCAGY-GINECO, conducted in 12 French centers, and funded by Regeneron. Clinical trial information: EuCT 2025-524232-20-00. Research Sponsor: Regeneron.

RAINFOL-04 (ENGOT-OV96/GOG-3134): A phase 3, open-label, randomized study of rinatabart sesutecan (Rina-S) plus standard of care (SOC) vs SOC as maintenance treatment after second-line platinum-based chemotherapy in patients with recurrent platinum-sensitive ovarian cancer.

Toon Van Gorp, Yoland Catherine Antill, Kosei Hasegawa, Ibrahima Soumaoro, Manlei Wu, Alexander Olawaiye, on behalf of ENGOT/GOG Investigators; Division of Gynaecological Oncology, University Hospital Leuven, Leuven Cancer Institute, Leuven, Belgium; and BGOG, Leuven, Belgium; Peninsula Health, Monash University, Melbourne, VIC, Australia; Saitama Medical University International Medical Center, Hidaka, Saitama, Japan; Genmab, Princeton, NJ; University of Pittsburgh Medical Center and Magee-Women's Hospital of UPMC, Pittsburgh, PA

Background: Ovarian cancer (OC) is the eighth leading cause of cancer-related death in women globally. In patients with advanced OC, 70%-80% develop recurrent platinum-sensitive OC (PSOC) within 3 years after initial therapy. Standard treatment for recurrent PSOC includes platinum-based chemotherapy $\pm$ bevacizumab (BEV), but in most patients, disease progression occurs within a year. Rina-S is an antibody-drug conjugate targeting folate receptor alpha (FR α) with a novel hydrophilic protease-cleavable linker and a topoisomerase I inhibitor, exatecan, payload. In cohort B1 of the phase 1/2 RAINFOL-01 study (NCT05579366), Rina-S showed encouraging antitumor activity and was tolerated in patients with heavily pretreated advanced OC. We report the design of ENGOT-OV96/GOG-3134 (RAINFOL-04), a phase 3, randomized study of Rina-S + standard of care (SOC) vs SOC as maintenance treatment for patients with recurrent PSOC (NCT07225270). **Methods:** This phase 3 open-label study will enroll ~528 patients with platinum-sensitive high-grade serous or endometrioid epithelial OC, primary peritoneal cancer, or fallopian tube cancer regardless of their FR α expression. Patients must have disease progression >6 months after the last dose of first-line platinum chemotherapy and have achieved at least stable disease following completion of second-line platinum-based chemotherapy $\pm$ BEV. Patients will be randomized 1:1 to receive Rina-S 120 mg/m² intravenously every 3 weeks plus SOC or SOC (BEV or observation) until disease progression, unacceptable toxicity, or discontinuation. The primary endpoint is progression-free survival (PFS) per RECIST v1.1 by investigator assessment. The key secondary endpoint is overall survival. Additional secondary endpoints include PFS per RECIST v1.1 by blinded independent central review, PFS2 (time from randomization to the second progression or death), safety, and patient-reported outcomes. The trial is currently recruiting. Clinical trial information: NCT07225270. Research Sponsor: Genmab.

A phase 3, randomized, open-label study of INCB123667 versus investigator's choice of chemotherapy in patients with platinum-resistant ovarian cancer with cyclin E1 overexpression (MAESTRA 2, ENGOT-OV95, GOG-3137).

Rebecca Kristeleit, Kosei Hasegawa, Domenica Lorusso, Mark M. Jones, Maikel van der Velden, Jay Zhao, R. Wendel Naumann; Guy's and St Thomas' NHS Foundation Trust, Great Maze Pond, London, United Kingdom; Saitama Medical University International Medical Center, Hidaka, Saitama, Japan; Humanitas University, Pieve Emanuele, Italy; Incyte Corporation, Wilmington, DE; Incyte Biosciences International, Morges, Switzerland; Wake Forest University School of Medicine, Charlotte, NC

