2022-RA-956-ESGO 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 moths (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.

2022-RA-961-ESGO 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.

2022-RA-965-ESGO 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.

Methodology This is a single-center mixed methods study design consisting of a literature overview, a retrospective chart study and qualitative semi-structured interviews. Patients with advanced stage epithelial ovarian cancer who had primary or interval cytoreductive surgery including LAR were included. Main outcome was the postoperative LARS-score and postoperative documentation of functional bowel symptoms and impact on quality of life.
Results Forty-seven patients who underwent debulking surgery with a LAR between 2009 and 2019 were included for retrospective chart analysis. The LARS-score could not be determined retrospectively except in one case, because of non-specific documentation about defecation. However, in the majority of patients (76.6%) evidence of functional bowel symptoms was found. We interviewed nine patients for the interview part of the study. One patient suffered from major LARS, three patients from minor LARS. Qualitative analysis showed evidence for significant impact of LARS on quality of life.
Conclusion Evidence on LARS in EOC patients is limited. This study contributes to creating attention and awareness for postoperative functional bowel problems. Prospective research is recommended in order to gain more insight in prevalence and impact on quality of life of LARS in patients with epithelial ovarian cancer after cytoreductive surgery.

2022-RA-966-ESGO TOLERANCE OF INTRAPERITONEAL (IP) NIVOLUMAB AFTER CYTOREDUCTIVE SURGERY (CRS) AND HYPERTHERMIC INTRAPERITONEAL CHEMOTHERAPY (HIPEC) IN PATIENTS (PTS) WITH RELAPSE ADVANCED OVARIAN CARCINOMA: A PHASE I STUDY WITH EXPANSION COHORT (ICONIC)

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Introduction/Background Cytoreductive surgery and HIPEC combination with intraperitoneal immunotherapy may have a synergic effect, through an increase of tumor-antigen expression and of mutational load. We aimed to determine the safety of IP nivolumab after CRS and HIPEC in pts with relapsed ovarian carcinoma (NCT03959761).
Methodology Patients were treated according to three dose-levels of IP nivolumab following a 3+3 design (0.5 mg/kg, 1 mg/kg, and 3 mg/kg), starting 5 to 7 days after DS and HIPEC and repeated every 2 weeks for 4 infusions. The primary objective was to establish the maximum tolerated dose (MTD) of IP nivolumab based on dose limiting toxicity (DLT) occurrence during the 28 days after the first IP nivolumab infusion. Secondary objectives were to assess disease progression, tolerance of DS, HIPEC and post procedure intravenous chemotherapy.
Results A total of 9/10 pts enrolled into the dose escalation were evaluable for DLT (1 peritoneal catheter fall-out after the 2nd infusion). No DLTs have been observed at either dose level according to an independent data safety monitoring board (DSMB), and 7 pts were included into an expansion cohort. In total, six pts (35.3%) did not complete all planned cycles. No deaths due to treatment occurred. Nine pts (52.9%) experienced severe adverse events (SAEs), 4 related to peritoneal catheter implant. SAEs were transaminases elevation (6 pts, grade 3–4, related to DS), hemodynamic shock (1 pt, related to DS), hypokalemia (1 pt, related to DS and HIPEC), portal vein thrombosis (1 pt, related to DS). There were no SAEs related to IP nivolumab. With a median follow-up of 10.1 months (95%CI 8.2-NA), median progression-free-survival was 7.4 months (95% CI 6.0-NA).
Conclusion IP nivolumab was feasible and well tolerated, supporting the pursuit of studies investigating this pioneering approach with other immunotherapy combination for example.

2022-RA-970-ESGO THERE IS NO BENEFIT FOR PREOPERATIVE HYPERHYDRATATION BEFORE CYTOREDUCTIVE SURGERY AND HIPEC WITH CISPLATIN WHEN COMBINED WITH SODIUM THIOSULFATE

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Introduction/Background Cytoreductive surgery associated with hyperthermic intraperitoneal chemotherapy (HIPEC), using cisplatin, is an option in advanced ovarian cancer treatment. Cisplatin may cause renal failure, both after systemic or intraperitoneal administration. It can accumulate and lead to nephrotoxicity in one third of intravenous prescription and up to 40% of acute renal failure for the IP route with progressive and irreversible chronic renal failure.In addition to preoperative hyperhydration, Sodium Thiosulfate (ST) has been used in the prevention and treatment of Cisplatin-induced toxicity, particularly to prevent renal toxicity.The objective of our study was to evaluate the interest of preoperative intravenous hydration alone or in combination with sodium thiosulfate to prevent nephrotoxicity induced during the use of intraperitoneal Cisplatin in patients who have undergone a cytoreductive surgery with HIPEC.
Methodology A retrospective single-tertiary-center analysis of all consecutive patients treated by cytoreductive surgery with Cisplatin-based HIPEC between January 01, 2015 and July 30, 2020. All types of PC were included. There were three consecutive periods of study corresponding to 3 different treatments. A first group was treated with preoperative hyperhydration alone (group 1 – PHH), a second-one with preoperative hyperhydration (3L/24 h of Ringer-Lactate) with addition of ST (group 2 – PHH + ST) and a third-one with ST alone (group 3 – ST).
Results Period study included 230 consecutive patients underwent. Median age was 59 years (interquartile range 49 – 68 years), with 76% women. Higher rate of complete cytoreduction (CC0) were achieved in PHH + TS and TS alone (92% and 97%, respectively, vs 77%, $p < 0.001$). PHH + TS and TS alone had better postoperative renal function without acute injury compared to group 1 ($p<0.001$).
Conclusion In addition to the nephroprotective benefit, sodium thiosulfate also appears to be associated with better cytoreduction results. Hyperhydration does not provide any additional benefit.