Abstracts

2022-LBA-325-ESGO PATIENTS WITH NEWLY DIAGNOSED OVARIAN CANCER TREATED WITH MAINTENANCE RUCAPARIB: EXPLORATORY BIOMARKER ANALYSIS FROM THE PHASE 3 ATHENA-MONO STUDY (GOG-3020/ENGOT-OV45; NCT03522246)

1 Anna Oaknin, 2 Rebecca S Kistleren, 3 Haider S Mahdii, 4 Myong C Chad Lim, 5 Bacco de Vivo, 6 Erin A Salinas, 7 Michelle K Wilson, 8 Michalis I Liostos, 9 Alessandro D Santi, 10 Diane M Provencer, 11 Fatu Demirkiran, 12 Lyndsay J Williott, 13 Anita M Chudecka-Glaz, 14 Thomas J Herzog, 15 Mario E Beiner, 16 Larry J Copeland, 17 Iain A McNeish, 18 Kevin K Lin, 19 Bradley J Monk. 20 Gynecologic Cancer Programme, Vall d’Hebron Institute of Oncology (VHIO), Hospital Universitari Vall d’Hebron, Vall d’Hebron Barcelona Hospital Campus, Barcelona, Spain; 21 Department of Oncology, Guy’s and St Thomas’ NHS Foundation Trust, London, UK; 22 Department of Obstetrics and Gynecology, Cleveland Clinic, Cleveland, OH; 23 Current location: Department of Obstetrics, Gynecology and Reproductive Sciences, University of Pittsburgh, Pittsburgh, PA; 24 Gynecologic Oncology, National Cancer Center Korea, Goyang-si, Gyeonggi-do, Republic of Korea, Korea, Republic of; 25 Department of Oncology, San Bartolo General Hospital, Azienda ULSS Berica, Vicenza, Italy; 26 Department of Gynecologic Oncology, Northwest Cancer Specialists PC, Vancouver, WA; 27 Department of Cancer and Blood, Auckland City Hospital, Auckland, New Zealand; 28 Department of Clinical Therapeutics, National and Kapodistrian University of Athens, Alexander Hospital, Athens, Greece; 29 Department of Obstetrics and Gynecology, Yale University School of Medicine, New Haven, CT; 30 Department of Obstetrics-Gynecology, Centre hospitalier de l’Université de Montréal (CHUM), Institut du cancer de Montréal, Montréal, QC, Canada; 31 Gynecologic Oncology Department, Medical Faculty, Istanbul University, Cerrahpasa, Istanbul, Turkey; 32 Arizona Center for Cancer Care, University of Arizona College of Medicine, Creighton University School of Medicine, Phoenix, AZ; 33 Department of Gynecologic Surgery and Gynecological Oncology for Adults and Adolescents, Pomeranian Medical University, Szczecin, Poland; 34 Department of Gynecologic Oncology, University of Cincinnati, Cincinnati, OH; 35 Gynecology-Oncology Department, Meir Medical Center, Kfar-Saba, Israel; 36 Department of Gynecologic Oncology, James Cancer Hospital and Solove Research Institute, The Ohio State University, Columbus, OH; 37 Department of Surgery and Cancer, Imperial College London, London, UK; 38 Molecular Diagnostics, Clovis Oncology, Inc., Boulder, CO; 39 GOG Foundation, HonorHealth Research Institute, University of Arizona College of Medicine, Creighton University School of Medicine, Phoenix, AZ

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Introduction In ATHENA-MONO, first-line (1L) maintenance treatment with rucaparib improved progression-free survival (PFS) versus placebo in patients with ovarian cancer (OC), regardless of molecular characteristics (Monk et al. J Clin Oncol. 2022). This exploratory analysis evaluated the PFS benefit of 1L maintenance rucaparib in subgroups defined by genomic biomarkers of homologous recombination deficiency, including homologous recombination repair (HRR) gene mutations, zygosity, and germline/somatic status.

Methods Patients with high-grade OC who underwent cytoreductive surgery and completed 1L platinum-doublet chemotherapy with a partial or complete response were randomised 4:1 to oral rucaparib 600 mg BID or placebo. Mutations in BRCA1, BRCA2, and 28 other genes in the HRR pathway (Coleman et al. Lancet. 2018), and zygosity status, were identified via next-generation sequencing of tumor tissues (Foundation Medicine). BRCA germline/somatic status were determined by germline sequencing (Ambry Genetics). The primary endpoint was investigator-assessed PFS per RECIST.

