IGCS 2025 CAPE TOWN

Annual Global Meeting, November 5–7, 2025

IGCS 2025 Abstracts: E-Poster Viewing (Trials-in-Progress)

Registered delegates will have access to all submitted Trial-in-Progress E-Posters via the IGCS 2025 mobile application, IGCS 360 Educational Portal, and the onsite E-Poster stations.

Poster presenters were given the option to submit an audio file with a short presentation together with their E-Posters. Submitted audio files will be available together with their E-Posters via the IGCS 360 Educational Portal.

TP001 / #1090

Topic: *AS01. Basic Sciences / AS01b. Basic & Translational Science*

TRIAL-IN-PROGRESS: A PHASE II INTERVENTIONAL STUDY OF HPV L1 VACCINE IN COMBINATION WITH IMIQUIMOD AND METFORMIN IN GYNECOLOGIC SQUAMOUS CANCERS

Caroline Davitt, Savannah Barkdull, Kathleen Pennington, Kenisha Lane, Jan Sunde
Baylor College of Medicine, Houston, United States of America

Introduction: This study aims to determine whether additional immune-boosting treatments can enhance the body's ability to fight HPV-related cancers when combined with standard therapy.

Objectives: The primary objective of this phase II trial is to evaluate 24-month progression-free survival (PFS) in patients with locally advanced cervical, vaginal, or vulvar carcinoma receiving intratumoral HPV vaccination, topical imiquimod, and oral metformin alongside standard chemoradiation (whole pelvic radiotherapy, chemotherapy, and brachytherapy). Tumor response, symptom relief, safety, and tolerability will also be assessed. Secondary objectives include identifying unexpected toxicities and evaluating immune mechanisms enhanced by the immunotherapy combination. The study will also assess immune biomarkers to understand how the treatment supports the immune response when paired with standard care.

Methods: This single-center, window-of-opportunity study uses the 9-valent HPV vaccine, imiquimod, and metformin to stimulate tumor immunity. Eligible participants are women aged 18–64 with histologically confirmed, locally advanced or metastatic cervical, vaginal, or vulvar cancer not suitable for primary surgery. Intratumoral vaccines are administered during weeks 2 and 4 of radiation, and post-radiation at weeks 8, 10, 12, and 16. Imiquimod and metformin are applied and taken before and after each visit. Immune biomarkers are collected at baseline, mid-treatment, and end of treatment. PFS outcomes will be compared to a historical control using Kaplan-Meier and log-rank tests.

Current Status & Future Directions: Enrollment began in August 2024. Ten patients are enrolled, with a target of 85 by August 2028. If successful, this strategy may inform a new standard for treating HPV-related squamous cell carcinomas.

TP002 / #937

Topic: *AS02. Clinical Disciplines / AS02d. Radiation Oncology*

HYPOFRACTIONATED RADIATION THERAPY WITH ADAPTIVE PLANNING FOR THE TREATMENT OF ENDOMETRIAL AND CERVICAL CANCER (HERA TRIAL)

Rojine Ariani, Puja Venkat
University of California Los Angeles, Radiation Oncology, Los Angeles, United States of America

Introduction: Conventional pelvic radiotherapy for gynecologic cancers involves prolonged treatment courses and treatment volumes accounting for organ motion that contribute to quality-of-life (QOL) burdens. Stereotactic body radiotherapy (SBRT) offers a condensed regimen but has shown variable toxicity profiles. Adaptive planning offers higher precision allowing for smaller treatment volumes. The Hypofractionated External Beam Radiotherapy With Adaptive Planning for Endometrial and Cervical Cancers (HERA) trial investigates the feasibility and safety of 30 Gray in 5 fractions of adjuvant pelvic SBRT using adaptive planning.

Objectives: The primary objective is to evaluate acute toxicity within 12 weeks of adaptive SBRT using CTCAE v5.0. Secondary objectives include assessment of patient-reported QOL (EORTC QLQ-C30 and EN24), late toxicity, and survival endpoints.

Methods: This is a single-arm, non-randomized phase I trial enrolling 60 patients with FIGO Stage IA–IVB endometrial or Stage IA–IIA cervical cancer following surgery. Eligible patients receive 6 Gray x 5 fractions of SBRT with CT- or MRI-guided adaptive planning. Toxicity, QOL, and disease control will be evaluated through clinical, radiographic, and survey-based follow-up for 5 years. Clopper-Pearson exact method, paired t-test, Wilcoxon signed-rank test, the Benjamini-Hochberg procedure, and Kaplan-Meier analysis will be used as indicated.

Current Status & Future Directions: Accrual began in 2024, with a target enrollment of 60 patients expected by 2027. No interim reports have been performed to date. This trial may support the integration of adaptive SBRT into standard adjuvant treatment for select gynecologic cancer patients to reduce treatment burden while preserving and/ or improving safety and efficacy.

TP003 / #308

Topic: *AS04. Prevention & Downstaging / AS04a. Pre-Invasive Disease*

TRIAL IN PROGRESS: A RANDOMIZED CLINICAL TRIAL TO ASSESS THERMAL ABLATION VS LOOP ELECTROSURGICAL EXCISION PROCEDURE IN WOMEN LIVING WITH HIV IN MOZAMBIQUE

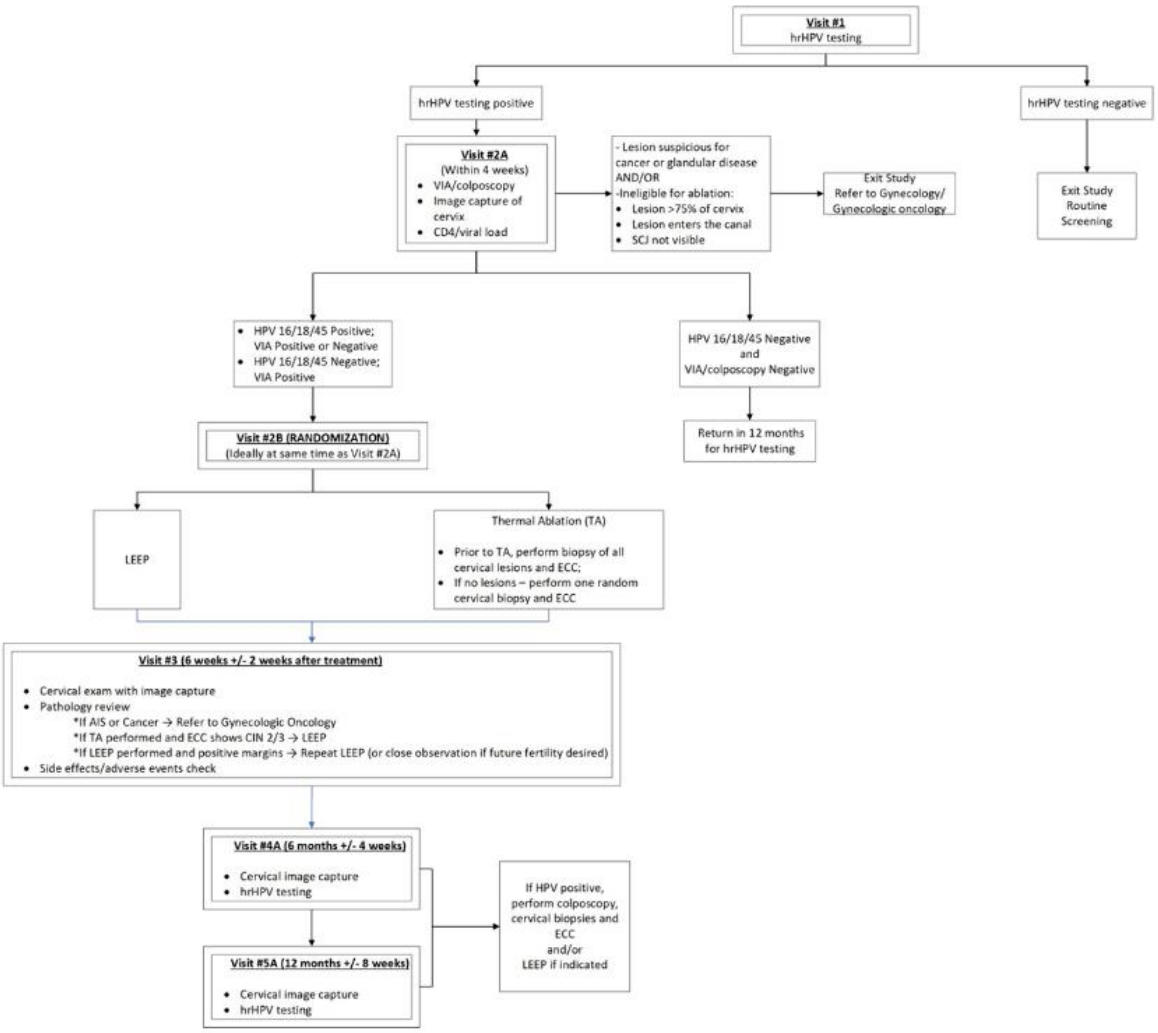
Parisa Fallah[1], Edna Nhacule[2,3], Yolanda Utui[2], Marcia Massinga[2], Nafissa Osman[4], Guilhermina Tivir[2,3], Carla Carrilho[4], Eliane Monteiro[5], Ricardina Rangeiro[5], Andrea Neves[6], Dercia Changule[5], Arlete Mariano[7], Alberto Machaze[2,3], Celso Castiano[2,3], Ellen Baker[1], Jose Jeronimo[8], Elizabeth Chiao[9], Mark Munsell[10], Melissa Varon[11], Jessica Milan[11], Joseph Thomas[10], Rebecca Richards-Kortum[12], Cesaltina Lorenzoni[2,13], Edna Viegas[2,3], Philip Castle[8], Kathleen Schmeler[1,11], Mila P. Salcedo[1]
[1]The University of Texas MD Anderson Cancer Center, Gynecologic Oncology And Reproductive Medicine, Houston, United States of America, [2]Instituto Nacional de Saude (INS) - National Institute of Health Mozambique, Maputo, Mozambique, [3]Centro de Investigacao e Treino em Saude de Polana Canico (CISPOC), Maputo, Mozambique, [4]Universidade Eduardo Mondlane Faculdade de Medicina, Maputo, Mozambique, [5]Hospital Central de Maputo, Maputo, Mozambique, [6]Hospital Geral Jose Macamo, Maputo, Mozambique, [7]Hospital Geral de Mavalane, Maputo, Mozambique, [8]National Institutes of Health, National Cancer Institute, Bethesda, United States of America, [9]The University of Texas MD Anderson Cancer Center, Epidemiology, Houston, United States of America, [10]The University of Texas MD Anderson Cancer Center, Biostatistics, Houston, United States of America, [11]The University of Texas MD Anderson Cancer Center, Global Oncology, Cancer Network, Houston, United States of America, [12]Rice University, Institute For Global Health Technologies, Houston, United States of America, [13]Mozambique Ministry of Health, National Cancer Control, Maputo, Mozambique

