

Abstract 0009/#786 Table 1

| Efficacy endpoint/ Statistical test | Efficacy population | | ITT population | |
|--|---|--------------------------|---|---------------------------|
| | Rucaparib (n=220) | CT (n=105) | Rucaparib (n=233) | CT (n=116) |
| Median PFS ^a (95% CI), months | 7.4 (7.3–9.1) | 5.7 (5.5–7.3) | 7.4 (6.7–7.9) | 5.7 (5.5–6.7) |
| Stratified Cox proportional hazard model | HR 0.639 (95% CI 0.489–0.835); P=0.0010 | | HR 0.665 (95% CI 0.516–0.858); P=0.0017 | |
| RECIST ORR ^b , n/N (%) [95% CI] | 85/211 (40.3) [33.6–47.2] | 31/96 (32.3) [23.1–42.6] | 85/224 (37.9) [31.6–44.7] | 32/106 (30.2) [21.7–39.9] |
| Stratified Cochran-Mantel-Haenszel test | P=0.1287 | | P=0.1250 | |

^aPrimary endpoint; ^bSecondary endpoint; only patients with measurable disease were included in this analysis. CT, chemotherapy; HR, hazard ratio; ITT, intent to treat; ORR, objective response rate; PFS, progression-free survival; RECIST, Response Evaluation Criteria In Solid Tumors, version 1.1.

Results 233 pts were randomized to rucaparib and 116 to CT (visit cutoff Sep 30, 2020); 179 (51.3%) had platinum-resistant, 96 (27.5%) had partially platinum-sensitive, and 74 (21.2%) had fully platinum-sensitive disease. 23 pts (6.6%) with BRCA reversion mutations and 1 pt without a BRCA mutation were excluded from the efficacy population. Median PFS was significantly longer with rucaparib vs CT in both the efficacy and ITT populations (Table). In an exploratory analysis of pts with BRCA reversion mutations, median PFS was shorter with rucaparib (n=13) vs CT (n=10); 2.9 vs 5.5 months, hazard ratio 2.769 (95% CI, 0.989–7.755). ORR was not significantly different between the rucaparib and CT arms in both populations (Table). Adverse events were consistent with the known safety profiles of rucaparib and CT.

Conclusions Patients with BRCA-mutated advanced, relapsed OC who received rucaparib had a significant improvement in PFS vs SOC CT. No new safety signals were identified. This is the first prospective report from a randomized trial demonstrating that the presence of a BRCA reversion mutation predicts for primary resistance to rucaparib.

0010/#784

ADJUVANT CHEMOTHERAPY FOLLOWING CHEMORADIATION AS PRIMARY TREATMENT FOR LOCALLY ADVANCED CERVICAL CANCER COMPARED TO CHEMO-RADIATION ALONE: THE RANDOMISED PHASE 3 OUTBACK TRIAL

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Background Cervical cancer is a common cause of cancer-related death among women worldwide. Standard treatment for locally advanced disease is chemoradiation. However, a significant percentage of women still relapse and die from the development of distant metastatic disease. OUTBACK was designed to determine the effects of giving adjuvant chemotherapy after chemoradiation on survival.

Methods OUTBACK is an international randomized phase 3 trial of the Gynecologic Cancer InterGroup (GCIg). Participating groups (countries) included ANZGOG (Australia and New Zealand), NRG (USA, Saudi Arabia, Canada, China), and Singapore. Eligible women had locally advanced cervical cancer (FIGO 2008 stage IB1 & node positive, IB2, II, IIIB or IVA) that was suitable for primary treatment with chemoradiation with curative intent. Women were randomly assigned to either standard cisplatin-based chemo-radiation (control) or standard cisplatin-based chemo-radiation followed by adjuvant chemotherapy (ACT) with 4 cycles of carboplatin and paclitaxel, after stratification for nodal status,

participating site, FIGO stage, age, and planned extended-field radiotherapy. The primary end point was overall survival (OS) at 5 years. Secondary endpoints included progression-free survival (PFS); adverse events (AE); and patterns of disease recurrence. The target sample size of 900 provided 80% power with 95% confidence to detect an improvement in OS at 5 years from 72% (control) to 80% (ACT), with some over-accrual to account for non-compliance with ACT and loss to follow-up.

Results 919 of 926 women recruited from April 2011 to June 2017 were eligible and included in the primary analysis: 463 assigned ACT, 456 control. ACT was started in 361 (78%) women assigned to receive it. Median follow-up was 60 months (IQR 45–65). OS at 5 years was similar in those assigned ACT versus control (72% vs 71%, difference <1%, 95% CI -6 to +7; P = 0.91). The hazard ratio for OS was 0.91, (95% CI 0.70 to 1.18). PFS at 5 years was similar in those assigned ACT versus control (63% vs 61%, difference 2%, 95% CI -5 to +9; P = 0.61). The hazard ratio for PFS was 0.87, (95% CI 0.70 to 1.08). AE of grade 3–5 within a year of randomisation occurred in 81% who were assigned and received ACT versus 62% assigned control. There was no evidence of differences between treatment groups in AE beyond 1 year of randomisation. Patterns of disease recurrence were similar in the two treatment groups.

Conclusion Adjuvant chemotherapy given after standard cisplatin-based chemoradiation for women with locally advanced cervical cancer did not improve OS or PFS.

Plenary 5: Oral Abstract Presentations

0011/#287

PROGNOSTIC SIGNIFICANCE OF 'P53 SIGNATURE' (FIELDS OF DYSPLASIA) AND IN SITU MARGIN STATUS IN ORGAN-CONFINED HPV-INDEPENDENT P53 ABNORMAL VULVAR SQUAMOUS CELL CARCINOMA

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Objectives Vulvar squamous cell carcinomas (VSCCs) can be stratified by HPV and TP53 mutation status to prognostically significant risk groups using p16 and p53 IHC. Treatment guidelines do not address optimal management of high molecular risk (TP53 mutated) pre-invasive neoplasia found at resection margins. Herein, we used p53 IHC to evaluate margin status in a retrospective cohort of HPV-independent (HPV-I) p53abn VSCCs.

Methods Surgically staged I-II HPV-I p53abn VSCCs from a single institution underwent margin (re)assessment using p53 IHC. Cases were segregated to i) morphologic dVIN at margin ii) vulvar skin with abnormal p53 IHC staining at margin and subtle morphologic features insufficient for dVIN iii) margins clear by morphology & p53 IHC TP53 mutation status was evaluated by next-generation sequencing (group ii). Clinicopathologic and outcome data was collated using a standardized collection tool.