Results Deleterious mutations in BRCA1 and BRCA2 were detected in 13.9% (75/538) and 7.4% (40/538) of patients, respectively. PFS was longer with rucaparib compared with placebo in both BRCA1 (HR=0.39; 95% CI=0.14–1.08) and BRCA2 (HR=0.46; 95% CI=0.13–1.69) subgroups. Rucaparib PFS benefit was observed regardless of BRCA mutation type: short variants (frameshift, nonsense, splice site, missense) or large structural events (homozygous deletions, large rearrangements). BRCA mutations were further classified by germline (12.6%; 68/538), somatic (6.1%; 33/538), or unknown (2.6%; 14/538). PFS was longer with rucaparib compared with placebo in germline (HR=0.33; 95% CI=0.10–1.12) and somatic (HR=0.65; 95% CI=0.18–2.39) BRCA subgroups. Deleterious mutations in non-BRCA HRR genes were detected in 11.2% (60/538) of patients, with a PFS benefit of rucaparib versus placebo (HR=0.59; 95% CI=0.24–1.43).

Conclusions Exploratory biomarker analyses confirmed benefit with 1L maintenance rucaparib in patients with advanced OC harbouring different types of deleterious mutations in BRCA and non-BRCA HRR genes.

2022-LBA-414-ESGO PRELIMINARY CLINICAL OUTCOME OF ADP-A2M4CD8, A NEXT-GENERATION AUTOLOGOUS T-CELL RECEPTOR T-CELL THERAPY, IN PATIENTS WITH ADVANCED EPITHELIAL OVARIAN CANCER

1 Kathleen Moore, 2 Adam Asch, 3 Victor Moreno, 4 Emiliano Calvo, 5 Marcus Butler, 6 Jon Zigazagoitia, 7 David Hong, 8 Ahmed Galan, 9 Lorena Ostios, 10 Maria de Miguel, 11 Quan Lin, 12 Thejo Annareddy, 13 Francine Brophy, 14 Marisa Rosenberg, 15 Theresa Seiders, 16 RevaShnee Naidoo, 17 Natalie Bath, 18 Jesse Nory, 19 Jeffrey Clarke. 20 U2 Health Stephenson Cancer Center, Oklahoma City, OK; 21 START Madrid-FID, Madrid, Spain; 22 START Madrid-CiOC, Madrid, Spain; 23 Princess Margaret Cancer Centre, Toronto, ON, Canada; 24 Hospital Universitario 12 de Octubre, Madrid, Spain; 25 MD Anderson Cancer Center, Houston, TX; 26 Duke Cancer Center, Durham, NC; 27 Adaptimmune, Philadelphia, PA; 28 Adaptimmune, Abingdon, Oxfordshire, UK

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Introduction ADP-A2M4CD8, a next-generation specific peptide enhanced affinity receptor (SPEAR) T-cell therapy supplemented with a CD8α co-receptor, is being evaluated in the Phase 1 SURPASS trial (NCT04444589) in multiple solid tumours, including ovarian cancer. Promising anti-tumour activity, including a 36% overall response rate (1 complete response [CR], 7 partial responses [PR] in 22 evaluable patients; 2 August 2021 data cut-off) and a favourable benefit to risk profile were reported.1 We report preliminary anti-tumour activity in ovarian cancer and updated safety in all tumours.

Methods SURPASS is a first-in-human trial evaluating ADP-A2M4CD8 using a modified 3+3 design, with 2 dose cohorts and an expansion cohort.1 T-cells are collected by leukapheresis, transduced, and infused into the patient after lymphodepletion. Eligible patients express human leukocyte antigen (HLA)-A*02 with melanoma-associated antigen (MAGE)-A4-positive tumours. Patients with ovarian cancer must have received platinum-based chemotherapy and progressed ≤12 months post platinum therapy.

Results As of 1 August 2022, 14 patients with ovarian cancer had received 1.14–9.95×10⁹ transduced T-cells. Median age was 59 years (range, 40–75); median number of prior systemic therapy regimens was 4 (range, 2–8); median MAGE-A4 expression H-score was 237.5 (range, 95–300). Adverse events in the overall population were consistent with lymphodepletion chemotherapy or cellular therapy; similar safety results were seen in the ovarian cancer subgroup (table 1). There was 1 Grade 5 cytokine release syndrome. Best overall responses were 1 CR, 4 PR, 6 stable disease (SD), 2 progressive disease and 1 not evaluable, giving a 36% overall response rate and a 79% disease control rate (CR+PR+SD, figure 1).