Introduction: Mozambique experiences one of the highest burdens of cervical cancer globally. Women living with HIV (WLWH) carry a six-fold higher risk of cervical cancer compared to the general population. Effectiveness of thermal ablation (TA) versus loop electrosurgical excision procedure (LEEP) in WLWH is uncertain.

Objectives: We aim to compare the effectiveness of TA versus LEEP for the management of abnormal screening results in WLWH. Our primary endpoint is the rate of persistent/recurrent cervical intraepithelial neoplasia grade 2 or worse (CIN 2+) and high-risk human papillomavirus infection (hrHPV) at 12 months after treatment.

Methods: This is a randomized non-inferiority trial. Participants include 25–49-year-old WLWH in Mozambique. Exclusion criteria are pregnancy, history of total hysterectomy, prior treatment for CIN, or cervical cancer. Participants undergo screening with primary hrHPV testing. If positive, they undergo visual inspection with acetic acid (VIA). Those

who are hrHPV positive and VIA positive, or HPV 16/18 positive regardless of VIA result, are randomized to TA or LEEP. Participants then undergo follow-up at 4-8 weeks, 6 months, and 12 months post-procedure.



Current Status & Future Directions: To meet our primary endpoint, we need to randomize 126 participants with ablation-eligible CIN 2/3 to TA or LEEP. To date we have screened 175 participants, of which 8 were found to have CIN 2/3 and underwent randomization and treatment. As TA becomes widely adopted in low-resource settings for the management of CIN, it is essential to know its effectiveness in WLWH, so that women receive appropriate and feasible treatment.

TP004 / #429

Topic: *AS04. Prevention & Downstaging / AS04b. Prevention & Vaccination*

STUDY TO COMPARE THE EFFECTIVENESS OF CERVICAL CYTOLOGY WITH MOLECULAR SCREENING IN DETECTING REACTIVE CELL CHANGES IN THE CERVIX IN AN OPEN POPULATION

Leopoldo Enrique Gatica Galina[1], Olando Santillan Godinez[2], Mercedes Gutierrez Smith[1]
[1]TIMSER, CIUDAD DE MEXICO, Mexico, [2]ATSO PHARMA, CIUDAD DE MEXICO, Mexico

Introduction:

Figura 1. Western blot para detectar la ribonucleoproteína heterogénea nuclear en sueros de pacientes con CaCu (muestras 1 – 8) y en donadoras sanas (muestras 9 – 15). Abreviaturas: Expos, tiempo de exposición (en segundos) de la membrana en el sistema de revelado; MPM, marcador de peso molecular.

Figura 2. Western blot para detectar el Factor eucariótico de inicio de la traducción en sueros de pacientes con CaCu (muestras 1–7) y donadoras sanas (muestras 8 – 15). El tiempo de exposición de revelado fue de 10 segundos. Abreviaturas: Expos, tiempo de exposición.

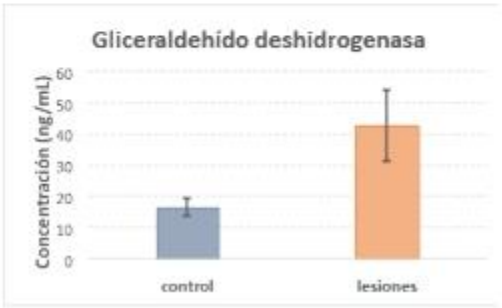


Figura 3. Concentración de la Gliceraldehído deshidrogenasa estimada mediante ELISA.

The official test for cervical cancer screening is cytology. Screening is an evaluation of apparently healthy individuals (an open population) to detect a condition or disease. Cytology presents several limitations, including its invasive nature, low sensitivity (51–55.4%), limited coverage of the target population (31.4% in 2020), and various sociocultural and economic barriers. Blood biomarkers is known that can be used for

molecular screening of precursor lesions and cervical cancer. The present study aims to compare the effectiveness of cervical cytology with molecular screening.

Objectives: Due to the multiple limitations of cervical cytology, it is important to identify tests capable of increasing the detection capacity of precursor lesions and cervical cancer. To achieve this, this study will compare the efficacy of cervical cytology with molecular screening. The biomarkers studied—heterogeneous nuclear ribonucleoprotein, eukaryotic translation initiation factor, and glyceraldehyde dehydrogenase—are associated with cellular alterations in the cervix.

Methods: The sensitivity of liquid-based cytology was estimated at 67.4%. The sensitivity of molecular screening (85.3%). The study population consisted of women in good general health, aged 18–85 years, who fasted for 6–12 hours, who had not received treatment for cervical cancer within the previous 6 months, who had not had sexual intercourse in the previous 24 hours, and who attended gynecological screening at the participating center.

Current Status & Future Directions: Approved by regulatory bodies in Mexico, awaiting a change of research center to begin sample collection, which we will be able to carry out in less than two months after approval.

TP005 / #971

Topic: *AS04. Prevention & Downstaging / AS04c. Screening & Early Detection*

NON-INVASIVE STRATEGIES FOR EARLY ENDOMETRIAL CANCER DETECTION IN PATIENTS WITH ABNORMAL UTERINE BLEEDING

Karman Johal[1], Pamela Bai[2], Arabella Helgason[1], Dollina Dodani[1], Jennifer Ellis-White[1], Andrea Neilson[1], Aline Talhouk[1]
[1]University of British Columbia, Department Of Obstetrics And Gynaecology, Vancouver, Canada, [2]University of British Columbia, Department Of Medicine, Vancouver, Canada

Introduction: Abnormal uterine bleeding (AUB) is a common first symptom of endometrial cancer (EC) and its precursors, prompting endometrial biopsy for diagnostic evaluation. However, AUB is a nonspecific symptom experienced by 30% of women, most commonly during perimenopause. Better indicators are needed to effectively risk-stratify patients with AUB at high EC risk and limit unnecessary biopsies.

Objectives: The DETection of Endometrial Cancer Through Risk modelling (DETECTR) trial aims to integrate self-reported health history with vaginal biomarkers to train a model that predicts malignancy, and to identify persistent EC-associated DNA mutations that lead to later endometrial hyperplasia or endometrial pathology.

