Comparison analysis Between TSO500 Panel Sequencing and Whole Exome Sequencing in Patients with High-Grade Serous Carcinoma

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High-grade serous carcinoma (HGSC) is the most common histologic type of ovarian cancer, with a median 5-year survival rate of between 15% and 55%. Recently, targeted therapies for DNA damage repair with poly (ADP-ribose) polymerase (PARP) inhibitors have significantly improved progression-free survival for patients with homologous recombination deficiency (HRD). The Cancer Genome Atlas (TCGA) reported HRD in approximately 50% of patients with HGSC, and the major causes of HRD was BRCA1/2 mutation (~20%). Because patients with HRD could benefit from PARP inhibitors, identifying patients with HRD is essential for ovarian cancer treatment selection. For identifying patients with HRD, we utilized whole exome sequencing and Illumina's the TruSight Oncology (TSO) 500 HRD panel. TSO500 HRD panel can assess HRD status by measuring genomic instability score (GIS) using the same algorithm of MyChoice CDx HRD Companion Diagnostic test. We performed both sequencing and compared the results in 24 patients with HGSC. This analysis revealed three results. Firstly, we identified 50% (12/24) of patients with HGSC are HRD based on HRR mutations in WES data. Secondly, utilizing TSO500 HRD results, we could identify that an additional 9 patients were also HRD based on GIS score, and 87.5% (21/24) of patients with HGSC were HRD. The frequency of patients with HRD (87.5%) was significantly higher than the TCGA report (50%). Lastly, because it is possible to estimate HRD score based on WES data, we measured the prediction performance of WES-based HRD scores. Using GIS of TSO500 HRD panel as the gold standard, WES-based HRD score showed high sensitivity (100%, 21/21) and good positive predictive value (PPV) (91%, 21/23). In conclusion, the frequency of HRD in patients with HGSC was significantly higher with 87.5% than the 50% of TCGA, and HRD scores based on WES data showed the acceptable concordance with GIS by TSO500 HRD panel. However, further research with a larger cohort is needed.