Background: Epithelial ovarian cancer (EOC) accounts for ~90% of ovarian cancers, with high-grade serous ovarian cancer (HGSOC) the most common histology. Despite high initial response rates to platinum-based therapy, ~70% of patients (pts) with advanced EOC relapse and nearly all recurrent disease ultimately becomes platinum resistant. Platinum-resistant ovarian cancer (PROC) remains a major therapeutic challenge with poor prognosis and limited treatment options. Standard therapies include single-agent, non-platinum chemotherapy with or without bevacizumab (bev), and mirvetuximab soravtansine (mirv) for pts with folate receptor alpha (FR α)-positive HGSOC. Approximately 50% of ovarian cancers overexpress cyclin E1. Cyclin E1 overexpression and increased cyclin-dependent kinase 2 (CDK2) activity are associated with poor outcomes and treatment resistance in ovarian cancer. A synthetic lethal relationship between CDK2 inhibition and cyclin E1 overexpression provides a strong biological rationale for selective CDK2 inhibition in this molecularly defined population. INCB123667 is a potent, selective, oral, small-molecule CDK2 inhibitor. In an ongoing phase 1 study, INCB123667 demonstrated manageable safety and objective response rates >30% in heavily pretreated pts with PROC and cyclin E1 overexpression [Damian S, et al. *J Clin Oncol.* 2025;43(16 suppl):5514; Simonelli M, et al. *Ann Oncol.* 2024;35(suppl 2):S495]. **Methods:** MAESTRA 2 (NCT07214779) is a global, multicenter, randomized, open-label phase 3 study evaluating the efficacy and safety of INCB123667 vs investigator's choice chemotherapy (ICC) in ~466 female pts with platinum-resistant, high-grade serous epithelial ovarian, fallopian tube, or primary peritoneal cancer with tumor cyclin E1 overexpression by immunohistochemistry (IHC; $\geq 75\%$ of tumor cells with IHC score $\geq 1+$). Eligible pts must have received 1-4 prior lines of systemic therapy, for whom single-agent chemotherapy is an appropriate next treatment. Pts should have received prior bev, and pts with FR α -positive disease should have received prior mirv. Pts are randomized 1:1 to INCB123667 50 mg twice daily or ICC (weekly paclitaxel, pegylated liposomal doxorubicin, gemcitabine, or topotecan). Randomization is stratified by primary platinum-free interval, ICC, and number of prior lines of systemic therapy. Dual primary endpoints are progression-free survival (PFS) by blinded independent central review (BICR) per RECIST v1.1 and overall survival. A key secondary endpoint is objective response by BICR per RECIST v1.1. Additional secondary endpoints include safety and tolerability, duration of response, PFS and objective response by investigator assessment, and health-related quality of life. The first pt was enrolled in Dec 2025. Clinical trial information: NCT07214779. Research Sponsor: Incyte Corporation.

Rationale and study design of the KOV-HIPEC-04: A phase III randomized controlled trial in primary stage three and four ovarian cancer after interval cytoreductive surgery (FOCUS).

Myong Cheol Lim, Ji Hyun Kim, Boram Park, Jaekyung Bae, Jung-Yun Lee, Heon Jong Yoo, Yun Hwan Kim, Jae Yun Song, Yong Jung Song, Suk-Joon Chang, Dae Hoon Jeong, Jeong-Yeol Park, Ki Hyung Kim, Ju-Won Roh, Jae-Kwan Lee, Sang-Soo Seo, Sang-Yoon Park; Center for Gynecologic Cancer, National Cancer Center, Goyang, South Korea; Gynecologic Cancer Center, National Cancer Center Korea, Goyang-Si, Gyeonggi-Do, South Korea; Department of Medical Education and Medical Humanities, College of Medicine, Inha University, Incheon, South Korea; National Cancer Center, Goyang-Si, South Korea; Yonsei Cancer Center and Severance Hospital, Yonsei University College of Medicine, Seoul, South Korea; Chungnam National University Sejong Hospital, Sejong, South Korea; Department of Obstetrics and Gynecology, Ewha Womans University College of Medicine, Seoul, South Korea; Department of Obstetrics and Gynecology, Korea University College of Medicine, Seoul, South Korea; Department of Obstetrics and Gynecology, Pusan National University Yangsan Hospital, Pusan, South Korea; Department of Obstetrics and Gynecology, Ajou University School of Medicine, Yeongtong-Gu, Suwon-Si, South Korea; Inje University Busan Paik Hospital, Busanjin-gu, Busan, South Korea; Department of Obstetrics and Gynecology, Asan Medical Center, Seoul, Seoul, South Korea; Department of Obstetrics and Gynecology, Pusan National University Hospital, Pusan, South Korea; CHA Ilisan Medical Center, Goyang-Si, South Korea; Korea University Guro Hospital, Seoul, South Korea; Center for Gynecologic Cancer, National Cancer Center, Goyang-Si, South Korea