Methods: Participants aged ≥ 35 years who are scheduled to undergo diagnostic assessment for AUB via endometrial biopsy are eligible. Before their endometrial biopsy, patients provide vaginal swabs to investigate microbial changes and EC-associated somatic mutations, a vaginal pH kit, and self-reported health history via a questionnaire. A subset of participants is invited for longitudinal follow-up over six months via weekly questionnaires and a wearable device to track health data. These participants will complete a second vaginal collection at the six-month marker to assess for persistent somatic changes.

Current Status & Future Directions: DETECTR has enrolled 31 participants across five BC clinics, expecting 1000 participants by spring 2027. Data analysis will be conducted continuously until study completion. It is anticipated that this non-invasive approach to EC screening in a symptomatic population can effectively risk-stratify patients to reduce the number of endometrial biopsies, enhance screening accessibility and identify opportunities for intervention.

TP006 / #708

Topic: *AS05. Social Responsibility: Global Health, Economic Challenges & Inequity*

FEASIBILITY AND ACCEPTABILITY OF ULTRASOUND TRAINING AND EDUCATION VIA LONG-DISTANCE E-LEARNING FOR CERVICAL CANCER STAGING (US-TELE)

Anisa Mburu[1], Floriana Mascilini[2], Antonia Testa[2], Maja Pakiz[2], Lorena Quagliozzi[2], Anna Fagotti[2]
[1]Aga Khan Hospital, Mombasa, Kenya, [2]Dipartimento Scienze della Salute della Donna, del Bambino e di Sanità Pubblica, Fondazione Policlinico Universitario Agostino Gemelli, IRCCS, Rome, Italy, Rome, Italy

Introduction: Cervical cancer remains a major burden in LMICs, where access to advanced imaging is limited by cost, infrastructure, and personnel. As a low-cost, widely available tool, ultrasound offers a practical alternative for staging, with growing evidence supporting its accuracy in assessing tumor size, invasion, and lymph node involvement—making it especially valuable in resource-constrained settings.

Objectives: The primary objective is to evaluate whether the implementation of an e-learning program for ultrasound training in cervical cancer staging is feasible, the secondary aim is to determine the acceptability of the distance learning module in key stakeholders

Methods: This pilot study, part of the ESGO-ENYGO mentorship program, is a prospective feasibility project by gynecologic oncologists from Policlinico Gemelli, Rome, and Aga Khan Hospital, Mombasa (March 2024–ongoing). It comprises three phases: a literature review on ultrasound use in pelvic anatomy and cervical cancer staging; supervised scanning of healthy volunteers via videoconferencing; and ultrasound assessment of patients with advanced cervical cancer. For each phase, the trainee completes scored modules. The study concludes with an on-site visit where the trainee performs 5–10 supervised scans to assess skill and competency.

Current Status & Future Directions: Maturation began in March 2024. Enrolment is expected to be completed by June 2025, with analysis in August 2025. Currently, Parts I and II, involving the examination of five patients from Italy and five from Kenya, have been completed. The collected video data and modules have been submitted to the ultrasound expert for evaluation. Part III is ongoing, with 15 patients with advanced cervical cancer examined so far.

TP007 / #1127

Topic: *AS06. Tumor Types / AS06b. Cervical Cancer*

NEOADJUVANT TREATMENT OF CADONILIMAB (ANTI-PD-1 AND CTLA-4 BISPECIFIC ANTIBODY) AND CHEMOTHERAPY IN IB2-IB3 CERVICAL CANCER PATIENTS WHO DESIRE FERTILITY PRESERVATION: AN OPEN-LABEL, SINGLE-ARM, PHASE II CLINICAL TRIAL

Jin Li[1], Xiaohua Wu[2]
[1]Fudan University Shanghai Cancer Center, Shanghai, China, [2]Department of Gynecologic Oncology, Fudan University Shanghai Cancer Center, Shanghai, China

Introduction: There is unanimous consensus that fertility-sparing surgery is a safe option for stage IB1 cervical cancer. However, the optimal fertility-sparing management for cervical cancer patient with stage IB2-IB3 disease are not well defined.

Objectives: Immunotherapy has made significant advances in cervical cancer treatment. We conducted this study to evaluate the efficacy and safety of neoadjuvant chemo + Cadonilimab (Ak104, a PD-L1 and CTLA4 inhibitor) in CC patients (IB2/IB3) who required fertility preservation.

Methods: This is an open label, single-arm, phase 2 trial in China. It is registered with ClinicalTrials.gov, NCT06209294, and is ongoing. CC (squamous cell/adenocarcinoma/adenosquamous carcinoma) patients aged 18-45 years with stage of IB2-IB3 and an Eastern Cooperative Oncology Group performance status of 0 or 1 were enrolled. Pts should desire for fertility preservation and their pre-treatment imagings show no distant metastasis or regional lymph node metastasis, and the tumor should limit to the cervix. Eligible patients will undergo six cycles of weekly doublet chemotherapy (Nab paclitaxel 125mg/m2 d1,8,15,22,29,36 intravenously, plus Carboplatin AUC=2 d1,8,15,22,29,36 intravenously), plus two cycles of AK104 on day 1 and d22 (10 mg/kg). Patients with response will be sent for fertility-sparing surgery after neoadjuvant immune-chemotherapy. The outcome measures includes the objective response rate, pathological complete sesponse (pCR) rate, safety of AK104 combined with nab-paclitaxel and carboplatin in the neoadjuvant treatment of cervical cancer.

Current Status & Future Directions: Eight patients were enrolled and the study is still recruiting eligible patients. Further research will use clinical samples to explore the predictors of efficacy and the mechanism of immunotherapy resistance in cervical cancer.

TP008 / #961

Topic: *AS06. Tumor Types / AS06b. Cervical Cancer*

TROFUSE-020/GOG-3101/ENGOT-CX20: A PHASE 3, RANDOMIZED, ACTIVE-CONTROLLED, OPEN-LABEL, MULTICENTER STUDY COMPARING SACITUZUMAB TIRUMOTECAN MONOTHERAPY VS TREATMENT OF PHYSICIAN'S CHOICE AS SECOND-LINE TREATMENT FOR RECURRENT/METASTATIC CERVICAL CANCER

Ritu Salani[1], Lin Zhongqiu[2], Shin Nishio[3], Ana Oaknin[4], Jean-Emmanuel Kurtz[5], Giorgio Valabrega[6], Stefania Canova[7], M. Valeria Cáceres[8], Philipp Harter[9], Lucy Gilbert[10], Azmat H. Sadozye[11], Lilian Arruda Do Rêgo Barros[12], Jung-Yun Lee[13], Toon Van Gorp[14], Ingrid Boere[15], Christian Marth[16], Radosław Mądry[17], Flora Zagouri[18], Linda Duska[19], Bradley Monk[20], Xin Tong Li[21], Agata M. Bogusz[21], Sarper Toker[21], Kristina Lindemann[22]
[1]Department of Obstetrics and Gynecology, University of California Los Angeles, Los Angeles, United States of America, [2]Sun Yat-sen Memorial Hospital, Sun Yat-sen University, Guangzhou, China, [3]Department of Obstetrics and Gynecology, Kurume University, Fukuoka, Japan, [4]Gynaecologic Cancer Programme, Vall d'Hebron Institute of Oncology (VHIO), Hospital Universitari Vall d'Hebron, Vall d'Hebron Barcelona Hospital Campus, Barcelona, Spain, [5]Department of Medical and Surgical Oncology & Hematology, ICANS, Strasbourg, France, [6]AO Ordine Mauriziano Torino and Department of Oncology, University of Torino, Torino, Italy, [7]Medical Oncology Unit, Fondazione IRCCS San Gerardo dei Tintori, Monza, Italy, [8]Department of Medical Oncology, Instituto de Oncología Ángel H. Roffo, Buenos Aires, Argentina, [9]Department of Gynecology and Gynecologic Oncology, Ev. Kliniken Essen-Mitte, Essen, Germany, [10]Division of Gynecologic Oncology, McGill University Health Centre, Gerald Bronfman Department of Oncology, McGill University, Montreal, Quebec, Canada, [11]Beatson West of Scotland Cancer Centre, Gartnavel General Hospital, Glasgow, United Kingdom, [12]Núcleo de Pesquisa e Ensino da Rede São Camilo, Sao Paulo, Brazil, [13]Yonsei Cancer Center and Severance Hospital, Yonsei University College of Medicine, Seoul, Korea, Republic of, [14]Division of Gynaecological Oncology, University Hospital Leuven, Leuven Cancer Institute; and BGOG, Leuven, Belgium, [15]Department of Medical Oncology, Erasmus MC Cancer Institute, Erasmus University Medical Center, Rotterdam, Netherlands, [16]Department of Obstetrics and Gynecology, Medical University Innsbruck, Innsbruck, Austria, [17]Department of Oncology, Poznan University of Medical Sciences, Poznań, Poland, [18]Department of Clinical Therapeutics, Alexandra Hospital, Medical School, Athens, Greece, [19]University of Virginia School of Medicine, Charlottesville, United States of America, [20]Florida Cancer Specialists and Research Institute, West Palm Beach, United States of America, [21]Merck & Co., Inc., Rahway, United States of America, [22]Unit for Gynecological Oncology, Department of Oncological Surgery, Oslo University Hospital, Oslo, Norway; Faculty of Medicine, Institute of Clinical Medicine, University of Oslo; and NSGO-CTU, Oslo, Norway

Introduction: Sacituzumab tirumotecan (sac-TMT; formerly MK-2870/SKB264) is an antibody–drug conjugate comprising an anti-TROP2 antibody, hydrolytically-cleavable linker, and cytotoxic drug KL610023 (average drug/antibody ratio, 7.4). In an ongoing phase 1/2 study (MK-2870-001), sac-TMT monotherapy showed promising antitumor activity in participants with locally advanced unresectable/metastatic solid tumors refractory to standard therapies.

