between chemo-naïve to chemo-exposed patients (figure 1, cPARG: 23.8% vs. 78.4%, p<0.001). cPARG was associated with a decreased proliferation score (Ki-67 8.0% vs. 19.5%, p=0.03) and decreased overall survival (figure 2). PARG expression could be induced by chemotherapy in chemo-sensitive cells but not in isogenic chemo-resistant cells.

Conclusions PARG localizes to the nucleus in ovarian cancer cells but shifts to the cytoplasm following chemotherapy. Localization of PARG to the cytoplasm is associated with poor survival. The association between PARG expression and resistance to chemotherapy or PARP inhibitors warrants further investigation.

Abstract EP244/#718 Figure 1 Representative micrographs of serous carcinomas stained with anti-PARG and anti-Ki-67 antibodies. cPARG, PARG localized to the cytoplasm; nPARG, PARG localized to the nucleus; Scale, 50μm

Abstract EP244/#718 Figure 2 Kaplan-Meier survival curve and Hazard Ratio for death in cPARG compared to nPARG patients. cPARG, PARG localized to the cytoplasm; nPARG, PARG localized to the nucleus; Dx, diagnosis.

Objectives To elucidate an off-target mechanism by which niraparib induces ovarian cancer cell apoptosis regardless of homologous recombination (HR) status through downregulation of the oncogenic SRC/STAT3 axis.

Methods A variety of techniques were used to determine the underlying mechanisms by which niraparib regulates the SRC/STAT3 axis including tumor organoid formation, cell viability assays, colony formation assays, real-time PCR, western blot, apoptosis assays, cell transfections, in-cell and in-vitro thermal shift assays, and confocal microscopy.

Results Niraparib exhibited more potent antitumor effects than olaparib in both HR deficient and proficient models. In addition to inhibiting PARP catalytic function, niraparib-promoted cell death in ovarian cancer cells was found to be mediated by its inhibitory effects on activated STAT3 (p-STAT3). Niraparib altered the expression of STAT3 downstream target genes, specifically those involved in apoptosis. The anti-apoptotic gene BCL-XL (BCL2L1), usually induced by STAT3 activation, was significantly reduced while the proapoptotic CASP3, CASP8, and CASP9 genes, which are suppressed by STAT3 activity, were markedly upregulated. Niraparib-mediated inhibition of the STAT3 pathway was found to be at least partially attributed to the downregulation of SRC kinase activity as demonstrated in all tested ovarian cancer cell lines and patient tumor-derived organoid models.

Conclusions Niraparib inhibits the growth of ovarian cancer cells, regardless of HR status, more effectively than olaparib. Unlike olaparib, which is known to activate STAT3, niraparib inhibits STAT3 activity by interfering with SRC tyrosine kinase. These findings provide a potential off-target mechanism by which niraparib may provide benefit to ovarian cancer patients regardless of HR biomarker status.

Abstracts

EP245/#993 NIRAPARIB INDUCES OVARIAN CANCER CELL APOPTOSIS REGARDLESS OF HOMOLOGOUS RECOMBINATION STATUS THROUGH DOWNREGULATION OF THE ONCOGENIC SRC/STAT3 AXIS

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Abstract EP246/#636 THE EFFICACY OF MEK INHIBITORS (MEKI) IN THE TREATMENT OF LOW-GRADE SEROUS OVARIAN CANCER (LGSC): A SYSTEMATIC REVIEW

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Objectives Low response rates of LGSC to traditional systemic therapies prompts the need for novel therapies. LGSC have 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.

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Methods Pubmed, EMBASE, Medline and the Cochrane Database were searched from inception to March 2022. Inclusion criteria were studies assessing the treatment of LGSC with a MEK inhibitor in the primary or recurrent setting, 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 Initial literature search identified 1815 papers; four met eligibility criteria. Three were randomized clinical trials and one was a phase II single-arm prospective cohort study. A total of 680 patients were included, of which 416 were treated with a MEK inhibitor alone. All patients were treated for recurrent LGSC. ORR ranged from 12.1 to 26.0% and median progression-free survival (PFS) ranged from 7.2 to 13 months.

Conclusions While one study demonstrated significantly improved efficacy of MEK inhibitor over physician-choice systemic therapy, another did not show benefit. Two additional studies did not compare MEK inhibitor to traditional therapies, limiting their clinical relevance. LGSC with BRAF and KRAF mutations have higher ORR to MEK inhibitor. Further prospective and randomized trials are needed to determine the efficacy of MEK inhibitor in treating LGSC.

Objectives Ovarian cancer survival rates, cancer progression and risk of death with this cause have not been studied in Georgia yet. Conducting the study based on population registry data has been possible since 2015. 5 years registry database allowed us to study 3 years survival and risks.

Methods 1,467 (5.0%) cases of ovarian cancer were registered in the Georgia in 2015–2019. Using dBase SPSS of the registry, 3-year survival of ovarian cancer and risks of cancer progression were studied; Risks of cancer progression and death were assessed 36 months after the incidence.

Results Compared to other cancer sites, 3-year survival rate of ovarian cancer is low in both Georgia (55.4%) and Tbilisi (55.2%). Risk of ovarian cancer progression, 36 months after the incidence was 3.3 times higher than cervical and 1.4 times higher than endometrial cancer in Tbilisi. Among gynecological cancers both in Tbilisi and in Georgia, No1 killer is ovarian cancer. The risk of ovarian cancer death in Tbilisi is 2.1 times higher compared to cervical and 2.4 times higher than endometrial cancer death.

Conclusions Research should be continued and study 5 years survival and risks of cancer caused death, according to treatment methods and schemes, as well as cytological, ultrasound (3D), cytological, histological, histochemical and molecular characteristics of cancer. Study of 5-year survival, in addition should determine ECOG Adjusted Survival, for which it is recommended that the Registry add ECOG follow-up to the registration variables.

Objective In the Indian population, endometriosis did not have any impact on the age at presentation, CA 125 levels, stage of the disease and survival out comes in EC and CCC ovary.

Conclusions In the Indian population, endometriosis did not have any impact on the age at presentation, CA 125 levels, stage of the disease and survival outcomes in EC and CCC ovary.

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