Abstract EP242/#861 Figure 1

subset of whom also underwent tumor next generation sequencing.

Methods Ovarian cancer patients who underwent HER2 testing were identified. Clinical information, including histology, germline BRCA status, and immunohistochemistry (IHC) profile were noted. For patients receiving multiple biopsies, each anatomical location, timing, and HER2 expression were counted.

Results Among 193 patients, expression of 2+ and 3+ were found in 28% and 6%, respectively, and 18 patients received HER2 targeted drug. HER2 3+ rate was 23% in mucinous, 11% in endometrioid, 9% in clear cell, and 3% in high grade serous type. HER2 3+ was exclusively identified in BRCA wildtype, MMR proficient, or PD-L1 low expressing patients. Genomic analysis showed that the TP53 mutation rate was lower and other mutations such as ARID1A, KRAS, and PIK3CA were relatively more common in HER2 2+ or 3+, compared to HER2 0+ or 1+ patients. CNV analysis showed that 4 out of 5 HER2 3+ patients showed ERBB2 amplification. Out of 20 patients with multiple time-lagged biopsy, 9 patients showed an increase in HER2 expression in the later biopsy sample.

Conclusions Ovarian cancer patients with HER2 overexpression show a distinct histological, IHC, and genomic profile. HER2 targeting agent may serve as a potential option for BRCA wildtype patients, especially in the later lines of treatment.

Abstract EP243/#1167

RELATIVE EXTENSIVENESS OF PERITONEAL SEEDING VERSUS LYMPH NODE METASTASIS AS A PROGNOSTIC FACTOR IN ADVANCED-STAGE OVARIAN CANCER

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10.1136/ijgc-2022-igcs.334

Objectives To evaluate the prognostic impact of relative extensiveness of peritoneal seeding versus lymph node metastasis in advanced stage ovarian cancer.

Methods Medical records of consecutive patients with advanced stage ovarian cancer who were treated in Seoul National University Bundang Hospital between 2013.1–2021.12 were retrospectively reviewed. The impact of clinicopathologic factors including relative extensiveness of peritoneal seeding versus lymph node metastasis on recurrence-free survival was evaluated.

Results A total of 241 patients was identified and analyzed. Median age was 59 years (35–81). Peritoneal seeding was grouped into three according to the area: none (8.7%, n=21) pelvis (5.8%, n=14), and above pelvis (85.5%, n=206). The extensiveness of lymph node metastasis was grouped into five according to the involved areas among pelvis, abdomen, chest, and neck: none (44.8%, n=108), single metastasis (15.3%, n=37), double metastasis (17.0%, n=41), and triple or more metastasis (22.8%, n=55). Relative extensiveness of peritoneal seeding versus lymph node metastasis was set as three categories according to the different combinations of the two groups: severe (44.8%, n=108), moderate (51.0%, n=123), and mild (4.1%, n=10). Relative extensiveness of peritoneal seeding versus lymph node metastasis did not have a significant prognostic impact on recurrence-free survival (mean, 67.8 months [95% CI, 58.7–75.5]; 56.5 [48.6–64.3]; 80.0 [46.3–113.6]; p=0.253). However, severe level of peritoneal seeding had poor prognostic impact on recurrence-free survival (mean, 77.8 months [95% CI, 63.9–91.8]; 67.3 [37.7–96.8]; 59.2 [53.1–65.4]; p=0.036).

Conclusions Relative extensiveness of peritoneal seeding versus lymph node metastasis did not have a significant prognostic impact on recurrence-free survival in advanced stage ovarian cancer.
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 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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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 oncogetic 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.

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.