Background: The addition of hyperthermic intraperitoneal chemotherapy (HIPEC) during interval cytoreductive surgery increases progression-free and overall survival for patients with stage III ovarian cancer in two randomized controlled trials (OV-HIPEC-01 and KOV-HIPEC-01). This trial aims to identify the survival benefit of HIPEC in stage III & IV ovarian cancer in the era of maintenance therapy of bevacizumab and/or PARP inhibitors. **Methods:** Ovarian cancer patients will be randomized at the time of interval cytoreductive surgery with achieving complete cytoreduction or cytoreduction with no more than 2.5mm size of residual disease to receive HIPEC (41.5 cisplatin 75mg/m², 90 minutes) or not (Control arm). After recovery from surgery, patients will receive postoperative platinum-based adjuvant chemotherapy followed by maintenance therapy with PARP inhibitor or bevacizumab. The primary objective of the trial is to evaluate OS in two groups. Secondary objectives are PFS, cancer-specific survival, time to first subsequent therapy (TFST), safety, CA-125 KELIM, and quality of life. Assuming that the enrollment period is 5 years and the follow-up period is 3 years, the total number of events required is 263. Based on the log-rank test, the total number of subjects required to prove HR 0.67 with a two-sided alpha of 0.05 and 90% power is 494. Considering 5% drop-out, 520 patients are finally studied. Clinical trial information: NCT05827523. Research Sponsor: National Cancer Center Korea (NCC2110790, NCC2110770).

FRAmework-01: A two-part phase 3 study of sofetabart mipitecan versus chemotherapy or mirvetuximab soravtansine in platinum-resistant ovarian cancer (PROC), and sofetabart mipitecan plus bevacizumab versus platinum-based chemotherapy plus bevacizumab in platinum-sensitive ovarian cancer (PSOC).

Isabelle Laure Ray-Coquard, Elena Ioana Braicu, Kosei Hasegawa, Jung-Yun Lee, Xiaohua Wu, Destin Black, Nicole Concin, Claire Frances Friedman, Karim Nacerddine, Roisin Eilish O'Cearbhaill, Bhavana Pothuri; Centre Léon Bérard, University Claude Bernard, Lyon, France; Department of Gynecology, Campus Virchow, Charité Universitätsmedizin Berlin and North Eastern German Society for Gynecologic Oncology (NOGGO), Berlin, Germany; Department of Gynecologic Oncology, Saitama Medical University International Medical Center, Hidaka, Saitama, Japan; Yonsei Cancer Center and Severance Hospital, Yonsei University College of Medicine, Seoul, South Korea; Fudan University Shanghai Cancer Center, Shanghai, China; Trials 365, LLC, Shreveport, LA; Department of Gynecology and Gynecological Oncology, Medical University of Vienna, Vienna, Austria; Eli Lilly and Company, Indianapolis, IN; Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, NY; Division of Gynecologic Oncology, Laura & Isaac Perlmutter Cancer Center, NYU Langone Health, New York, NY