Objectives: This phase 3, randomized, open-label, multicenter study (NCT06459180) evaluates the efficacy and safety of sac-TMT monotherapy vs treatment of physician's choice (TPC) as second-line treatment in participants with recurrent/metastatic cervical cancer.

Methods: Eligible participants are aged ≥18 years with progressive recurrent/metastatic cervical cancer, measurable per RECIST v1.1 by investigator, and had received 1 line of platinum doublet chemotherapy (±bevacizumab) and anti–PD-1/anti–PD-L1 therapy as a part of cervical cancer regimens. Participants must provide tissue from a core/excisional biopsy of an unirradiated tumor lesion. Approximately 666 participants will be randomly assigned 1:1 to receive sac-TMT 4 mg/kg IV Q2W or TPC (pemetrexed 500 mg/m^2 IV Q3W; tisotumab vedotin 2 mg/kg IV Q3W; 3-week cycles of topotecan 1 or 1.25 mg/m^2 on days 1–5, vinorelbine 30 mg/m^2 on days 1 and 8, gemcitabine 1000 mg/m^2 on days 1 and 8; or 6-week cycles of irinotecan 100 or 125 mg/m^2 on days 1, 8, 15, and 22). Tumor imaging will be performed ≤28 days before treatment allocation/randomisation, then Q9W until week 54 and Q12W thereafter. The primary endpoint is OS; secondary endpoints include PFS by BICR, ORR, DOR, safety, time to deterioration, and PROs.

Current Status & Future Directions: Enrollment began Q3 2024. Results will determine the efficacy and safety of sac-TMT.

TP009 / #190

Topic: *AS06. Tumor Types / AS06c. Endometrial & Uterine Corpus Cancers*

SELECTIVE OMISSION OF ADJUVANT THERAPY IN POLE-MUTATED ENDOMETRIAL CANCER: THE SIMPLE TRIAL

Seongmin Kim[1], Jae-Hoon Kim[2], Jae Yun Song[1]
[1]73 Goryeodae-ro, Seongbuk-gu, Seoul 02841, Korea, Seoul, Korea, Republic of, [2]Yonsei University Gangnam Severance Hospital, Seoul, Korea, Republic of

Introduction: POLE-ultramutated endometrial cancer is associated with excellent prognosis. While recent guidelines have suggested de-escalation of adjuvant therapy in early-stage POLEmut cases, high-grade histology and stage II–III disease remain clinical gray zones. This study aims to assess real-world patterns of adjuvant therapy omission and outcomes in POLEmut patients within a molecularly classified prospective cohort.

Objectives: The primary objective is to determine the proportion of patients with POLE-mutated endometrial cancer who do not receive adjuvant therapy. Secondary objectives include recurrence rate, survival outcomes, and treatment-related toxicities.

Methods: This is a prospective, multicenter observational cohort study including patients with stage IA3–III endometrial cancer. All participants undergo molecular classification for POLE, p53, and MMR status. POLE mutations are detected by droplet digital PCR (ddPCR), and MMR and p53 status are assessed via immunohistochemistry (IHC). Treatment decisions, including omission of adjuvant therapy, are made at the discretion of treating physicians. Toxicities will be reviewed retrospectively using CTCAE v5.0 criteria.

Current Status & Future Directions: The study has been approved by the Scientific Review Board (SRB) of the Korean Gynecologic Oncology Group (KGOG), and IRB submissions are currently underway at participating institutions. Patient enrollment is scheduled to begin in the second half of 2025 across multiple centers in the capital region of South Korea. A total of 200 patients will be recruited.

TP010 / #487

Topic: *AS06. Tumor Types / AS06c. Endometrial & Uterine Corpus Cancers*

GOG-3119/ENGOT-EN29/TROFUSE-033: A PHASE 3, RANDOMIZED STUDY OF SACITUZUMAB TIRUMOTECAN PLUS PEMBROLIZUMAB VS PEMBROLIZUMAB ALONE AS FIRST-LINE MAINTENANCE THERAPY FOR MISMATCH REPAIR-PROFICIENT ENDOMETRIAL CANCER

Shibani Nicum[1], Christian Marth[2], Dearbhaile C. Collins[3], Jan Kümmel[4], Flora Zagouri[5], Yakir Segev[6], Maria Cristina Petrella[7], Heini J. Lassus[8], Keiichi Fujiwara[9], Jian Liu Wang[10], Chien-Hsing Lu[11], Atthapon Jaishuen[12], M. Valeria Cáceres[13], Ruffo Freitas-Junior[14], Sarah Crafton[15], Destin Black[16], Brian M. Slomovitz[17], Robert Orlowski[18], Stephan Kruger[18], Lili Yao[18], Bradley Monk[19]
[1]GTG-UK and Department of Oncology, University College London Cancer Institute, London, United Kingdom, [2]AGO-A and Department of Obstetrics and Gynecology, Medical University of Innsbruck, Innsbruck, Austria, [3]Cancer Trials Ireland and Department of Medical Oncology, Cork University Hospital, Cork, Ireland, [4]CEEGOG, University Hospital Ostrava, and Faculty of Medicine University of Ostrava, Department of Obstetrics and Gynecology, Ostrava, Czech Republic, [5]HeCOG and Department of Clinical Therapeutics, Alexandra Hospital, Medical School, Athens, Greece, [6]TRSGO and Gynecology Oncology Division, Department of Obstetrics and Gynaecology, Carmel Medical Center, Haifa, Israel, [7]MITO and Oncologia Medica Ginecologica, Azienda Universitaria Ospedaliera Careggi, Firenze, Italy, [8]NSGO and Department of Obstetrics and Gynecology, Helsinki University Hospital and University of Helsinki, Helsinki, Finland, [9]Department of Gynecologic Oncology, Saitama Medical University International Medical Center, Hidaka, Saitama, Japan, [10]Department of Obstetrics and Gynecology, Peking University People's Hospital, Beijing, China, [11]Department of Gynecology and Obstetrics, Taichung Veterans General Hospital, Taichung, Taiwan, [12]Division of Gynecologic Oncology, Department of Obstetrics and Gynecology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand, [13]Department of Medical Oncology, Instituto de Oncología Ángel H. Roffo, Buenos Aires, Argentina, [14]Universidade Federal de Goias, Faculdade de Medicina Goiania, Goias, Brazil, [15]GOG Foundation and Division of Gynecologic Oncology, Department of Obstetrics and Gynecology, West Penn Hospital, Allegheny Health Network, Pittsburgh, United States of America, [16]GOG Foundation and Department of Obstetrics and Gynecology, Willis-Knighton Cancer Center, Shreveport, United States of America, [17]GOG Foundation and Mount Sinai Medical Center, Miami Beach, United States of America, [18]Merck & Co., Inc., Rahway, United States of America, [19]GOG Foundation and Florida Cancer Specialists and Research Institute, West Palm Beach, United States of America

Introduction: Pembrolizumab plus chemotherapy then maintenance pembrolizumab is a standard of care regimen for primary advanced/recurrent endometrial cancer (EC). Most PFS events in pMMR EC occur 6–18 months after treatment initiation, suggesting a need for improved first-line maintenance therapies. Sac-TMT (SKB264/MK-2870) is an investigational ADC composed of a humanized anti–TROP2 monoclonal antibody, a hydrolytically and enzymatically cleavable linker, and the cytotoxic drug KL610023. TROP2 is expressed in EC and sac-TMT and pembrolizumab have complementary mechanisms of action. The phase 3 GOG-3119/ENGOT-en29/TroFuse-033 study (EU CT, 2024-519331-42) is evaluating first-line maintenance therapy with sac-TMT plus pembrolizumab vs pembrolizumab alone in advanced/recurrent pMMR EC.

