Methods We retrospectively reviewed medical records of patients who received splenectomy as part of cytoreductive surgery in advanced ovarian cancer from 2007–2022. Patients were divided into the parenchymal invasion group and capsular/hilar invasion group. Clinical characteristics including histologic invasion patterns and survival outcomes were analyzed.

Results A total of 100 ovarian cancer patients received splenectomy; 55 (55%), 40 (40%) and 5 (5%) cases were performed during primary debulking surgery, interval debulking surgery and at the time of disease recurrence respectively. The median age was 54.5 yrs, and all patients had FIGO stage IIIC-IV disease. 27 (27%) patients had parenchymal invasions and all the lesions were accompanied by capsular or hilar metastasis without solitary parenchymal invasion. Among the patients with primary disease(n=95), 42 (44.2%) patients had stage IV disease including 17 (17.8%) patients with splenic parenchymal metastasis. There was no difference in residual disease (p=0.392), progression-free survival (p=0.339) and overall survival (p=0.841) between the patients with parenchymal invasion and capsular/hilar metastasis.

Conclusions Although splenic parenchymal metastasis reflected widespread tumor dissemination, all the lesions were followed by hilar or capsular involvement and surgically treatable disease. The prognosis of splenic parenchymal metastasis was not inferior to the capsule or hilar invasion, therefore, it needs to be considered as FIGO stage IIIC disease.

EP240/#814 PROGNOSTIC SIGNIFICANCE OF CLINICAL FACTORS, INCLUDING BRCA MUTATION STATUS, IN EPITHELIAL OVARIAN, PERITONEAL, AND FALLOPIAN TUBE CANCERS

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Objectives We analyzed the survival outcomes of patients with epithelial ovarian, peritoneal, or fallopian tube cancer (EOPFTC) with BRCA1/2 mutations and the clinical factors associated with the prognosis of these cancers.

Methods Based on the data collected from Clinical Data Warehouse of Catholic university of Korea, we investigated patients who had been diagnosed and treated for EOPFTC, and undergone germline BRCA test in 6 hospitals between January 2012 and December 2019.

Results In total, 378 patients were identified and 76 (20.1%) women carried BRCA 1/2 mutation. There was no significant difference in progression-free survival (PFS; p = 0.562) and overall survival (p = 0.677) between BRCA 1/2 mutation and wild-type groups. In multivariate analysis, however, PFS of BRCA 1/2 mutation group for 18 month from primary treatment was significantly superior to wild-type group (p = 0.024). In subgroup analysis for high grade serous carcinoma patients, BRCA 1/2 mutation was an independent favorable prognostic factor for PFS (p = 0.035). Subgroup analysis for stage III to IV disease also demonstrated an independent PFS gain in patients with BRCA 1/2 mutation (p = 0.015). Neoadjuvant chemotherapy as primary treatment was related with poor PFS (p < 0.001) and reduced OS (p = 0.005).

Conclusions Germline BRCA 1/2 mutation improved short-term PFS in patients with EOPFTC. Elevated initial CA125 level and primary neoadjuvant chemotherapy were related to poor prognosis.

EP241/#853 HIGH EXPRESSION OF TRAFFICKING PROTEIN TRANSMEMBRANE P24 TRAFFICKING PROTEIN9 PROMOTES POOR PROGNOSIS OF EPITHELIAL OVARIAN CANCER

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Objectives Transmembrane emp24 domain-containing protein9 (TMED9) belongs to the TMED/p24 family which regulates the innate immune and protein transport via the ER-Golgi cargo pathway. TMED9 role in epithelial ovarian cancer (EOC) has not been clarified yet. Therefore, in this study we aim to evaluate the function, molecular mechanism and clinicopathological significance of TMED9 in EOC.

Methods Expression levels of functional role of TMED9 were respectively evaluated by Immunohistochemistry staining of EOC, borderline, benign and normal epithelial tissues, qPCR, western blotting, and public data sets. The functional roles of TMED9 were evaluated by MTS, colony formation, and transwell migration/invasion assays in EOC cell lines.

Results TMED9 protein was elevated in EOCs according to a GEO and TCGA datasets. High mRNA and protein levels of TMED9 were observed in EOCs. Importantly, high expression level of TMED9 was associated poor overall survival and disease free survival compared with low expression of TMED0 in EOCs (p = 0.006, p < 0.001, respectively). In vitro results also demonstrated the knockdown of TMED9 was associated with decreased cell invasion (p < 0.001), migration (p < 0.001), proliferation (p < 0.001), and colony forming abilities (p < 0.001) supporting the oncogenic role in EOC.

Conclusions Our study is the first work to identify an oncogenic role of TMED9 in EOC tissues and cell lines which may provide insights into the application of TMED9 as a novel predictor of clinical outcome and a potential therapeutic target in EOC patients.

EP242/#861 HUMAN EPIDERMAL GROWTH FACTOR RECEPTOR-2 (HER2) RECEPTOR EXPRESSION AND ITS DYNAMIC CHANGE IN OVARIAN CANCER PATIENTS

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Objectives HER2 targeted drugs are increasingly introduced in non-breast cancers, yet studies on HER2 expression in ovarian cancer patients is lacking. Therefore, we studied HER2 receptor status and its dynamic change in ovarian cancer patients, a
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) profiles 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.

EP243/#1167 RELATIVE EXTENSIVENESS OF PERITONEAL SEEDING VERSUS LYMPH NODE METASTASIS AS A PROGNOSTIC FACTOR IN ADVANCED-STAGE OVARIAN CANCER

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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.

EP244/#718 POLY-(ADP-RIBOSE)-GLYCOHYDROLASE LOCALIZES TO THE CYTOPLASM FOLLOWING NEOADJUVANT CHEMOTHERAPY IN OVARIAN SEROUS CARCINOMA

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Objectives Poly-(ADP-ribose)-glycohydrolase (PARG) regulates the parylation of DNA and poly(ADP-ribose)-polymerases (PARPs) during the single-strand DNA repair process. PARG deregulation causes resistance to PARP inhibitors in several cancer cell lines. We studied the clinical significance of PARG expression in ovarian carcinomas.

Methods Epithelial ovarian cancer tissue microarrays including 86 high-grade serous carcinomas were stained with anti-PARG antibody. PARG expression was classified as cytoplasmic (cPARG) or nuclear (nPARG). Demographic and survival data was collected from the medical records. We compared overall survival, DNA damage response (gamma-H2AX, RAD51) and proliferation (Ki-67) between the PARG groups. Ovarian cancer cell lines were treated with cisplatin for 24–48 hours and their nuclear and cytoplasmic extracts were assessed for PARG levels by western blot and immunofluorescence.

Results While normal and borderline histologies expressed PARG exclusively in the cytoplasm, tissues from cancer patients expressed nuclear PARG in up to 57% of the cases. Interestingly, we detected a shift from nucleus to cytoplasm 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.