Background: Folate receptor alpha (FR α) is overexpressed in ovarian cancer and is a validated therapeutic target. Mirvetuximab soravtansine (MIRV), an antibody drug conjugate (ADC) targeting FR α , is approved for the treatment of patients with PROC and high FR α expression ($\geq 75\%$ tumor cells with 2+ and/or 3+ staining intensity). Given MIRV's limited indication and its association with specific side effects, including ocular adverse events and peripheral neuropathy, there remains a significant medical need to improve outcomes for a broader population of patients with ovarian cancer. Sofetabart mipitecan is an FR α -targeting ADC composed of an Fc-silenced, humanized IgG1 antibody, a novel polysarcosine hydrophobicity masking agent with a dipeptide cleavable linker, and the topoisomerase I inhibitor payload exatecan at a drug-antibody ratio of 8. Data from the Phase 1 study indicate that sofetabart mipitecan monotherapy demonstrates promising and durable clinical activity, with high objective response rates and a tolerable safety profile, in heavily pretreated patients with PROC. Responses were observed across all FR α levels, including in patients who received prior MIRV treatment, and there were no reports of keratopathy or significant peripheral neuropathies. Sofetabart mipitecan was recently granted Breakthrough Therapy Designation by the FDA. **Methods:** In Part A, 530 participants with PROC who received ≤ 3 prior lines of systemic cytotoxic therapy (or ≤ 4 lines if MIRV was included), will be randomized in a 1:1 ratio to receive either sofetabart mipitecan, or the investigator's choice (IC) of chemotherapy (paclitaxel, pegylated liposomal doxorubicin [PLD], gemcitabine, or topotecan) or MIRV (if eligible per local label). In Part B, 550 participants with PSOC who received ≤ 2 prior lines of systemic cytotoxic therapy and had disease progression either during or within six months of completing treatment with a poly (ADP-ribose) polymerase inhibitor (PARPi), will be randomized in a 1:1 ratio to receive either sofetabart mipitecan plus bevacizumab (bev), or the IC of carboplatin-based chemotherapy (paclitaxel, PLD, or gemcitabine) plus bev. Study Parts A and B will enroll participants irrespective of their tumor's FR α expression level. Each part has progression-free survival as its primary endpoint, while overall survival is a key secondary endpoint. Study parts will be conducted separately, and statistical analyses will be performed independently. Trial Status: The study is actively enrolling participants in Part A and B. Clinical trial information: NCT07213804. Research Sponsor: Eli Lilly and Company.

Fern-EC-01 (BNT323-01): A phase 3 trial of trastuzumab pamirtecán (HER2 ADC) versus investigator's choice of chemotherapy in patients with previously treated, HER2-expressing, recurrent endometrial cancer (EC).

Floor Jenniskens Backes, John McGrane, Bhavana Pothuri, Susie Kit Sze Lau, Keri-Lee Geneser, Michael Liontos, Jae-Hoon Kim, Peng-Hui Wang, Xiaohua Wu, Rami Eitan, Monika Ducceschi, Joannie Neveu, Stephan Polterauer, Vicky Soomers, Ji Hyun Lee, Zifang Guo, Kathleen N. Moore, Hanna Dahlstrand; Division of Gynecologic Oncology, Ohio State University Wexner Medical Center, Columbus, OH; Royal Cornwall Hospital NHS Trust, Cornwall, United Kingdom; NYU Langone Laura and Isaac Perlmutter Cancer Center, New York, NY; Segal Cancer Center Gynecologic Oncology Program, Montréal, QC, Canada; Western Health, Medical Oncology - Sunshine Hospital, St. Albans, Australia; National and Kapodistrian University of Athens, Department of Clinical Therapeutics, Athens, Greece; Gangnam Severance Hospital, Seoul, South Korea; Taipei Veterans General Hospital, Taipei, Taiwan; Fudan University Shanghai Cancer Center, Shanghai, China; Rabin Medical Center, Petah Tikva, Israel; Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; Division of Gynecologic Oncology, Newfoundland and Labrador Health Services, Eastern Health, St. Johns, NF, Canada; Department of Obstetrics and Gynecology, Medical University Vienna, Vienna, Austria; Radboud Univ Nijmegen Med Ctr, Nijmegen, Netherlands; BioNTech US Inc., Cambridge, MA; Fred and Pamela Buffett Cancer Center at the University of Nebraska Medical Center, Omaha, NE; Karolinska University Hospital, Stockholm, Sweden

