p=0.0123, HR=3.029; 95%CI: 1.4–6.5). Median time from OC diagnosis to BM and from disease recurrence to BM, was longer for BRCA+ compared to BRCA-(44.3mo vs. 32.3mo and 11.8mo vs. 0.7mo, respectively). Median survival(mOS) was not significantly different in patients with BM or without BM(59.4mo vs. 71.2mo, p=0.36). Following diagnosis of BM, mOS was 20.6mo among BRCA+ and 12.3mo among BRCA (p=0.4266). No correlation was found with PARP inhibitors or bevacizumab treatment.

Conclusion* BM are an infrequent among OC patients. However, the risk is three-folds higher among BRCA+. Interestingly, BM do not significantly alter survival among OC patients; might be related to longer survival in BRCA+ or higher tropism or else.

978 CONCORDANCE OF THE FDA-APPROVED COMPANION DIAGNOSTIC AND A NEXT-GENERATION SEQUENCING ASSAY KIT FOR ASSESSING HOMOLOGOUS RECOMBINATION DEFICIENCY IN OVARIAN CANCER

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Introduction/Background* Olaparib+bevacizumab is approved as first-line maintenance treatment of advanced homologous recombination deficiency (HRD)-positive ovarian cancer (OC), defined by the presence of a deleterious or suspected deleterious BRCA mutation (BRCAm) and/or genomic instability (evaluated with a United States Food and Drug Administration-approved companion diagnostic). We evaluated the performance of an in-development next-generation sequencing assay, based on Illumina's RUO TSO 500 content, that identifies variants in tumour tissue and HRD genomic scars (Illumina test). Herein, we report the performances of the in-development Illumina test versus the Myriad myChoice PLUS assay (Myriad test).

Methodology OC tissue samples were analysed with Illumina (n=227; 40ng DNA) and Myriad tests (n=254; 200ng DNA). Samples that failed QC during the first run using the Illumina test were retested with higher DNA input. Agreement rates for BRCAm, genomic instability score (GIS), and HRD status (includes BRCA and GIS [cutoff, 42]) were analysed. For the overall and the non-BRCAm cohorts, correlation between the continuous GIS of the Illumina and Myriad tests was determined. The analytical sensitivity and specificity of the Illumina-derived GIS to correctly classify genomic instability status as determined by the Myriad test (cutoff, 42) was evaluated using area under the receiver operating characteristic (AUROC).

Result(s)* Agreement rates are reported in the Table. The GIS correlation between the 2 tests was 0.980 (all samples) and 0.975 (non-BRCAm cohort). AUROC was 0.992 (all samples) and 0.988 (non-BRCAm cohort). Prevalence (Illumina and Myriad tests) was 51.0% and 49.2% for overall HRD and 27.6% and 25.5% for BRCAm. Success rates (Illumina and Myriad tests) were 86.8% (197/227) and 94.1% (239/254) (overall HRD), 88.1% (200/227) and 97.6% (248/254) (BRCAm), and 91.2% (207/227) and 94.1% (239/254) (GIS); after re-running the failed samples with the Illumina test, rates were 90.3%, 92.5%, and 93.4%, respectively.

Abstract 978 Table 1 Agreement rates for the illumina test versus the myriad test

	Positive Percentage Agreement, % (95% CI)	Negative Percentage Agreement, % (95% CI)	Overall Percentage Agreement, % (95% CI)
HRD (positive vs negative) (N=194)	92.3 (85.6-96.1)	96.7 (90.7-98.9)	94.3 (90.1-96.8)
*BRCA*m (positive vs negative) (N=197)	92.9 (83.0-97.2)	98.6 (95.0-99.6)	96.9 (93.5-98.6)
GIS (<42 vs ≥42) (N=204)	91.3 (84.2-95.3)	98.0 (93.1-99.5)	94.6 (90.6-97.0)

Conclusion* Illumina test and Myriad test HRD, BRCAm, and GIS detection results were in >91% agreement. With both tests, GIS was highly correlated (0.98), and prevalence estimates of HRD and BRCAm rates were similar. Data suggest that a distributable solution such as the Illumina test may replicate the performance of the Myriad myChoice HRD assay.

1167 OLAPARIB IN COMBINATION WITH INHIBITORS OF ATR/CHK1 PATHWAY LEADS TO INCREASED CELL DEATH IN OVARIAN CANCER CELLS SENSITIVE AND RESISTANT TO PARPI

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Introduction/Background* Ovarian cancer (OC) is believed to be one of the most lethal gynaecologic malignancies worldwide. Despite advances in the treatment of OC after the introduction of poly(ADP-ribose) polymerase inhibitors (PARPi) in the frontline setting as maintenance therapy and in the recurrent setting, the 5-year survival rate of high-grade serous ovarian cancer (HGSOC) ranges between 35 and 40%. PARPi exhibit meaningful activity against OC, however resistance to these agents emerges ultimately. Thus, there is a need to develop more effective treatments for OC. Recent reports highlighting increased OC cell reliance on ATR/CHK1 pathway gives hope to overcome PARPi resistance and prolong patient's survival.

Methodology The aim of this study was to estimate cytotoxic activity of PARPi (olaparib), the ataxia telangiectasia and Rad-3 related protein (ATR) inhibitor (ATRi, ceralasertib), and the checkpoint kinase 1 (CHK1) inhibitor (CHK1i, MK-8776) alone or in combinations in PEO1 (BRCA2MUT) OC cell line, and in PEO1-derived olaparib-resistant (PEO1-OR) cell line developed by continuous incremental long-term treatment with olaparib. Here, we evaluated the effect of tested drugs on cell survival in respect of metabolic activity by MTT assay and colony forming capacity. We also preliminarily elucidated mechanisms conferring resistance to olaparib in OC cells by assessment of expression of key proteins (ATR, CHK1, PARP1, P-glycoprotein) by western blot analysis. Statistical analyses were performed using Student's t-test and ANOVA followed by the Tukey's multiple comparisons post-hoc test.

Result(s)* OC cells are more sensitive to combination of the drugs in comparison with monotherapy with each agent alone. What is more, treatment with single-agent PARPi or combination of PARPi/ATRi or PARPi/CHK1i activates ATR/CHK1