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% (75/558) 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.

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 (NCT0444859) 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. 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. 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 23.7 (range, 9.5–300). 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).