Background: Despite advancements in frontline therapies for EC, treatment options for recurrent/refractory disease remain limited. HER2 overexpression in EC is associated with rapid disease progression, tumor invasiveness, a high risk of recurrence, and poor prognosis. Trastuzumab pamirtecán (T-Pam; BNT323/DB-1303) is an investigational HER2-targeting antibody-drug conjugate (ADC) with a DNA topoisomerase I inhibitor payload and a drug-to-antibody ratio of ~8. In a phase 1/2a trial (NCT05150691), T-Pam demonstrated encouraging clinical benefit in patients with HER2-expressing EC, efficacy was observed across all HER2 expression levels and patient subgroups with a manageable safety profile. **Methods:** Following a protocol amendment, this open-label, randomized, multi-site, phase 3 trial (Fern-EC-01; BNT323-01) is enrolling patients with recurrent, HER2 expressing EC (assessed by central laboratory testing using IHC) who have measurable disease defined by RECIST v1.1, an ECOG PS of 0-2, and have received ≥ 1 prior line of platinum-based therapy (in any setting) and prior immune-checkpoint inhibitor treatment. Up to three lines of prior therapy are permitted. Prior hormonal therapy and radiation are allowed but do not count as prior lines of therapy. Prior exatecan-containing treatment is not allowed. All patients will receive treatment until RECIST v1.1 defined progressive disease, unacceptable toxicity, withdrawal of consent, or other discontinuation criteria are met. The trial is enrolling two cohorts. In Cohort 1, ≈ 420 patients with HER2-expressing (IHC 1+ or 2+) EC will be randomized 2:1 to evaluate the efficacy and safety of T-Pam vs investigator's choice of chemotherapy (doxorubicin, paclitaxel, or docetaxel in case of contraindication to paclitaxel and availability at the site). Stratification is based on HER2 expression (IHC 1+; 2+) and prior lines of therapy (1; 2+). The primary endpoint for Cohort 1 is progression-free survival (PFS) by blinded independent central review (BICR); overall survival is a key secondary endpoint. In Cohort 2, ≈ 60 patients with HER2 IHC 3+ EC will receive T-Pam; the primary endpoint for this cohort is objective response rate by BICR. Enrollment is ongoing globally. Clinical trial information: NCT06340568. Research Sponsor: BioNTech SE in collaboration with Duality Biologics.

RAINFOL-03 (ENGOT-EN-31/GOG-3128): A global, phase 3, open-label, randomized study of rinatabart sesutecan (Rina-S) vs investigator's choice of chemotherapy in patients with endometrial cancer after platinum-based chemotherapy and programmed death-ligand 1 inhibition.

Antonio Gonzalez Martin, Elena Ioana Braicu, Pallavi P. Kumar, Kosei Hasegawa, Allan Covens, Fernanda Damian, Birute Brasiuniene, David Shao Peng Tan, Giorgio Valabrega, Alison Stillie, Mala Talekar, Xuan Zhou, Noelle Cloven, On behalf of the Grupo Español Investigación Cáncer Ovario (GEICO) Group; Department of Medical Oncology, Cancer Center Clínica Universidad de Navarra, Madrid, Spain; Charité - Universitätsmedizin Berlin and NOGGO, Berlin, Germany; Sinai Hospital of Baltimore/Life Bridge Health, Baltimore, MD; Saitama Medical University International Medical Center, Hidaka, Saitama, Japan; Sunnybrook Research Institute, Toronto, ON, Canada; Hospital São Lucas da PUCRS, Hospital Nossa Senhora da Conceição - Grupo Hospitalar Conceição, Latin American Cooperative Oncology Group, Brazilian Gynecologic Oncology Group (EVA), Universidade Federal do Rio Grande do Sul, Porto Alegre, Brazil; Center of Medical Oncology, National Cancer Center of Vilnius University Hospital Santaros Clinics; Faculty of Medicine, Vilnius University, and Nordic Society of Gynaecological Oncology (NSGO), Vilnius, Lithuania; National University Cancer Institute, Singapore, Singapore, Singapore; University of Turin, A.O. Ordine Mauriziano, Turin, Italy; Edinburgh Cancer Centre, Western General Hospital, Edinburgh, United Kingdom; Genmab, Princeton, NJ; Texas Oncology, Fort Worth, Fort Worth, TX

