

Introduction/Background Lysyl oxidase (LOX) is an enzyme engaged in the cross-linking of the extracellular matrix proteins. LOX proenzyme is secreted to extracellular space, then proteolytically cleaved resulting in the LOX enzyme and LOX propeptide (LOX-PP). Various studies showed contradictory results, indicating that LOX may act either as an oncogene or a tumor suppressor. More detailed analyses suggest that LOX enzyme may be responsible for oncogenic effects, while LOX-PP may act as tumor suppressor. Our aim was to investigate LOX-PP role in ovarian cancer cells.

Methodology Ovarian cancer cell lines (SKOV3, A2780, ES2) with stable LOX-PP overexpression were established using lentiviral transfer system. Cell lines were validated by semi-quantitative RT-PCR and immunoblotting. Cells proliferation were assessed by MTS assay. In vitro cytotoxicity assay was performed with two major drugs used in ovarian cancer treatment: cisplatin (0,1–20 μ M range) and paclitaxel (1,56 nM – 30 μ M range).

Results RT-PCR showed that the LOX-PP-containing cells had higher LOX-PP expression compared to control cells with an empty vector. Immunodetection was successful both in cells lysates and in culture medium suggesting that the protein is efficiently secreted. Cell proliferation assay showed lower proliferation rate of A2780_LOX-PP as compared to controls. No differences in proliferation rate was observed among cell lines SKOV3 and ES2. In vitro cytotoxicity assay demonstrated that LOX-PP overexpressing SKOV3 and A2780 cells were more sensitive to both cisplatin and paclitaxel. The A2780_LOX-PP cells showed a 8,5% and 16% higher sensitivity to paclitaxel and cisplatin, respectively, while SKOV3-LOX-PP cells showed 15% and 24% higher sensitivity to those drugs.

Conclusion LOX-PP seems to exert an anti-cancer function in ovarian cancer, either by decreasing cells proliferation rate and/or by sensitizing of cells to chemotherapeutic agents.

Disclosures The authors have no conflicts of interest to declare.

#822

EXPANDING USE OF HIPEC AT TIME OF INTERVAL DEBULKING SURGERY. A PROSPECTIVE ANALYSIS ON PERIOPERATIVE AND ONCOLOGIC OUTCOMES

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Introduction/Background In advanced ovarian cancer, randomized data showed that hyperthermic intraperitoneal chemotherapy (HIPEC) after interval debulking surgery (IDS) determined improvement in both progression free (PFS) and overall survival (OS). However, data include only patients with FIGO stage III disease receiving \leq IV cycles of neoadjuvant chemotherapy (NACT). We aimed to assess perioperative outcomes and PFS of FIGO stage IV and/or patients receiving up to VI cycles of NACT undergoing IDS+HIPEC.

Methodology This study included prospectively collected cases from 01/01/2019 to 31/07/22. Patients were suitable for HIPEC if: age $>$ 18 but \leq 75 years, Body Mass Index (BMI) \leq 35 kg/m², ASA score \leq 2, FIGO stage III/IV epithelial disease treated with up to 6 cycles of NACT, residual disease at IDS $<$ 2.5 mm.

Participation to clinical trials and uncontrolled medical conditions were exclusion criteria.

Results 205 patients were included. 76 (37.1%) had FIGO stage IV disease and 44 (21.5%) received $>$ 4 cycles of NACT. No significant difference was found in patients' and disease' characteristics between FIGO Stage III and FIGO Stage IV cases, while rate of stable disease after NACT ($p=0.004$), mean surgical complexity score (SCS) at IDS ($p=0.001$) and bowel resection rate ($p=0.046$) were higher in patients undergoing delayed IDS. No difference in both perioperative outcomes and complication rate were identified among the populations, however a trend towards a higher rate of severe postoperative complications was shown in case of delayed IDS ($p=0.07$) and FIGO stage III disease ($p=0.052$), the latter remaining the only independent risk factor for severe postoperative complications at multivariate analysis ($p=0.02$). No difference in PFS was identified neither between FIGO stage III and FIGO Stage IV patients ($p=0.44$), nor between patients receiving 3–4 cycles vs $>$ 4 cycles of NACT ($p=0.85$).

Conclusion In relation to the absence of additional complications and positive survival outcomes, we offer a background to consider the use of HIPEC in selected FIGO stage IV patients and women receiving $>$ 4 cycles of NACT.

Disclosures none

#823

COMPREHENSIVE CHARACTERIZATION OF NAÏVE TREATMENT SAMPLES OF HIGH GRADE SEROUS OVARIAN CANCER ADDRESSED TO NEOADJUVANT CHEMOTHERAPY: A HYPOTHESIS-GENERATING STUDY ON BIOMARKERS OF RESPONSE TO PLATINUM-BASED CHEMOTHERAPY

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Introduction/Background Neoadjuvant chemotherapy (NACT) followed by interval debulking surgery (IDS), has been shown to be not oncologically inferior to primary debulking surgery for patients affected by advanced epithelial ovarian cancer (EOC). However, 20% of patients don't respond and therapeutic options are limited. The genomic landscape could, at least partially, explain this phenomenon. By correlating mutational profiles with clinical outcomes, we aimed at identifying genomic features of resistance to platinum-based chemotherapy.

Methodology FPG500 (IRB 3837) is a comprehensive cancer genome profiling programme at Fondazione Policlinico Agostino Gemelli IRCCS. An evaluation of 523 genes (TSO500HT, Illumina) is provided. All EOC patients addressed to NACT and enrolled in FPG500 were included. Response to NACT was scored following the chemotherapy response score (CRS): no/minimal tumor response (CRS1), partial response (CRS2), and total response (CRS3). Age, residual tumour at IDS, and stage were also considered.

