Conclusion These observations add to the collective body of evidence regarding the changing treatment landscape in aOC.

HOMOLOGOUS RECOMBINATION DEFICIENCY (HRD): A NEW OVARIAN CANCER BIOMARKER – VALIDATION OF DECENTRALIZED GENOMIC PROFILING, WITH A FOCUS ON GENOMIC LARGE REARRANGEMENTS (LRs)

Introduction/Background The diagnostic evaluation of HRD is central to define targeted therapy strategies for patients with ovarian carcinoma, so advances in decentralized genomic profiling are mandatory to allow for broader testing. We show the feasibility of implementing HRD assays in academic setting laboratories, and evaluate prevalence of genomic large rearrangements (LRs) in real life cohorts of high-grade ovarian cancer patients.

Methodology We evaluated HRD in 514 ovarian carcinoma samples by a hybrid capture next-generation sequencing assay using the standardized Myriad Mychoice cdx HRD test. Each patient’s HRD status was evaluated by measuring the BRCA1/2 mutational status and the Genomic Instability Score (GIS). All samples were measured twice, in the central Myriad laboratory and in an academic molecular pathology laboratory, and the concordance was analyzed. Afterwards, the cohort was extended to 1163 ovarian cancer samples to determine real world prevalence of LRs in HRR genes.

Results Combining GIS and BRCA-mutations, a total of 200 (38.9%) of 514 tumors were HRD-positive. High-grade serous histology (p<0.000001), grade 3 tumors (p=0.001) and patient age <60 years (p=0.0003) were significantly associated with a positive GIS. Concordance between both laboratories for the HRD-status was 97.1% (499/514 tumors) with a sensitivity of 94.6% and a specificity of 98.4%.

LRs were found in 88/1163 (7.5%) of ovarian cancer samples. Interestingly, RAD51B, CDK12, BRCA1, ATM and BRCA2 were found to constitute 74% of all observed LRs.

Conclusion The percentage of HRD-positive tumors found was similar to that observed in the PAOLA-1 trial, with a high concordance between central and local laboratories. These results support introduction of standardized HRD assay in academic molecular pathology laboratories, to allow for broad access to personalized oncology strategies for patients with ovarian cancer. Genomic LRs are observed in a small portion of ovarian cancer samples, with a skewed occurrence towards 5/15 genes.