Objectives: Primary endpoints are PFS per RECISTv1.1 by BICR and OS. Secondary endpoints include PFS2 per investigator (time from randomization to subsequent PD after new anticancer therapy or death due to any cause, whichever occurs first), safety, and PROs.

Methods: Adults with primary stage III (measurable) or stage IV or recurrent (measurable or nonmeasurable) pMMR EC per RECISTv1.1 by investigator and no prior systemic therapy (except 1 prior line of platinum-based [neo]adjuvant chemotherapy in the curative-intent setting) will receive 6 cycles of induction treatment with pembrolizumab, carboplatin, and paclitaxel (≤2 additional cycles of pembrolizumab allowed). After induction, participants are randomized 1:1 to maintenance sac-TMT 4mg/kg IV Q2W plus pembrolizumab 400mg Q6W or pembrolizumab alone Q6W for ≤14 cycles. Participants with PD confirmed by BICR during or after induction (ie, ineligible for maintenance therapy) may receive randomized subsequent treatment with sac-TMT plus pembrolizumab or sac-TMT alone.

Current Status & Future Directions: Enrollment begins in May 2025.

TP011 / #941

Topic: *AS06. Tumor Types / AS06c. Endometrial & Uterine Corpus Cancers*

RINATABART SESUTECAN MONOTHERAPY IN PATIENTS WITH ADVANCED ENDOMETRIAL CANCER: PART F OF THE PHASE 1/2 RAINFOL™-01 STUDY

Debra Richardson[1], Gottfried Konecny[2], Elizabeth Lee[3], Ira Weiner[4], Lyndsay J. Willmott[5], Justin Call[6], Jessica Thomes Pepin[7], Andrea Jewell[8], Cara Mathews[9], Leigh Seamon[10], Joseph Buscema[11], Bradley Monk[12], Elizabeth Guancial[13], Douglas Orr[14], Anton Melnyk[15], Michael Gillespie[16], Nurgul Kilavuz[16], Teng Jin Ong[16], Edward Kavalerchik[16], Noelle Cloven[17]
[1]Stephenson Cancer Center, University of Oklahoma Health Science Center/SCRI, Gynecologic Oncology Department, Oklahoma City, United States of America, [2]UCLA Health, Gynecologic Medical Oncology, Los Angeles, United States of America, [3]Dana-Farber Cancer Institute, Boston, United States of America, [4]Karmanos Cancer Institute, Detroit, United States of America, [5]Honor Health, Usor, Phoenix, United States of America, [6]Medical Oncology, START Mountain Region, West Valley City, United States of America, [7]Minnesota Oncology, Maplewood, United States of America, [8]University of Kansas Medical Center, Kansas City, United States of America, [9]Women and Infants Hospital, Legorreta Cancer Center, Alpert Medical School of Brown University, Medical Oncology, Providence, United States of America, [10]START Center for Cancer Care - Midwest, Grand Rapids, United States of America, [11]Arizona Oncology, Tucson, United States of America, [12]Florida Cancer Specialists and Research Institute, West Palm Beach, United States of America, [13]Florida Cancer Specialists and Research Institute, Internal Medicine, Medical Oncology/hematology, Sarasota, United States of America, [14]Mary Crowley Cancer Research, Dallas, United States of America, [15]Texas Oncology-Abilene, Abilene, United States of America, [16]Genmab AS, Princeton, United States of America, [17]Texas Oncology/Sarah Cannon Research Institute, Fort Worth, United States of America

Introduction: Endometrial cancer (EC) is the most prevalent gynecologic cancer in the United States; novel treatments are needed for patients who progress on current therapies. Rinatabart sesutecan (Rina-S®) is an antibody-drug conjugate targeting folate receptor alpha with a novel hydrophilic, protease-cleavable linker and topoisomerase I inhibitor exatecan payload. Efficacy and safety of Rina-S are under investigation in the multipart phase 1/2 RAINFOL™-01 trial (NCT05579366) for patients with locally advanced and/or metastatic solid tumors, including EC. In the dose-expansion phase of RAINFOL-01, Rina-S monotherapy administered every 3 weeks (Q3W) showed encouraging antitumor activity in patients who have received prior platinum-based chemotherapy and a programmed death-ligand 1 (PD-L1) inhibitor. Similarly, findings from dose-expansion cohort B2 showed a confirmed objective response rate (ORR) of

50% and a disease control rate of 100% with Rina-S 100 mg/m^2 in patients with heavily pretreated unresectable or metastatic EC.

Objectives: Part F of RAINFOL-01 will evaluate single-agent Rina-S 100 mg/m^2 Q3W in patients with advanced, recurrent, or metastatic EC. Primary endpoint: ORR per blinded central review. Secondary endpoints: duration of response, progression-free survival, overall survival, adverse events, and laboratory abnormalities.

Methods: Part F will enroll up to 100 eligible patients with advanced, recurrent, or metastatic EC that progressed after 1-3 lines of therapy. Prior therapies must include platinum chemotherapy and a PD-L1 inhibitor (Table). ORR will be evaluated using the Fisher exact test (2-sided; α=0.05).

Current Status & Future Directions: The trial is currently enrolling. Study outcomes may provide further insights into whether Rina-S could be a safe and efficacious treatment for patients with EC.

Table. Key Inclusion/Exclusion Criteria

Inclusion Criteria	Exclusion Criteria
• Confirmed advanced, recurrent, or metastatic EC • Measurable disease per RECIST v1.1 • Prior treatment: ○ 1-3 lines of therapy, including platinum chemotherapy and a PD-L1 inhibitor	• Uncontrolled diabetes mellitus • Documented history of a cerebral vascular event or cardiovascular disease • History of noninfectious interstitial lung disease/pneumonitis that required steroids for ≤2 years • Prior antitumor small molecule or antibody-based treatment without washout period • Hospitalization or clinical symptoms due to, or radiographic evidence of, gastrointestinal obstruction

EC, endometrial cancer; PD-L1, programmed death-ligand 1; RECIST v1.1, Response Evaluation Criteria in Solid Tumors, version 1.1.

TP012 / #940

Topic: *AS06. Tumor Types / AS06c. Endometrial & Uterine Corpus Cancers*

A PHASE 2 STUDY OF AVUTOMETINIB (VS-6766; DUAL RAF/MEK INHIBITOR) PLUS DEFACTINIB (FAK INHIBITOR) IN RECURRENT GYNECOLOGICAL CANCERS (DURAFAK)

Christina Washington[1], Tara Castellano[2], Carolyn Muller[3], Robert Holloway[4], Kathleen N. Moore[5]
[1]University of Oklahoma, Gynecologic Oncology, University of Oklahoma, United States of America, [2]Louisiana State University, Gynecologic Oncology, New Orleans, United States of America, [3]University of New Mexico, Gynecologic Oncology, Albuquerque, United States of America, [4]AdventHealth, Gynecologic Oncology, Orlando, United States of America, [5]University of Oklahoma, Gynecologic Oncology, Oklahoma City, United States Minor Outlying Islands

Introduction: Worldwide gynecological cancers account for approximately 16% of the cancer burden in women. Molecular analysis of endometrial, cervical, and ovarian cancers reveals RAS as a clinically significant indicator of disease state. Aberrant RAS signaling mediates tumor transformation through the RAF/MEK/ERK (MAPK) pathway. Single-agent inhibition of the MAPK pathway may result in chemoresistance through FAK activation, permitting tumor progression. The scientific rationale for the study design is based on the complementary anticancer mechanisms of action of Avutometinib (RAF/MEK inhibition) and defactinib (FAK inhibition).The combination of a Avutometinib and defactinib could significantly improve on single-agent MEK inhibitor activity due to the inhibition of both RAF and MEK and blockage of FAK-mediated adaptive resistance. Evidence from multiple clinical trials support the use of this combination in patients with RAS mutated gynecologic cancer.

Objectives: The primary endpoint is objective response rate. Key secondary endpoints include safety and tolerability, progression free survival, disease control rate, duration of response, and overall survival.

Methods: A phase 2, multicenter, clinical trial evaluating single stage exploratory trial will evaluate the therapeutic efficacy of Avutometinib + defactinib in RAS mutated, BRAF mutated (type I, II, and/or III), NF-1 (Neurofibromin-1) loss of function, and/or RAS activated gynecological cancers.

