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TREATMENT PATTERNS AND OUTCOMES AFTER PROGRESSION ON POLY-ADP RIBOSE POLYMERASE INHIBITOR MAINTENANCE THERAPY

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Introduction/Background poly-ADP ribose polymerase inhibitors (PARPi) are approved as maintenance therapy in epithelial ovarian cancer (EOC) after response to last platinum-based therapy both in first line and in the platinum-sensitive relapse. Although they have modified clinical practice, few data are available on post-progression treatments and response.

Methodology we evaluated, in a real-life population, treatment patterns and response after PARPi therapy, evaluating duration of response (DOR) to first line after PARPi, progression free survival (PFS) from the beginning of PARPi to progression on the subsequent chemotherapy and overall survival (OS). we retrospectively analyzed patients treated with PARPi maintenance therapy and progressed on it. Clinico-pathological characteristics and treatment outcomes were collected from medical records.

Results 80 EOC patients were identified. 13% started PARPi after front-line chemotherapy, while 87% in the relapsed setting. 21% received olaparib, 73% niraparib, 6% rucaparib. 25% were BRCA mutated. Median duration of PARPi was 7.7 months (IQR 5.4–16.0). In the BRCA-mutated cohort (25%) it was 12.3 months (IQR 9.1–15.8), 7.1 (IQR 4.4–17.5) in the non BRCA-mutated. Following PARPi progression, 75% of patients received chemotherapy, 26% receiving platinum. Response rate (RR) to first line therapy after PARPi was 31%. DOR was 3.8 months (IQR 2.8–5.3). Based on chemotherapy subgroups, it was 3.8 months (IQR 3.5–4.4) for platinum-doublet, 4.8 (IQR 2.5–6.6) for platinum monotherapy, 3.8 (IQR 2.8–6.0) for trabectedin and pegylated liposomal doxorubicin (PLD) and 4.0 (IQR 3.1–5.3) for other non-platinum agents. Median PFS was 19.1 months (95%CI 14.4–23.0); 8.2 (95%CI 6.5–11.3) and 17.0 months (95%CI 14.4–20.8) for platinum-resistant and sensitive disease, respectively. OS was 25 months (95%CI 20.3–31.7).

Conclusion post-progression treatments and response after PARPi suggest that RR and DOR to subsequent therapy are lower than expected even for platinum-sensitive patients. With the intrinsic limits of this study, it highlights the need of clinical research in post PARPi treatments.

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REAL-WORLD PROSPECTIVE CHARACTERIZATION OF HOMOLOGOUS RECOMBINATION DEFICIENCY IN ADVANCED OVARIAN CANCER

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Introduction/Background Approximately 50% of high-grade serous ovarian, tubal, or primary peritoneal carcinomas (HGSC) harbor homologous recombination deficiency (HRD). HRD predicts sensitivity for platinum-based chemotherapy and is particularly crucial in selection of patients who could benefit from poly ADP-ribose polymerase inhibitor (PARPi) maintenance treatment after first-line adjuvant chemotherapy. HRD can result from genetic or epigenetic loss of HR genes such as BRCA1/2, however not all genomic alterations leading to HRD are known. We recently developed an optimized HRD test for HGSC (ovaHRDscar) using somatic allelic imbalances; loss of heterozygosity (LOH), large-scale state transitions (LSTs), or telomeric allelic imbalance (TAI). However, the clinical characteristics and real-world significance of HRD remains unknown.

Methodology We prospectively collected tumor samples from more than 100 patients diagnosed with advanced HGSC or endometrioid ovarian cancer, during primary or interval debulking surgery performed at the Helsinki University Hospital between October 2019 and June 2022. We isolated DNA from fresh-frozen and formalin-fixed paraffin-embedded (FFPE) tumor samples and tested for BRCA1/2 mutations and genomic scarring with ovaHRDscar.

Results The median age at diagnosis was 67 (range 37–85) years. Of all patients, 33% were diagnosed with Stage III and 67% with Stage IV disease, and 43.5% of patients were treated with neoadjuvant chemotherapy. In 15% of the patients, we found a deleterious BRCA1/2 mutation, two thirds of which were germline mutations. Of the samples, 63.2% were HRD according to ovaHRDscar, including as expected all tumors with BRCA1/2 mutations. Interestingly, 56.3% of the tumors were HRD even in the absence of a BRCA1/2 mutation.

Conclusion The analysis of the clinical significance of HRDs, including the association with progression-free survival (PFS), platinum-free interval (PFI), and the responses to PARPi are currently ongoing. The results will reveal the real-world clinical outcomes of HRD in advanced ovarian cancer patients.

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PREVALENCE OF LOW ANTERIOR RESECTION SYNDROME IN PATIENTS WITH ADVANCED STAGE EPITHELIAL OVARIAN CANCER

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Introduction/Background Cytoreductive surgery combined with platinum-based chemotherapy is the standard treatment for advanced stage epithelial ovarian cancer (EOC). A Low Anterior Resection (LAR) can be necessary to achieve complete cytoreductive surgery. Low anterior resection syndrome (LARS) is a well-known long-term complication in rectal cancer patients undergoing a LAR but evidence on prevalence of LARS in ovarian cancer patients is limited. The aim of this study is to investigate the prevalence of LARS in a cohort of patients with advanced stage epithelial ovarian cancer after a LAR.