Results At data cut-off of the 9th of January 2023, 96 EOC patients were included in this preliminary analysis. 85 patients had at least one genomic alteration (78%). The overall mean of alterations was 1.75 (SD=1.37). CCNE1 amplifications were associated with older age (17% age $<$ 64 years vs

26.5% > 64 years), and worse CRS (24% CRS 1–2 vs 15% CRS 3), similar to PIK3CA (mainly single nucleotide variants [SNVs] or insertion/deletions [Indels]) (37% CRS 1–2 vs 19% CRS 3). MYC amplifications and PIK3CA alterations were associated with a more advanced stage (respectively 37.5% and 39% stage IV vs 27% and 25% stage III). However, MYC was associated to with a better response to NACT (28% CRS 1–2 vs 42% CRS 3).

Conclusion CCNE1, MYC and PI3KCA genomic alterations seem to be associated with stages and response to chemotherapy, however, a sample size of 365 patients is required to obtain statistical significance. The enrollment is ongoing and results are expected in 2025.

Disclosures The authors declare no disclosures.

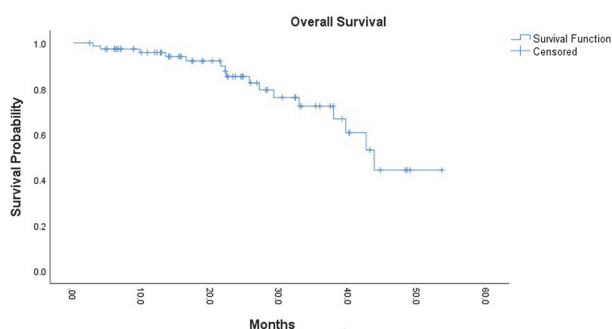
#832 HYPERTHERMIC INTRAPERITONEAL CHEMOTHERAPY WITH INTERVAL DEBULKING SURGERY FOR ADVANCED EPITHELIAL OVARIAN CANCER: A REAL-WORLD EXPERIENCE FROM AN INDIAN CENTRE

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Introduction/Background Hyperthermic intraperitoneal chemotherapy (HIPEC) has improved survival in advanced epithelial ovarian cancer (EOC) in randomised controlled trials when administered with interval debulking surgery (IDS). There is limited data on IDS HIPEC in EOC from India. This study aimed to assess the perioperative and survival outcomes of IDS HIPEC in Indian women with EOC.

Methodology In this prospective observational study, women who underwent IDS HIPEC for advanced EOC between March 2018 and December 2022 at Tata Medical Center were included. HIPEC (cisplatin 100 mg/m²) was offered to eligible women as per institutional protocol and multidisciplinary team recommendation. The Clavien-Dindo classification and Common Terminology Criteria for Adverse Events (CTCAE) version 5.0 were used for complications. Appropriate descriptive and survival statistics were used in the analysis.



Abstract #832 Figure 1 Overall Survival

Results A total of 77 women (median age 54; IQR 46–63) underwent IDS HIPEC during the study period. The majority

had stage IIIC (92.2%) and high-grade serous histology (94.8%). All had optimal cytoreduction at IDS (CC0 94.8%, CC1 5.2%) before HIPEC. Bowel resection and diversion rates were 20.8% and 11.7%, respectively. Surgical complications of Clavien-Dindo grade 3 or higher occurred in 19.5% of patients. CTCAE grade 3 or higher anaemia and hypokalaemia developed in 32.5% and 13%, while 39% had postoperative infections. Thirty-day readmission and 30-day death rates were 19.5% and 3.9%, respectively. The median hospital stay was 11 days (IQR 8–13) and the median time to adjuvant chemotherapy was 30 days (IQR 25–35). The median progression-free survival was 26.4 months (95% CI 22.4–30.4), and the median overall survival was 43.7 months (95% CI 37.7–49.8).

Conclusion HIPEC administered at the time of IDS in women with advanced EOC had acceptable safety and encouraging survival outcomes.

Disclosures none

#841 GENETIC ALTERATIONS IN EPITHELIAL OVARIAN CARCINOMA

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Introduction/Background Ovarian carcinoma results from a succession of genetic alterations involving proto-oncogenes and tumor suppressor genes, which have a critical role in normal cell growth regulation. Alterations of the c-erbB-2 and c-Myc proto-oncogenes and p53 and BRCA1 tumor suppressor genes, have been frequently observed in a sporadic ovarian carcinoma. The aim of this study was to investigate the frequency of heterozygosity loss (LOH) in the p53 and BRCA1 genes regions, so as the frequency of the c-Myc and c-erbB-2 oncogenes amplification in the sporadic epithelial ovarian carcinomas, together with the association of this alterations with the stage and prognosis of the disease.

Results LOH in the p53 gene region was detected in 31% of tumor samples of which all were in the FIGO IIIC stage. In the BRCA1 gene region, LOH was detected in 39% of tumor samples. By the FIGO classification 60% of this cancers were in the stage IIIC. LOH in both of the analyzed regions was detected in 7.7% of samples, in the FIGO IIIC stage.

Both the amplification of the c-myc and c-erbB-2 oncogenes were found in 27% of the analyzed samples, ranging from 50% to 250%. It is worth to mention that erb was deleted in four samples (27%). In one of them, amplifications of both myc and erb genes were found at the same time (6.6%). Most of the ovarian carcinomas (60%) with alterations in c-Myc and c-erbB-2 belonged to advanced FIGO stages (IIIC).

Conclusion Both types of gene alterations, LOH in the p53 and BRCA1 genes and amplification of c-Myc and c-erbB-2 oncogenes, are most likely late events in pathogenesis of the sporadic epithelial ovarian cancers that correlate with an