587 PROGNOSTIC ROLE OF CHEMOTHERAPY RESPONSE SCORE SYSTEM IN TUBO – OVARIAN HIGH GRADE SEROUS CARCINOMA

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10.1136/ijgc-2021-ESGO.433

Introduction/Background* Epithelial ovarian cancer is a lethal gynaecological cancer with a 5 year survival of < 30% in advanced stages. Recently, NACT followed by surgery is being increasingly used to treat advanced tubo-ovarian high-grade serous carcinoma (HGSC) following the results of randomized trials that demonstrated non- inferior overall survival and morbidity compared to primary surgery.The chemotherapy response score (CRS) has been described to assess the chemotherapy response in patients with HGS tubal & ovarian carcinoma. Studies have shown that the three-tier CRS based on omental assessment of residual disease helps in predicting progression free survival (PFS) and overall survival.

Methodology A retrospective study to assess the prognostic significance of CRS in patients who undergo surgery after 3-4cycles NACT and obtained optimal cytoreduction from January 2016 to July 2018 for HGS ovarian carcinoma in a tertiary care centre in India. CRS was analysed by a single pathologist in omental samples. Patients were followed up for the first 3 years and PFS calculated from diagnosis to radiological evidence of progression or starting of chemotherapy for recurrence. Progression free survival was estimated using the Kaplan - Meier method and compared using the log-rank test.

Result(s)* A total of 76 patients with omental slides were included in the analysis. The median follow up period was 44 months. Ten Patients had CRS 1, 36 had CRS 2 and 30 patients had CRS 3. The median progression free survival for patients with CRS 1, 2 and 3 were 7 months , 16 months and 33 months respectively (p value 0.001) The progression free survival probability at 4 years for patients with CRS1 was 0, CRS 2 was 16.7% and CRS 3 was 44.4% (p value0.001).

Conclusion* The CRS was significantly associated with PFS. The CRS scoring of omental samples provides clinicians prognostic information on patients with HGS ovarian cancer undergoing IDS. This helps in early detection of non-responders and triaging patients for further management.

592 INPP4B GENE IS FREQUENTLY DEREGULATED VIA COPY NUMBER ALTERATION AND UNDEREXPRESSION IN OVARIAN CANCER

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10.1136/ijgc-2021-ESGO.434

Introduction/Background* The PI3K/AKT signaling pathway is activated in a wide spectrum of human cancers. *INPP4B* is a tumor suppressor gene encoding lipid phosphatase type II - a negative regulator of the PI3K signaling. We aimed to determine mechanisms of *INPP4B* inactivation in ovarian cancer.

Methodology Among 194 ovarian cancers studied, there were 126 serous, 23 endometrioid, 18 clear cell, 10 mucinous and 17 other type carcinomas. *INPP4B* mutations were analyzed in 52 carcinomas using Sanger sequencing method. Analyses of copy number alteration (CNA), mRNA expression and promoter methylation were performed with the use of quantitative PCR (qPCR) method for 194, 144 and 125 ovarian carcinomas, respectively. Five specimens of noncancerous fallopian tube constituted a control group. Statistical analyses were done with Fisher's exact test, χ^2 and Mann-Whitney U tests.

Result(s)* One *INPP4B* missense mutation, c.1659G>A, p.(Gly554Ser), was detected in two carcinomas (3.8%, 2/52) of clear cell and serous type.

The *INPP4B* CNA was found in 82 out of 194 (42.3%) ovarian cancers. There were 25.3% (49/194) allelic losses and 17% (33/194) amplifications at the *INPP4B locus*. Allelic loss was associated with high-grade (P = 0.031) and advanced FIGO stage (P = 0.011) tumors. Reduced copy number was more common in carcinomas with *PIK3CA* amplification (P = 0.014) and *PIK3R1* allelic loss (P = 0.001). The *INPP4B* copy loss was mutually exclusive with *PTEN* mutations (P = 0.035).

The *INPP4B* mRNA expression was significantly decreased in ovarian cancers compared with control tissues (P = 0.004). The difference in mean expressions between carcinomas and normal tissues was 57% (0.099 ± 0.12 vs 0.231 ± 0.11). We did not observe an association between decreased mRNA level and copy number loss of the gene. Lower levels of *INPP4B* mRNA were more frequent in cancers with wt *PTEN*, *PIK3R1* and *KRAS* genes (P = 0.038).

INPP4B promoter wasn't methylated in any of 125 ovarian carcinomas.

Conclusion* A part of ovarian cancers have a reduced *INPP4B* copy number and mRNA expression. This may be an alternative pathway of PI3K activation in these tumors. Copy number loss is more common in cancers with aggressive tumor phenotype.

This study was supported by the grant no. 2016/23/B/NZ5/00572 of the National Science Centre, Poland

599 REAL-LIFE TOLERABILITY OF PARP INHIBITORS USING SPECIFIC PRO-CTCAE QUESTIONNAIRES: A SINGLE CENTRE EXPERIENCE IN OVARIAN CANCER

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10.1136/ijgc-2021-ESGO.435

Introduction/Background* Maintenance therapy with PARP inhibitors (PARPis) in Epithelial Ovarian Cancer (EOC) is associated with outstanding results in progression free survival but has to be weighted on patients' quality of life (QoL). Objective of the analysis of specific questionnaires from the Patient-Reported Outcomes version of the Common Terminology Criteria for Adverse Events (PRO-CTCAE) is to achieve an applicable measure of patients outcomes.