Background: Patients with recurrent endometrial cancer (EC) whose disease progresses after platinum-based chemotherapy (PBC) and programmed death (ligand) 1 [PD-(L)1] inhibition have a poor prognosis and limited, ineffective treatment options. Single-agent chemotherapy in this setting has been associated with low objective response rates (ORRs; ~15%) and median progression-free survival (PFS) of ~3-4 months. Rina-S is an investigational antibody-drug conjugate targeting folate receptor alpha (FR α) with a novel hydrophilic protease-cleavable linker and topoisomerase I inhibitor, exatecan, payload. In the phase 1/2 RAINFOL-01 trial (NCT05579366), Rina-S 100 mg/m² showed encouraging antitumor activity, with a 50% confirmed ORR, including 2 complete responses, and a manageable safety profile in patients with heavily pretreated EC after progression on PBC and a PD-(L)1 inhibitor (Winer IS, et al. *J Clin Oncol.* 2025;43[16 suppl]:3039). We report the design of RAINFOL-03, a global, open-label, randomized phase 3 study of Rina-S vs investigator's choice (IC) therapy in patients with EC who have progressed on PBC and a PD(L)-1 inhibitor (NCT07166094). **Methods:** This phase 3 open-label study will enroll ~544 patients with recurrent or progressive EC (any subtype excluding neuroendocrine tumors, carcinosarcoma, or endometrial sarcoma), measurable per RECIST v1.1, who have received 1-3 prior lines of therapy, including PBC and a PD(L)-1 inhibitor. Patients will be randomized 1:1 to receive Rina-S 100 mg/m² intravenously every 3 weeks or IC therapy (paclitaxel or doxorubicin) until disease progression or unacceptable toxicity. Patients will be enrolled regardless of FR α expression level; however, FR α expression levels will be required for stratification at randomization. Dual primary endpoints are PFS per RECIST v1.1 by investigator assessment and overall survival. The key secondary endpoint is ORR per RECIST v1.1 by investigator assessment. Additional secondary endpoints include PFS and ORR per RECIST v1.1 by blinded independent central review (BICR), duration of objective response per RECIST v1.1 by investigator assessment and BICR, safety, and quality of life outcomes. The trial is currently recruiting. Clinical trial information: NCT07166094. Research Sponsor: Genmab A/S.

Puxitatug samrotecan (AZD8205) vs chemotherapy in patients with B7-H4-selected advanced/metastatic endometrial cancer: The phase 3 randomized Bluestar-Endometrial01 (BE01)/GOG-3110/ENGOT-EN28 trial.

Stephanie Gaillard, Evelyn Cantillo, David Cibula, Andrew R. Clamp, Sarah Crafton, Hannelore Denys, Karen Finkelstein, Marta Gil-Martin, Lars Christian Hanker, Kosei Hasegawa, Olivia Le Saux, Bradley J. Monk, Fernanda Musa, Leslie Randall, Vanda Salutari, Brian M. Slomovitz, Yang Xiang, Deepali Verma, Andreea Varga, Nicole Concin; Johns Hopkins Sidney Kimmel Cancer Center, Baltimore, MD; Department of Obstetrics and Gynecology, Division of Gynecology Oncology, Weill Cornell Medicine, New York, NY; Department of Gynaecology, Obstetrics and Neonatology, General University Hospital in Prague, First Faculty of Medicine, Charles University, Prague, Czech Republic; The Christie NHS Foundation Trust and University of Manchester, Manchester, United Kingdom; Division of Gynecologic Oncology, Department of Obstetrics and Gynecology, West Penn Hospital, Allegheny Health Network, Pittsburgh, PA; Ghent University Hospital, Department of Medical Oncology, Ghent, Belgium; Optimum Clinical Research Group, Albuquerque, NM; Department of Medical Oncology, Institut Català d'Oncologia L'Hospitalet- IDIBELL, Barcelona, Spain; Department of Gynecology & Obstetrics, University Hospital Münster, Münster, Germany; Saitama Medical University International Medical Center, Department of Gynecologic Oncology, Hidaka, Saitama, Japan; Medical Oncology, Centre Léon Bérard, Lyon, France; Florida Cancer Specialists & Research Institute, West Palm Beach, FL; Swedish Medical Center-First Hill, Seattle, WA; Gynecologic Cancer Service Institute, Inova Schar Cancer Center, Inova Health System, Fairfax, VA; Department of Women, Children and Public Health Sciences, Gynecologic Oncology Unit, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Italy; Gynecologic Oncology, Mount Sinai Medical Center, Miami Beach, FL; Department of Obstetrics and Gynecology, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing, China; Oncology R&D, AstraZeneca, Cambridge, United Kingdom; Department of Gynecology and Gynecological Oncology, Medical University of Vienna, Vienna, Austria

