RECYCLING OF DISCARDED OVARIAN CANCER ASCITES TO MONITOR THERAPY RESISTANCE

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Introduction/Background Ovarian cancer ascites is one of the signs of ovarian cancer (OC) metastasis in the peritoneum and is found in patients at the time of diagnosis and in disease relapse. This serous fluid is used for the initial cytopathological diagnosis and is frequently drained from the peritoneal cavity at advanced stages only for symptomatic relief (and is discarded). In the ovarian cancer context, the presence of ascites is a unique opportunity to monitor the tumor kinetics during disease progression without additional invasive procedures. The main aim of this work was to evaluate the potential of this usually discarded biological material to evaluate the expression of proteins associated with therapy resistance in ovarian cancer ascites cells during disease progression.

Methodology We received ascites from OC patients at diagnosis (n=7) and during treatment (n=8). After centrifugation, samples were formalin-fixed and embedded in Histogel before standard histological processing. Next, immunocytochemistry was performed to assess the expression of three biomarkers associated with chemoresistance in ovarian cancer (ALDH1, SOX2, and PgP).

Results The majority of our samples had a sufficient number of cells to perform a diversity of histological-based techniques and other molecular studies. The expression of cancer stem cell markers ALDH1 and SOX2 was frequently negative. However, SOX2 and ALDH1 were expressed in samples obtained after chemotherapy. Multi-drug resistance marker (Pgp) expression was negative in samples at diagnosis but was found positive, especially in samples from patients with refractory ascites and without clinical response to treatment.

Conclusion The multidimensional potential ovarian cancer ascites as a spontaneous liquid biopsy remains underexplored. Our results show that the use of immunocytochemistry to evaluate resistance biomarkers in tumor cells present in ascites drained from patients during treatment has the potential to predict response to treatment.

THE EFFICACY OF MEK INHIBITORS IN THE TREATMENT OF LOW-GRADE SEROUS OVARIAN CANCERS: A SYSTEMATIC REVIEW

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Introduction/Background It’s very important to identify individuals with high genetic risk of developing cancer for prevention of familial ovarian cancer forms, their follow-up management and timely preventive care. A burdened family history (BFH) of cancer is unquestionable and most important indication for genetic testing. Objective: To assess the BFH in patients with ovarian cancer (OC), fallopian tube carcinoma (FTC), primary peritoneal carcinoma (PPC).

Methodology All women with OC, FTC and PPC, who treated at oncogynecologic department N.N. Alexandrov National Cancer Centre of Belarus between January 2022 and May 2022 were retrospectively identified. The main criteria were serous carcinoma, endometrioid carcinoma and clear cell carcinoma. All patients filled out BFH questionnaires. Analysis of the normality of data distribution was carried out on the basis of the Shapiro-Wilk’s W test. The Mann-Whitney U-test was used to compare two independent samples.

Results A total of 92 patients were analyzed: 81 patients with OC, 9 with FTC, 2 with PPC. The mean was 54.5 years, high grade serous carcinoma was the predominant (87%). The majority of patients were of Belarusian (93.5%). 53 (57.6%) women were in menopause at the time of diagnosis, in premenopause was less (28.3%). Most of the study participants had pregnancies, children, lactation were noted (88.0%, 84.8%, 71.7%, respectively). Only 15.2% of women indicated the use of contraceptives. A BFH was noted in 38 (63.0%) patients, it was absent in 34 (17%) patients. The average age of women with a BFH was 53.2 years, without – 56.7 years. There were no statistically significant differences in the groups of patients without and with a BFH, depending on age, diagnosis, histological variant of the tumor (p>0.05).

Conclusion Presence of burdened family history revealed in most cases (63% patients with OC, FTC, PPC) requires further genetic testing.

BURDENED FAMILY HISTORY IN PATIENTS WITH OVARIAN CANCER: RETROSPECTIVE MONOCENTRIC STUDY

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Introduction/Background The low response rates to traditional systemic therapies prompts the need for novel therapies in the treatment of LGSC. LGSC tumors have demonstrated a high frequency of mutations in the MAPK cascade, which is targeted by MEKi. The primary objective of this systematic review was to assess the overall response rate (ORR) of LGSC to MEKi.

Methodology PubMed, EMBASE, Medline and the Cochrane Database were searched from inception to March 2022. Inclusion criteria were studies assessing the treatment of LGSC in the primary or recurrent setting with the use of a MEKi, published in English. Case reports, case series, conference proceedings, in vitro studies and animal studies were excluded. Studies were screened and assessed for eligibility by two independent reviewers (AK, CC), with conflicts resolved by a third reviewer (TZ). Data was extracted using pre-established criteria.
Results The initial literature search identified 1815 papers; four met the eligibility criteria. Three were randomized clinical trials and one was a phase II single-arm prospective cohort study. MEKI investigated included: pimasertib, selumetinib, trametinib, and binimetinib. A total of 680 patients were included in these studies, of which 416 were treated with a MEKi alone. All patients were treated for recurrent LGSOC. Objective response rates (ORR) to MEKi ranged from 12.1 to 26% and median progression-free survival (PFS) ranged from 7.2 to 13 months.

Conclusion While one study demonstrated significantly improved efficacy of a MEKi over physician-choice systemic therapy in the treatment of recurrent LGSC, another did not show significant benefit. Two additional studies did not compare MEKi to current traditional chemotherapy or hormonal therapies used in the management of LGSC, limiting their clinical relevance. Mutation profiles within the tumors may affect the ORR to various MEKi. Further prospective and randomized trials are needed to determine the efficacy of MEKi in treating LGSC.

Introduction/Background Platinum-resistant ovarian cancer (PROC) is associated with a substantial humanistic and economic burden due to disease symptoms, treatment-related side effects and costs. Cost-utility analyses that inform healthcare decision-makers require a set of health state utility values (HSUVs). As part of a systematic literature review (SLR), published evidence of HSUVs associated with PROC were described.

Methodology The scope of the SLR was defined using the Patient population, Intervention, Comparators, Outcomes measures and Study design (PICOS) statement, and performed using pre-defined search terms in accordance with PRISMA guidelines. Key biomedical literature databases (Medical Literature Analysis and Retrieval System Online [MEDLINE®] and Excerpta Medica Database [Embase®]), EconLit and Cochrane were searched for records dated up to July 6, 2021. Relevant congresses (2017–2021), previous health technology assessment submissions, and previously conducted SLRs were also searched to capture relevant data.

Results Out of 34 studies from the SLR, 17 publications reporting HSUVs were identified. Of these, nine studies gathered EQ-5D values directly from ovarian cancer patients, four mapped EQ-5D HSUVs from FACT-O or FACT-G values, three studies mapped utility values from other solid tumor indications and one modeled EQ-5D HSUVs using Bayesian regression from patient registry data. HSUVs were relatively high at pre-progression (range 0.610 to 0.718) while patients are receiving routine chemotherapy, with a lower value for those experiencing grades 3 and 4 toxicity (0.500). HSUVs increased in those receiving maintenance therapy with PARP inhibitors after chemotherapy (range: 0.710 to 0.838). There was a decrease observed those progressed on platinum chemotherapy (range 0.40 to 0.649), with a median disutility from pre- to post-progression of 0.093.