Poster #10 | Frequency of homologous recombination deficiency in a large community-based cohort of epithelial ovarian cancer cases
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Topic: Genetics

Objectives
Homologous recombination deficiency (HRD) is a useful predictor of treatment response in patients with epithelial ovarian cancer (EOC). Reported data on the frequency of HRD in EOC is largely based on analysis of patients treated at academic medical centers or who participated in clinical trials. We sought to characterize the frequency of HRD based on mutations in homologous recombination repair (HRR) genes, genomic instability (GI) and loss of heterozygosity (LOH) scores in a large community-based cohort of EOC patients who received genomic testing in the context of routine clinical care.

Methods
Information including patient demographic, tumor stage and histology data, and results from ovarian cancer tumor tissue sequencing tests was obtained from the diverse dataset within the Providence St. Joseph Health (PSJH) Electronic Medical Record (EMR) and the system-wide cancer registry data. Patients with an invasive EOC diagnosis (ICD C56.x) during the time interval between January 2015 and January 2020 were included. Structured genomic data was sourced from laboratory information systems and manual abstraction of molecular sequencing reports. Alterations in the following HRR genes were analyzed, along with LOH and GI scores: ATM, BARD1, BRCA1, BRCA2, BRIP1, CDK12, CHEK1, CHEK2, FANCL, PALB2, PPP2R2A, RAD51B, RAD51C, RAD51D, RAD54L.

Results
Within this EOC cohort of 1,015 patients who received genomic testing, 794 patients underwent germline testing and 507 patients had somatic tumor tissue testing (TTT) ordered in the context of clinical care. The number of patients who received Somatic TTT increased over time (79/558 vs 176/603 for 2015 vs 2019, X²=38.2, p < 0.00001) and was more frequent in patients with advanced stage disease (33/389 vs 150/657 for Stage I-II vs Stage III-IV, X²=34.8, p < 0.00001) or who had a tissue biopsy or hysterectomy at a PSJH facility (214/1071 vs 137/947 for biopsy/hysterectomy vs neither, X²=10.6, p=0.001). Pathogenic somatic mutations in HRR genes were identified in 87 (17%) patients including BRCA1 (n=47), BRCA 2 (n=23), ATM (n=8), CHEK2 (n=4), PALB2 (n=2), RAD51B (n=1), CDK12 (n=1) and BRIP1 (n=1). LOH and GI scores reflective of HRD were noted in 34/116 (29%) and 9/40 (23%) of patients tested, respectively. HRR gene mutations and/or GI/LOH were identified in tumors of all stages. Treatment data was available for a subset of patients. Patients with mutations or GI/LOH were far more likely to receive PARPi maintenance therapy than patients without these findings (Table 1).

Conclusions
In this large, community based cohort of EOC cases, commercial somatic TTT identified evidence of HRD in 130 of 507 (26%) patients tested. Molecular alterations were identified in tumors of all stages, suggesting that broad based somatic TTT may be of value. A large fraction of patients with HRD may not be receiving indicated PARPi therapy.

Abstract Table or Graph

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