Background: The transmembrane glycoprotein B7-H4 is highly expressed in endometrial cancer (EC), with limited expression in normal tissue; therefore, B7-H4 is an attractive antibody–drug conjugate (ADC) target in the treatment of advanced/recurrent EC. Puxitatug samrotecan (Puxi-Sam), a novel B7-H4-directed topoisomerase I inhibitor ADC, was assessed as monotherapy in the first-in-human, Phase 1/2a BLUESTAR trial in several B7-H4-expressing tumors, and showed manageable toxicity and promising efficacy during dose escalation in heavily pre-treated patients (pts).¹ In pts with advanced/recurrent EC, who progressed after available standard of care therapy (including chemotherapy and/or a programmed death [PD]–ligand [L] 1 inhibitor), objective response rates (ORRs) were 34.6% and 38.5% with 2.0 and 2.4 mg/kg Puxi-Sam, respectively, after ≥13 weeks of follow-up.² The safety profile of Puxi-Sam was favorable, with manageable hematologic and gastrointestinal toxicities, no adverse events (AEs) leading to discontinuation, and low dose reduction rates due to treatment-related AEs.² Following these encouraging results, Bluestar Endometrial01, a global Phase 3 trial, will investigate Puxi-Sam monotherapy versus physician's choice of chemotherapy in pts with B7-H4-selected EC whose disease has progressed following prior platinum-based chemotherapy and immunotherapy. **Methods:** This Phase 3, randomized, open-label, multicenter study includes pts with B7-H4-selected advanced/metastatic EC that progressed following platinum-based chemotherapy and anti-PD-1/anti-PD-L1 therapy. Approximately 700 pts will be randomized 1:1 to either Arm A: Puxi-Sam (2.4 mg/kg; intravenous [IV] on Day 1 every 3 weeks [q3w]) or Arm B: either doxorubicin (60 mg/m² IV on Day 1 q3w) or paclitaxel (80 mg/m² IV on Days 1, 8, and 15 in 28-day cycles). The primary outcomes are progression-free survival (PFS) and overall survival (OS). Secondary outcomes include ORR, duration of response (DoR), second PFS, time until first subsequent anticancer therapy (TFST) and second subsequent anticancer therapy (TSST) after discontinuation of the randomized treatment, or death, and time until discontinuation of treatment (TDT) for any reason, or death. All outcomes are to be assessed for Arm A versus Arm B. Safety will be assessed throughout. Clinical trial information: NCT07044336. First Patient In date: Aug 1, 2025. 1. Meric-Bernstam F, et al. *Ann Oncol*. 2024;35:S485–S486. 2. Gaillard S, et al. *Gynecol Oncol*. 2025;200:347–348. Editorial acknowledgment: Medical writing assistance was provided by Lewis C Rodgers, PhD, of Omnicom Health Medical Communications, and was funded by AstraZeneca. Clinical trial information: NCT07044336. Research Sponsor: AstraZeneca.