Abstract 2 Table 1

	BRCA mutant		ITT	
	Rucaparib (n=130)	Placebo (n=66)	Rucaparib (n=375)	Placebo (n=189)
Prespecified exploratory analyses				
Investigator-assessed TFST				
Median, mo	19.0	7.2	12.5	7.4
HR (95% CI); P value	0.29 (0.20–0.42); P<0.0001		0.43 (0.35–0.53); P<0.0001	
Investigator-assessed PFS2				
Median, mo	26.1	17.9	21.1	16.5
HR (95% CI); P value	0.44 (0.29–0.69); P=0.0003		0.62 (0.48–0.79); P=0.0001	
Investigator-assessed TSST				
Median, mo	NR	19.4	22.2	18.6
HR (95% CI); P value	0.49 (0.31–0.78); P=0.0024		0.70 (0.54–0.91); P=0.0064	
Post hoc exploratory analyses				
QA-PFS ^a				
Mean, mo	15.28	5.92	12.02	5.74
Mean difference (95% CI)	9.37 (6.65–11.85)		6.28 (4.85–7.47)	
Q-TWiST ^b				
Mean, mo	16.42	6.70	13.32	6.44
Expected mean difference (95% CI)	9.73 (7.10–11.94)		6.88 (5.71–8.23)	

Visit cutoff April 15, 2017 (date of unblinding for primary efficacy analyses).

^aQA-PFS was calculated as PFS function × EQ-5D index score function.

^bQ-TWiST was calculated as (μTOX × TOX) + TWiST; TOX represents duration with grade ≥3 adverse events (AEs); TWiST represents progression-free duration without AEs or symptoms of progression (ie, PFS minus time with toxicities); μTOX represents the utility weight for the TOX state; observed utility data from EQ-5D was incorporated as a per-person utility weight (0.90 for the BRCA-mutant cohort and 0.89 for the ITT population).

HRs estimated with a Cox proportional hazards model.

CI, confidence interval; HR, hazard ratio; NR, not reached.

investigator-assessed PFS (QA-PFS) and quality-adjusted progression-free time without symptoms or toxicity (Q-TWiST). Analyses are presented for the predefined BRCA-mutant cohort and the intent-to-treat (ITT) population.

Results The visit cutoff dates for efficacy and safety were April 15, 2017, and December 31, 2017, respectively. Post-progression and patient-centered outcome data are given in the table 1. The most common treatment-emergent adverse events (TEAEs) of any grade (rucaparib vs placebo) were nausea (75.8% vs 36.5%), asthenia/fatigue (70.7% vs 44.4%), dysgeusia (39.8% vs 6.9%), and anemia/decreased hemoglobin (39.0% vs 5.3%). Any grade TEAEs of nausea, asthenia/fatigue, and anemia/decreased hemoglobin led to discontinuation in only 2.7%, 1.6%, and 2.7% of rucaparib-treated patients.

Conclusions Rucaparib significantly improved clinically meaningful postprogression outcomes vs placebo in the BRCA-mutant cohort and ITT population. The quality-adjusted analyses, which incorporated patient-centered perspectives during rucaparib maintenance treatment, confirmed the benefit of rucaparib vs placebo. The updated safety profile of rucaparib in ARIEL3 was consistent with prior reports.

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3

TRANSLATING ENDOMETRIAL MOLECULAR RISK STRATIFICATION TO ENDOMETRIOID OVARIAN CARCINOMA: A NOVEL APPLICATION OF PRECISION MEDICINE

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Objectives Endometrioid ovarian carcinoma (ENOC) is generally associated with a more favorable prognosis compared to other ovarian carcinoma histotypes. Nonetheless, patients are

still treated according to a “one size fits all” approach. While tumor staging offers some stratification, the development of personalized treatment concepts remain elusive. Our group has recently validated the Proactive Molecular Risk Classifier for Endometrial Cancer (ProMisE), to distinguish clinically relevant prognostic groups. ENOC shares risk factors, genomics, and histology with its endometrial counterpart. The aim of our study was to apply and investigate ProMisE in ovarian endometrioid carcinoma.