Methodology Patients treated with PARPis between November 2016 and December 2020 were enrolled in this prospective study. PRO-CTCAE questionnaires were generated on the specific toxicities of PARPis using the form builder developed by the Division of Cancer Control and Population Science in the National Cancer Institute at the National Institute of Health and administered to the cohort. Patients toxicities, as recorded by physicians, were analyzed and compared with monthly PRO-CTAE questionnaires.

Result(s)* Thirty-one EOC patients underwent maintenance therapy with PARPis after 1 (24%), 2 (48%) and ≥3 (28%) lines of chemotherapy. The median age was 56 (range 35-77), 83.3% of patients had an ECOG Performance Status 0 and 14 (45.2%) were BRCA mutated. 50% received olaparib, 42.9% niraparib and 7,1% rucaparib. No patient discontinued treatment due to toxicity and 38.7% delayed the treatment due to anaemia (29%) or thrombocytopenia (9,7%). Haematological toxicities and asthenia were the most frequent adverse events recorded by physicians and occurred in 42.5% and 45.2% of patients, respectively. Concordance between the toxicity reported by patients and by physicians was observed in 40% of cases. PRO-CTCAE questionnaires contributed to the toxicity evaluation revealing symptoms under-reported by physicians, in particular: 35.7% of anorexia, 79.5% of nausea, 90% of vomiting, 63.7% of constipation, 79.8% of diarrhea, 35.3% of asthenia, 87.4% of arthralgia and 100% of headache and insomnia.

Conclusion* PRO-CTCAE is a toxicity assessment tool that should be required especially in the monitoring of maintenance treatments. The physician's evaluation of toxicities, enriched by the patient reported outcomes, could allow more targeted and earlier interventions and potentially affect the adherence to the treatment.

All authors have no conflict of interest

600 MULTIMODAL SCORING SYSTEM FOR R0 RESECTION IN OVARIAN CANCER

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10.1136/ijgc-2021-ESGO.436

Introduction/Background* Complete tumor resection (R0) at primary or interval debulking surgery is a main prognostic factor for overall survival in patients diagnosed with ovarian cancer. Neoadjuvant treatment has become standard of care in patients with advanced disease (FIGO stage IIIC/IV) or reduced performance status. Radiologic assessment of treatment response using CT scans has a low prediction for complete surgical tumor resection.

Here we aim to identify prognostic factors associated with R0-resection after neoadjuvant chemotherapy (NACT) for ovarian cancer and propose a multimodal scoring system using 3 Tesla diffusion-weighted MRI (DW-MRI), CA-125 and diagnostic laparoscopy for future investigation.

Methodology All patients treated with neoadjuvant chemotherapy for advanced primary ovarian, peritoneal or Fallopian tube cancer between 01/2012-12/2020 at the University Hospital Bern were included in this retrospective cohort study. Clinical and surgical data assessed include age, menopausal status, ECOG performance status, radiologic findings, histologic subtype, FIGO stage, CA-125, Fagotti-score, surgical resection status and chemotherapeutic regimen.

Multiple MR-graphic findings are scored number and distribution of intra-abdominal and thoracal lesions, qualitative and quantitative diffusion restriction, lymph nodal (LN) status, as well as prevalence and size of cardio-phrenic LN. Following treatment, change in tumor and metastatic lesion size are assessed.

Result(s)* Overall, 130 out of 475 women with primary ovarian cancer treated at the University Hospital Bern between 2012 – 2020 underwent NACT. Mean age was 66.2 years (range 24-90). Most patients were diagnosed with high-grade serous subtype (92%) at FIGO stage IIIC or IV (78%). Interval debulking surgery was performed and resection status was noted for 112 patients after a mean of 3 neoadjuvant cycles. R0 resection was achieved in 80 patients (71.4%), 10 patients (8.9%) had residual disease <1cm.

Until now, in our cohort, DW-MRI was performed in three patients during NACT.

Conclusion* We propose a multimodal scoring system for R0-resection based on DW-MRI, CA-125 and Fagotti-Score assessed during diagnostic laparoscopy. To validate this score, a prospective multicentre study including women with suspected primary or recurrent ovarian cancer is planned.

605 INFLUENCE OF SPLENECTOMY ON CHEMOTHERAPY TREATMENT AND ONCOLOGICAL PROGNOSIS IN WOMEN WITH ADVANCED OVARIAN CANCER

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10.1136/ijgc-2021-ESGO.437

Introduction/Background* To determine the effect of splenectomy on subsequent chemotherapy treatment and prognosis in women with advanced ovarian cancer.

Methodology We performed a retrospective study comparing two cohorts of patients. Data from 60 women who underwent splenectomy during cytoreductive surgery for primary or relapse ovarian cancer were compared with 62 controls who also underwent this type of surgery without splenectomy matched for baseline and surgical characteristics including type and date of surgery at University Hospital La Fe (Spain) between November 2011 and December 2019.

Result(s)* A total of 72/459 (15,7%) women who underwent splenectomy for advanced ovarian cancer were identified. Twelve women were excluded and finally 60 cases and 62 controls were identified.

No differences were observed regarding the following variables: postoperative complications (31.7% vs. 19.4%), mean time to start adjuvant chemotherapy (48.6 vs. 42.7 days), mean time to complete chemotherapy in women who received only adjuvant treatment (104 vs. 116 days) and percentage of six-cycle chemotherapy completion (78.8% vs. 98.4%) after adjusting for a potential confounding factors. No differences were observed between groups related to cycles delayed (50% vs. 32.3%; P=0.16) and reduction in the doses of chemotherapy (23.3% vs. 22.6; P=0,61); unlike the differences found according to cycles cancelled (30% vs. 11.3%; P=0.037). Two women died in the splenectomy group (3.3%). The mean