Current Status & Future Directions: There are currently 15 patients that have been enrolled. Based on the literature review of similar patient populations, ORR of at least 40% in endometrioid cancer patients, 25% in MOC patients, 25-30% in HGSOC patients, and 30% solid gynecological cancer patients will warrant future study.

TP013 / #1018

Topic: *AS06. Tumor Types / AS06d. Ovarian Cancer*

A PHASE 3, OPEN-LABEL RANDOMIZED TRIAL TO COMPARE RINATABART SESUTECAN VERSUS INVESTIGATOR'S CHOICE OF CHEMOTHERAPY IN PATIENTS WITH PLATINUM-RESISTANT OVARIAN CANCER: RAINFOL™-02 (ENGOT-OV86/GOG-3107)

Angeles Alvarez Secord[1], Elizabeth Lee[2], Michael Sundborg[3], Destin Black[4], David Starks[5], Edwin Alvarez[6], David Spigel[7], Noelle Cloven[8], Lynne Knowles[9], Anton Melnyk Jr.[10], William Winter Iii[11], Michael Mccollum[12], Peter Lim[13], Robert Neff[14], David O'Malley[15], Felix Hilpert[16], Dagmara Klasa-Mazurkiewicz[17], María Quindós Varela[18], Laurence Gladieff[19], Beryl Manning-Geist[20], Bhavana Pothuri[21], Ibrahima Soumaoro[22], Yan Liu[22], Christian Marth[23]
[1]Duke Cancer Institute, Durham, United States of America, [2]Dana-Farber Cancer Institute, Department Of Medical Oncology, Boston, United States of America, [3]FirstHealth Outpatient Cancer Center, Pinehurst, United States of America, [4]GOG Foundation and Department of Obstetrics and Gynecology, Willis-Knighton Cancer Center, Shreveport, United States of America, [5]Avera Cancer Institute, Sioux Falls, United States of America, [6]UCSF Helen Diller Family Comprehensive Cancer Center, San Francisco, United States of America, [7]SCRI Oncology Partners, Nashville, United States of America, [8]Texas Oncology, P.A., Fort Worth, United States of America, [9]Texas Oncology - Austin Central, Austin, United States of America, [10]Texas Oncology - Abilene, Abilene, United States of America, [11]Northwest Cancer Specialists, P.C. dba Compass Oncology - Rose Quarter Cancer Center, Portland, United States of America, [12]Virginia Oncology Associates, Norfolk, United States of America, [13]The Center of Hope, Reno, United States of America, [14]St. Elizabeth Healthcare - Edgewood, Edgewood, United States of America, [15]The Ohio State University and the James Comprehensive Cancer Center Columbus, Columbus, United States of America, [16]Mammazentrum Hamburg am Krankenhaus Jerusalem, Hamburg, Germany, [17]Uniwersyteckie Centrum Kliniczne w Gdańsku, Gdańsku, Poland, [18]Complejo Hospitalario Universitario A Coruña, La Coruña, Spain, [19]Institut Universitaire du Cancer de Toulouse (IUCT) Oncopole, Toulouse Cedex, France, [20]Winship Cancer Institute of Emory University, Atlanta, United States of America, [21]Laura & Isaac Perlmutter Cancer Center, NYU Langone Health, and GOG Foundation, Departments Of Obstetrics/gynecology And Medicine, Division Of Gynecologic Oncology, New York, Philadelphia, United States of America, [22]Genmab AS, Princeton, United States of America, [23]Medical University of Innsbruck, Ago And Department For Gynecology And Obstetrics, Innsbruck, Austria

Introduction: A substantial unmet need persists for effective and well-tolerated treatments for patients with platinum-resistant ovarian cancer (PROC). Rinatabart

sesutecan (Rina-S®) is an antibody-drug conjugate targeting folate receptor alpha with a topoisomerase I inhibitor exatecan, payload. Rina-S 120 mg/m^2 every 3 weeks (Q3W) showed encouraging antitumor activity in patients with heavily pretreated PROC in dose-expansion cohort B1 of a phase 1/2 study (RAINFOL™-01, NCT05579366), with a confirmed objective response rate (ORR) of 55.6% (95% CI, 30.8-78.5), including 4 complete responses (2 confirmed), and a well-tolerated safety profile.

Objectives: RAINFOL-02 (ENGOT-OV86/GOG-3107; NCT06619236) is an open-label, randomized, phase 3 study comparing Rina-S versus investigator's choice (IC) chemotherapy in patients with PROC. The primary endpoint of this study is progression-free survival. Secondary endpoints include overall survival, ORR, duration of response, CA-125 response, adverse events, and time to second disease progression. Overall change from baseline and time to deterioration in Global Health Status/Quality of Life, and patient-reported outcomes, will also be assessed.

Methods: The study will enroll ~530 patients with platinum-resistant, high-grade serous or endometrioid epithelial OC, primary peritoneal cancer, or fallopian tube cancer (**Table**). Patients will be randomized 1:1 to Rina-S 120 mg/m^2 IV Q3W or IC chemotherapy (paclitaxel, topotecan, pegylated liposomal doxorubicin, or gemcitabine). Follow-up visits are planned every 12 weeks for up to ~1 year after the treatment period.

Table. Key Inclusion and Exclusion Criteria for RAINFOL-02

Inclusion Criteria	Exclusion Criteria
• Patients with histologically or cytologically confirmed high-grade serous or endometrioid epithelial OC, primary peritoneal cancer, or fallopian tube cancer • Received 1-4 prior lines of therapy, including: – Platinum chemotherapy – Bevacizumab – PARP inhibitor (if applicable) – MIRV (if eligible) • Platinum-resistant disease defined as: – Patients who received ≥4 cycles of first-line platinum-based therapy, had a response, and then progressed 91-183 days after the last dose – Patients who received 2-4 lines of platinum-based therapy and had disease progression <183 days after the last dose	• Patients with primary platinum-refractory disease, defined as – OC that did not respond to a first-line platinum-containing regimen – OC that progressed ≤91 days after the last dose of a first-line platinum-containing regimen • History of another malignancy within ≤3 years or evidence of residual disease • Known active central nervous system metastases or carcinomatous meningitis

MIRV, mirvetuximab soravtansine; OC, ovarian cancer; PARP, poly-ADP ribose polymerase.

Current Status & Future Directions: The study is currently enrolling. Study outcomes may provide further insights into whether Rina-S could be a safe and efficacious treatment for patients with PROC.

TP014 / #750

Topic: *AS06. Tumor Types / AS06d. Ovarian Cancer*

OVATION-3: A RANDOMIZED PHASE III TRIAL EVALUATING THE SAFETY AND EFFICACY OF INTRAPERITONEAL IL-12 GENE THERAPY ADMINISTERED IN COMBINATION WITH STANDARD NEOADJUVANT AND ADJUVANT CHEMOTHERAPY IN NEWLY DIAGNOSED PATIENTS WITH ADVANCED EPITHELIAL OVARIAN CANCER

Premal Thaker[1], Christopher Darus[2], Megan Indermaur[3], Melanie Bergman[4], Charles Leath Iii[5], Douglas Faller[6], Lauren Musso[6], Stacy Lindborg[6], Khursheed Anwer[6], Kristin Longobardi[6], Melanie Quintana[7], Giorgio Paulon[7], Amir Jazaeri[8], William Bradley[9]
[1]Washington University School of Medicine, St. Louis, United States of America, [2]Earle A. Chiles Research Institute, Providence Cancer Institute, Portland, United States of America, [3]Women's Care Florida, St. Petersberg, United States of America, [4]Providence Sacred Heart, Spokane, United States of America, [5]University of Alabama, Birmingham, United States of America, [6]IMUNON, Lawrenceville, United States of America, [7]Berry Consultants, Austin, United States of America, [8]The University of Texas MD Anderson Cancer Center, Department Of Gynecologic Oncology And Reproductive Medicine, Houston, United States of America, [9]Froedtert Hospital & Medical College of Wisconsin, Milwaukee, United States of America

Introduction: IMNN-001, an IL-12 DNA-gene therapy nanoparticle formulated with a synthetic lipopolymer carrier, showed a favorable benefit/risk ratio when administered intraperitoneally (IP) in combination with Neo and Adjuvant IV chemotherapy (N/ACT) in women with advanced Epithelial Ovarian Cancer (EOC). In the OVATION-2 randomized phase 2 study, IMNN-001+SoC N/ACT demonstrated a clinically meaningful numerical OS benefit of 13 months (mo) vs N/ACT alone (46 vs 33 mo; HR 0.69). In the PARPi-treated subgroup of patients, OS HR was 0.38 (NE vs 37.1 mo). Local delivery of IL-12 with IMNN-001 was safe, with no serious immune-related adverse events. Herein, we present the OVATION-3 Phase 3 trial (NCT06915025), designed to confirm the OS benefit and safety of IMNN-001+SoC N/ACT for advanced EOC patients.

