Prognostic Role of Chemotherapy Response Score System in Tubo-Ovarian High Grade Serous Carcinoma

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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 scoring of omental samples provides clinicians prognostic information on 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 3-4 cycles 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 value 0.001).

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.

Innp4b Gene is Frequently Deregulated Via Copy Number Alteration and Underexpression in Ovarian Cancer

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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, χ² 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.

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Real-Life Tolerability of PARP Inhibitors Using Specific Pro-CTCAE Questionnaires: A Single Centre Experience in Ovarian Cancer

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Introduction/Background* Maintenance therapy with PARP inhibitors (PARPi) 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-CTCAE 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