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Distinct Genomic Characteristics and Ethnic Implications of Homologous Recombination Deficiency in High-Grade Serous Carcinoma

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Background: High-grade serous carcinoma (HGSC) is the most common ovarian cancer subtype, with limited survival outcomes. Poly (ADP-ribose) polymerase inhibitors (PARPi) had improved outcomes in patients with homologous recombination deficiency (HRD). While HRD occurs in approximately half of Western HGSCs, evidence in Korean patients remains limited. We investigated the prevalence of HRD and associated genomic features in Korean HGSC patients, with comparative analyses against multi-ethnic and Asian cohorts.

Methods: Tumor samples from 170 Korean HGSC patients using the TruSight Oncology 500 HRD panel, integrating comprehensive genomic profiling with HRD measurement. HRD was classified based on genomic instability score (GIS ≥42) and *BRCA* mutation status. Comparative analyses were conducted with TCGA (multi-ethnic) and Japanese cohorts.

Results: Among 170 patients, 70.6% harbored actionable alterations (OncoKB Level I). HRD was identified in 70% of patients, higher than TCGA (~50%, $p=1.3\times10^{-6}$). Frequent alterations included *BRCA1* mutations (24.7%, $p=3.5\times10^{-4}$), *MET* amplifications (9.4%, $p=9.7\times10^{-6}$), and *FGFR2* amplifications (6.5%, $p=1.0\times10^{-3}$), while *CCNE1* amplification was less common (11.2%, $p=4.0\times10^{-3}$). Of HRD cases, 51.9% carried *BRCA* mutations, and GIS-high (≥42) and *BRCA* wild-type patients demonstrated survival outcomes comparable to those with *BRCA* mutations, highlighting the importance of non-*BRCA* HRD. Compared with multi-ethnic cohorts, this cohort showed higher rates of both *BRCA* mutations ($p=2.5\times10^{-2}$) and HRD ($p=1.3\times10^{-6}$), while comparison with Japanese cohorts revealed a higher BRCA mutation frequency (p=0.04) but no significant difference in HRD

prevalence.

Conclusions:

This Korean HGSC cohort showed a distinct genomic profile not only from Western but also from Japanese cohorts, suggesting population-specific variation in HRD prevalence and therapeutic targets. Given that this is the first study addressing these differences, further investigations are warranted to validate these findings. Outcomes of GIS-high & *BRCA* wild-type patients comparable to those with BRCA mutations support the expansion of PARP inhibitor use beyond *BRCA* mutation carriers.