Methods ProMisE was applied to n=509 ENOC after bio-marker-assisted review of endometrioid histotype. Cases were aligned into four groups: low risk POLE mutant (POLE); moderate risk mismatch repair deficient (MMRd); high-risk p53 abnormal (p53abn); and a final moderate risk category lacking these biomarkers (p53wt). Kaplan-Meier and multivariable survival analyses were performed.

Results 4% of cases were POLE, 16% MMRd, 10% p53abn and 71% p53wt. Groups showed distinct progression-free and overall survival ($p<0.001$), near-identical to profiles of endometrial carcinoma. 5-year PFS was 54% in p53abn, 81% in MMRd, 84% in p53wt, and 100% in POLE cases. ProMisE classes of ENOC were independent of stage and residual disease in multivariable analysis.

Conclusions ProMisE risk classification provides additional prognostic information in a large cohort of ENOC. Our findings support the introduction of ProMisE-stratified treatment algorithms to ultimately improve endometrioid ovarian carcinoma patient care. Further, ENOC may benefit from parallel efforts under investigation in endometrial carcinoma.

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4 PROGNOSTIC IMPACT OF TUMOR INFILTRATING NATURAL KILLER CELLS IN OVARIAN CARCINOMA

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Objectives Whereas the prognostic impact of infiltrating T cells in ovarian cancer is established, the impact of other immune cells is largely unknown. The aim of the present study was to investigate the prognostic impact of intratumoral T cells, Natural Killer (NK) cells, neutrophils and PD-L1 expression.

Methods All patients diagnosed with high-grade serous carcinoma (HGSC) in Denmark in 2005 were included in the study (N=283). Immunohistochemical staining with antibodies for PD-L1, T cells (CD8), neutrophils (CD66b), and NK cells (CD57) were performed. Cell densities were analyzed using a digital image analysis method. The primary endpoint was overall survival (OS).

Results In patients with high levels of tumor infiltrating NK-cells the median OS was 45 vs 29 months (figure 1).

Abstract 4 Figure 1 NK cells high-grade serous carcinoma

The median OS was 37 vs 25 months ($p=0.0008$) for high vs low level of tumor infiltrating T cells, respectively. In multivariate analysis high numbers of NK-cells and T-cells remained independent markers of favorable OS with hazard ratios of 0.72 ($p=0.020$) and 0.67 ($p=0.041$) in favor of high T cell and high NK cell density respectively. A high level of PD-L1 expression was associated with improved OS (37 months vs 22 months, $p=0.0006$). PD-L1 was only borderline significant in the multivariate analysis (HR 0.77, $p=0.061$). Neutrophils had no significant association with OS.

Conclusions This population based cohort study demonstrated a favorable prognostic impact of high levels of tumor infiltrating NK-cells in patients with HGSC, and confirmed the importance of tumor infiltrating T cells. This may influence the future development of immunotherapy in ovarian carcinoma.

IGCS19-0726

5 THE GOOD PROGNOSIS OF IMMUNOREACTIVE SUBTYPE OF HIGH-GRADE SEROUS OVARIAN CANCER (HGSOC) IS NEGATIVELY IMPACTED WHEN OBESITY AND LIPID METABOLISM-RELATED GENES ARE HIGHLY EXPRESSED

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Objectives HGSOC is the deadliest gynecologic cancer. Molecular analysis to samples available at The Cancer Genome Atlas (TCGA) allowed the identification of 4 molecular subtypes with different biology/prognosis. Recently, our group demonstrated by bioinformatic analysis that patients expressing high levels of genes related to obesity and lipid metabolism (e.g. CD36/TGFB) experienced poorer outcomes in two international cohorts (TCGA and AOCs). Here, our goal was to establish if there was correlation between such patterns and