Objectives: The 500-patient planned sample will provide >95% power for the OS primary endpoint. Secondary endpoints include Chemotherapy Response Score, Surgical Response Score, ORR, and QoL. Exploratory endpoints include IMNN-001's local and systemic immune effects and ctDNA analysis.

Methods: Patients from ≈50 sites in Canada and USA will be randomized 1:1 to receive SoC N/ACT±IMNN-001, followed by olaparib or niraparib maintenance if HRD. Newly-diagnosed FIGO stage IIIC and IV high-grade non-mucinous EOC patients who are candidates for N/ACT and ECOG 0 – 2 will be eligible and stratified per HRD status and stage. Patients will receive three 21-day cycles of CT before and after interval

cytoreduction surgery. IMNN-001 (100 mg/m^2 IP) will be administered weekly through the last CT cycle for a total of 17 treatments.

Current Status & Future Directions: The trial will open in May 2025

TP015 / #962

Topic: *AS06. Tumor Types / AS06d. Ovarian Cancer*

PART C OF RAINFOL™-01: A PHASE 1/2 STUDY OF SINGLE-AGENT RINATABART SESUTECAN IN PATIENTS WITH ADVANCED AND/OR METASTATIC PLATINUM-RESISTANT OVARIAN CANCER

Elizabeth Lee[1], Justin Call[2], Ira Winer[3], Oladapo Yeku[4], Debra Richardson[5], Leigh Seamon[6], Erika Hamilton[7], Noelle Cloven[8], Jian Zhang[9], Edward Kavalerchik[10], Bradley Monk[11]

[1]Dana-Farber Cancer Institute, Department Of Medical Oncology, Boston, United States of America, [2]Medical Oncology, START Mountain Region, West Valley City, United States of America, [3]Karmanos Cancer Institute, Detroit, United States of America, [4]Massachusetts General Hospital, Boston, United States of America, [5]Gynecologic Oncology Department, Stephenson Cancer Center, University of Oklahoma Health Sciences Center/Sarah Cannon Research Institute, Oklahoma City, United States of America, [6]START Center for Cancer Care - Midwest, Grand Rapids, United States of America, [7]Sarah Cannon Research Institute, Nashville, United States of America, [8]Texas Oncology/Sarah Cannon Research Institute, Fort Worth, United States of America, [9]Phase I Unit, Fudan University Shanghai Cancer Center, Medicinal Chemistry & Bioinformatics, Shanghai, China, [10]Genmab AS, Princeton, United States of America, [11]Florida Cancer Specialists and Research Institute, West Palm Beach, United States of America

Introduction: The prognosis for patients with platinum-resistant ovarian cancer (PROC) is typically poor, with a median survival duration of <1 year. Rinatabart sesutecan (Rina-S®) is an antibody-drug conjugate targeting folate receptor alpha (FRα) with a novel hydrophilic protease-cleavable linker and a topoisomerase I inhibitor, exatecan. In Part A of the phase 1/2 RAINFOL™-01 study (NCT05579366), Rina-S showed antitumor activity and manageable safety in patients with pretreated ovarian cancer (OC) or endometrial cancer; the most common adverse events were cytopenias and low-grade gastrointestinal events. In Part B cohort 1, Rina-S 120 mg/m^2 every 3 weeks (Q3W) showed encouraging antitumor activity in patients with heavily pretreated PROC, with a confirmed objective response rate (ORR) of 55.6% (95% CI, 30.8-78.5); responses were observed regardless of FRα expression, with no new safety signals.

Objectives: Part C of RAINFOL-01 will evaluate single-agent Rina-S 120 mg/m^2 Q3W in patients with heavily pretreated PROC. Primary endpoint: ORR. Secondary endpoints: duration of response, progression-free survival, overall survival, CA-125 response, and adverse events.

Methods:

Table. Key Inclusion and Exclusion Criteria

Inclusion Criteria	Exclusion Criteria
• High-grade serous OC, primary peritoneal cancer, or fallopian tube cancer • Patients with 1 line of platinum-based therapy (≥4 cycles) and must have either had a response or had non-measurable disease at the start of platinum-based therapy, and then progressed between 91-183 days after last dose • Received 1 to 3 prior lines of therapy or 1 to 4 prior lines of therapy if MIRV was the last line of therapy (if eligible) – Received prior bevacizumab – Received prior PARP inhibitor (if applicable) • ECOG PS 0-1 • Measurable disease per RECIST v1.1	• Patients with primary platinum-refractory disease, defined as – OC that did not respond to a first-line platinum-containing regimen – OC that progressed ≤91 days after last dose of a first-line platinum-containing regimen • History of another malignancy within ≤3 years or evidence of residual disease • Known active central nervous system metastases or carcinomatous meningitis

ECOG PS, Eastern Cooperative Oncology Group performance status; MIRV, mirvetuximab soravtansine; OC, ovarian cancer; PARP, poly-ADP ribose polymerase; RECIST v1.1, Response Evaluation Criteria in Solid Tumors, version 1.1.

Part C will enroll up to 100 eligible patients with platinum-resistant, high-grade serous OC who have received 1-3 prior lines of therapy. Prior therapies can include bevacizumab, PARP inhibitors, or mirvetuximab soravtansine (Table). Patients will be treated with single-agent Rina-S 120 mg/m^2 IV Q3W.

Current Status & Future Directions: Part C is currently enrolling. Study outcomes may provide further insights on whether Rina-S could be a safe and efficacious treatment for patients with PROC.

TP016 / #425

Topic: *AS06. Tumor Types / AS06d. Ovarian Cancer*

REJOICE-OVARIAN02: A PHASE 1B/2 STUDY OF RALUDOTATUG DERUXTECAN WITH OTHER ANTICANCER AGENTS IN PARTICIPANTS WITH RELAPSED OVARIAN CANCER AFTER PLATINUM-BASED CHEMOTHERAPY

Ronnie Shapira-Frommer[1], Justin Call[2], Debra Richardson[3], Ora Rosengarten[4], Ruth Perets[5], Antonio González Martín[6], Marta Gil-Martin[7], Luis Manso Sánchez[8], Lucy Gilbert[9], Rebecca Redman[10], Paul Johannet[11], Rebecca Kristeleit[12], Rowan Miller[13], Susana Banerjee[14], Stephanie Lheureux[15], Tarrik Zaid[16], Qing Zhao[17], Sandra Re[18], Carmen Gonzalez[19], Ana Oaknin[20]
[1]Oncology Department, Sheba Medical Center, Ramat-Gan, Tel Aviv District, Israel, [2]Medical Oncology, START Mountain Region, West Valley City, United States of America, [3]Gynecologic Oncology Department, Stephenson Cancer Center, University of Oklahoma Health Science Center/SCRI, Oklahoma City, United States of America, [4]Oncology Department, Shaare Zedek Medical Center, Jerusalem, Israel, [5]Oncology Department, Rambam Health Care Campus, Haifa, Israel, [6]Medical Oncology Department, Cancer Center Clínica Universidad de Navarra, Madrid, Spain, [7]Medical Oncology, Institut Català d'Oncologia L'Hospitalet, Barcelona, Spain, [8]Medical Oncology Division, Hospital Universitario 12 de Octubre, Madrid, Spain, [9]Research Institute, McGill University Health Centre, Gerald Bronfman Department of Oncology, McGill University, Montreal, Canada, [10]The University of Louisville, Brown Cancer Center, Louisville, United States of America, [11]Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, United States of America, [12]Department of Oncology, Guy's & St Thomas' NHS Foundation Trust, London, United Kingdom, [13]Medical Oncology, Barts Health NHS Trust, London, United Kingdom, [14]Gynaecology Department, Royal Marsden NHS Foundation Trust and Institute of Cancer Research, London, United Kingdom, [15]Division of Medical Oncology and Hematology, Princess Margaret Cancer Centre, Toronto, Canada, [16]Department of Obstetrics and Gynecology, Houston Methodist Hospital and Weill Cornell Medical College, Houston, United States of America, [17]Medical Oncology, Merck & Co., Inc., Rahway, United States of America, [18]Oncology Clinical Development, Daiichi Sankyo, Inc., Basking Ridge, United States of America, [19]Medical Oncology, MSD, Madrid, Spain, [20]Medical Oncology Service, Vall d'Hebron Institute of Oncology, Vall d'Hebron Barcelona Hospital Campus, Barcelona, Spain

Introduction: Cadherin-6 is overexpressed in several cancers, including ovarian cancer (OC). Raludotatug deruxtecan (R-DXd) is an antibody-drug conjugate consisting of a humanized anti–cadherin-6 antibody, an enzymatically cleavable peptide linker, and a cytotoxic topoisomerase I inhibitor (target drug-to-antibody ratio, 8). In a first-in-human study (NCT04707248), R-DXd monotherapy showed promising antitumor activity and

manageable safety in participants with recurrent OC. We describe the phase 1b portion of a phase 1b/2, open-label, dose-escalation study (REJOICE-Ovarian02; NCT06843447) to assess safety, tolerability, and preliminary antitumor activity of R-DXd combined with carboplatin or paclitaxel in participants with platinum-sensitive recurrent OC (PSOC) or with bevacizumab in participants with platinum-resistant recurrent OC (PROC).

