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)

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10.1136/ijgc-2022-ESGO.1018

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

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10.1136/ijgc-2022-ESGO.1019

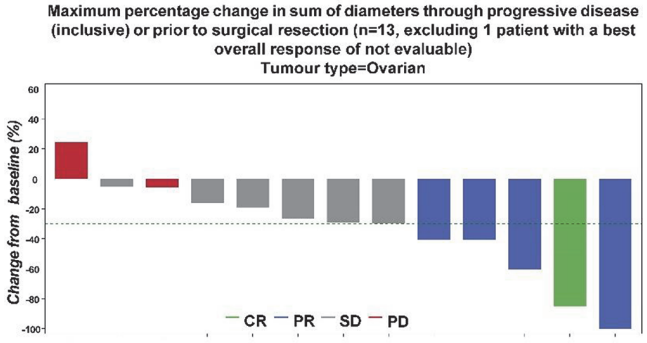
Introduction ADP-A2M4CD8, a next-generation specific peptide enhanced affinity receptor (SPEAR) T-cell therapy supplemented with a CD8α co-receptor, is being evaluated in the Phase 1 SURPASS trial (NCT04044859) in multiple solid tumours, including ovarian cancer. Promising anti-tumour activity, including 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 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 $1.14–9.95\times10^9$ 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).

Abstract 2022-LBA-414-ESGO Table 1 Adverse event (AE) summary

Preferred term	Serious AEs in ≥5% of patients overall, N=44	Serious AEs related to T-cell infusion in ≥5% of patients overall, N=44	Serious AEs in patients with ovarian cancer, N=14	Serious AEs related to T-cell infusion in patients with ovarian cancer, N=14
Any serious AE, n (%)	27 (61.4)	21 (47.7)	11 (78.6)	10 (71.4)
Cytokine release syndrome (CRS)	14 (31.8)	14 (31.8)	7 (50.0) [including 1 grade 5 event in a 60-year-old with large tumor burden in lungs and previous lung radiotherapy. Cause of death: pneumonia and CRS]	7 (50.0)
Hypoxia	3 (6.8)	3 (6.8)	3 (21.4)	3 (21.4)
Immune effector cell-associated neurotoxicity syndrome	3 (6.8)	3 (6.8)	1 (7.1)	1 (7.1)
Pyrexia	3 (6.8)	2 (4.5)	2 (14.3)	2 (14.3)
Preferred term	**AEs related to T-cell infusion in ≥12% of patients overall, N=44**	**AEs related to T-cell infusion in patients with ovarian cancer, N=14**		
Any AE	40 (90.9)	14 (100.0)		
Cytokine release syndrome	32 (72.7)	11 (78.6)		
Neutropenia/ neutrophil count decreased	13 (29.5)	4 (28.6)		
Anemia/RBC decreased	10 (22.7)	3 (21.4)		
Pyrexia	10 (22.7)	5 (35.7)		
Fatigue	9 (20.5)	4 (28.6)		
Leukopenia/WBC decreased	7 (15.9)	2 (14.3)		
Rash	7 (15.9)	3 (21.4)		
Thrombocytopenia/ platelet count decreased	7 (15.9)	2 (14.3)		
Dyspnoea	6 (13.6)	3 (21.4)		
Hypoxia	6 (13.6)	3 (21.4)		
Immune effector cell-associated neurotoxicity syndrome	6 (13.6)	1 (7.1)		
Pleural effusion	6 (13.6)	1 (7.1)		



Abstract 2022-LBA-414-ESGO Figure 1

Conclusions ADP-A2M4CD8 SPEAR T-cell therapy showed preliminary anti-tumour activity in heavily pre-treated patients with MAGE-A4+ advanced ovarian cancer, with tolerable emerging safety results. The trial now includes an anti-programmed death-ligand 1 combination treatment cohort. 1. Hong DS, et al. Ann Oncol. 2021;32(suppl5):540P.

2022-LBA-677-ESGO DISTRIBUTION AND PROGNOSTIC ROLE OF BRCA STATUS IN ELDERLY OVARIAN CANCER PATIENTS

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10.1136/ijgc-2022-ESGO.1020

Introduction Elderly patients with advanced ovarian cancer often receive suboptimal treatment with less radical surgery, due to the complexity and risks of primary debulking surgery (PDS). We know that complete resection is the most important independent factor affecting survival. There is an emerging role of BRCA status. BRCA mut patients are more chemosensitive while BRCA wt could better benefit of PDS. In this context it's important to evaluate the distribution of BRCA status in elderly patients and if its prognostic role is still maintained in this subgroup of patients.

Methods This is a retrospective single institution study evaluating patients with known germinal/somatic BRCA status. We are comparing clinical and surgical characteristics according to age groups. We are evaluating the prevalence of BRCA mut in the age groups, how it affects survival and chemosensitivity in order to understand if in elderly patients its prognostic role is still maintained

Results A total of 2089 patients were included in the analysis. Mean age of BRCAmut was 55.8 (SD=10.9) and 60.3 (SD=12) for BRCAwt ($p<0.0001$). The rate of BRCAmut decreases over age-range (figure 1). 1850 patients were stage IIIC-IV and older women were less likely submitted to PDS (from 62.1% for <50 y to 23.4% for ≥80 y), however the rate of complete resection was superimposable in all age