Objectives: Primary endpoints are DLTs, AEs, and treatment discontinuations due to AEs. The secondary endpoint is ORR.

Methods: The phase 1b portion will enroll ~78 participants with high-grade serous epithelial ovarian, primary peritoneal, or fallopian tube cancer who have relapsed disease after 1–3 prior lines of therapy and had progressed ≥6 months (PSOC) or <6 months (PROC) after the last dose of platinum-based therapy. Participants must have measurable disease per RECIST version 1.1, ECOG PS of 0 or 1, and adequate organ function. Individuals with primary platinum-refractory OC are ineligible. Participants are enrolled into different cohorts (**Table**). Dose escalation is done to determine the maximum tolerated dose based on DLTs using the Bayesian optimal interval design. Treatment with R-DXd or R-DXd + bevacizumab continues until disease progression, unacceptable toxicity, or participant withdrawal.

Disease Setting	Cohort	Treatment
PSOC	Cohort A-1 arm 1	R-DXd + carboplatin
PSOC	Cohort A-1 arm 2	R-DXd + paclitaxel
PROC	Cohort B-1	R-DXd + bevacizumab

Current Status & Future Directions: Enrollment is ongoing. Results will be used to determine recommended phase 2 doses.

TP017 / #473

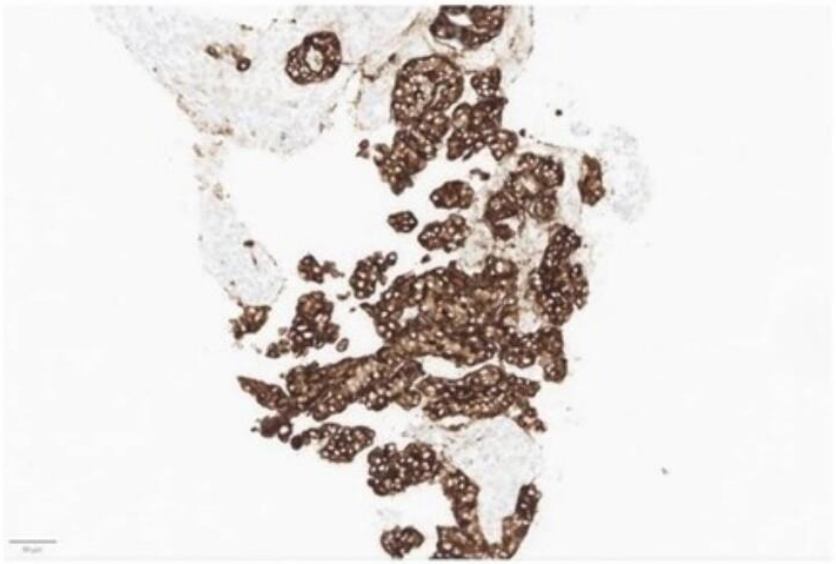
Topic: *AS06. Tumor Types / AS06d. Ovarian Cancer*

A PHASE 1/2 STUDY OF UBAMATAMAB (REGN4018) IN LOW-GRADE SEROUS OVARIAN CANCER COHORT

Els Van Nieuwenhuysen[1], Florence Joly[2], Judith Michels[3], Anna Reyners[4], Erika Hamilton[5], Oladapo Yeku[6], Crystal Stephens[7], Suk-Young Yoo[7], Bin Wang[7], Jurriaan Brouwer-Visser[7], Gloria Huang[7], Lindsay Joseph[7], Brigid Barnes[7], David Knorr[7], Israel Lowy[7], Thomas Uldrick[7], Elizabeth Miller[7]
[1]Leuven Cancer Institute, Leuven, Belgium, [2]Centre François Baclesse, Caen, France, [3]Institute of Cancer Gustave Roussy, Villejuif, France, [4]University Medical Center Groningen, University of Groningen, Groningen, Netherlands, [5]Sarah Cannon Research Institute, Nashville, United States of America, [6]Massachusetts General Hospital, Boston, United States of America, [7]Regeneron Pharmaceuticals, Inc., Tarrytown, United States of America

Introduction: Ubamatamab is a MUC16×CD3 bispecific antibody that bridges MUC16 on tumour cells and CD3 on T cells to promote T-cell–mediated cytotoxicity. In a first-in-human study (NCT03564340), ubamatamab demonstrated an acceptable safety profile and durable clinical activity in recurrent ovarian cancer, including low-grade serous ovarian cancer (LGSOC), both of which have high levels of MUC16 expression **(Figure 1)**. Here, we describe an LGSOC-specific expansion cohort.

Figure 1. Example of MUC16 Immunohistochemistry in LGSOC, 100% of cells express MUC16



LGSOC, Low-Grade Serous Ovarian Cancer; MUC16, Mucin 16.

Objectives: Primary endpoint: ORR (RECIST 1.1). Secondary endpoints include safety, PK, patient-reported outcomes and further efficacy assessments.

Methods: In the LGSOC-specific cohort, patients who have received ≥1 line of platinum-containing therapy and have relapsed or progressed after the most recent line of therapy will receive ubamatamab 800 mg IV 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.

Current Status & Future Directions: As of April 2025, 19 patients with LGSOC have been enrolled in the study. Initial data analysis of the LGSOC-specific cohort is expected by March 2027. Insights gained from the efficacy and safety of ubamatamab in patients with LGSOC from this cohort may further validate MUC16 as a novel therapeutic target for LGSOC.

TP018 / #731

Topic: *AS06. Tumor Types / AS06d. Ovarian Cancer*

EFFICACY OF DISITAMAB VEDOTIN, AK104, AND BEVACIZUMAB IN HER2-POSITIVE RECURRENT OVARIAN CLEAR CELL CANCER: PHASE 2 DAB-OCCC TRIAL

Dan Xie, Yanan Lu, Yuting Lai, Dongyan Wang, Yichun Xing, Hui Li, Miaofang Wu, Jing Li
Sun Yat-sen Memorial Hospital, Sun Yat-sen University, Guangdong Province, China

Introduction: Recurrent ovarian clear cell carcinoma (OCCC) has poor outcomes due to chemoresistance and HER2-driven aggressiveness. Disitamab vedotin (DV), an anti-HER2 ADC, provides targeted cytotoxicity and immune modulation. We hypothesized that combining DV, AK104 (a PD-1/CTLA-4 bispecific antibody), and bevacizumab could improve outcomes in OCCC.

Objectives: The primary endpoint was objective response rate (ORR). The secondary endpoints included disease control rate (DCR), progression-free survival (PFS), overall survival (OS), time to response (TTR), and safety.

Methods: This ongoing phase II, multicenter, single-arm, investigator-initiated trial enrolls patients with recurrent or persistent HER2-positive (IHC ≥1+) OCCC and a platinum-free interval ≤6 months or progression after platinum therapy. Eligible patients received DV (2.5mg/kg), AK104 (10mg/kg) and bevacizumab (15mg/kg) intravenously in 21-day cycles.The study uses Simon's two-stage design, proceeding to stage two if ≥2 responses are observed among the first 17-patient stage. Categorical and continuous variables will be summarized using counts (%) and descriptive statistics, respectively.

Current Status & Future Directions: As of April 20, 2025, 16 patients were enrolled, with 13 evaluable for efficacy. The confirmed ORR was 46.2% (n=6; 95% CI: 19.2–74.9%), all partial responses. The 6-month duration of response rate was 74.1% (95% CI: 39.1–90.9%). Stable disease was observed in 4 patients (44%) and progressive disease in 2 patients (7.7%), yielding a DCR of 51.4%. Treatment-related adverse events (TRAEs) occurred in 84.6% (n=11), with grade 3 events in 38.5% (n=5), including elevated transaminases (15.4%), granulocytopenia (7.7%), hyperglycemia (7.7%), and hypokalemia (7.7%). No grade ≥4 TRAEs or treatment-related deaths occurred. One patient (7.7%) required dose reduction due to TRAEs.