DISTRIBUTION OF BRCA1/2 MUTATIONS AND CLINICAL OUTCOMES IN EPITHELIAL OVARIAN, PERITONEAL, FALLOPIAN TUBE CANCER: BASED ON MULTICENTER REAL-WORLD DATA

Heekyoung Song, Jiyoung Hong, Yong-Ho Kim. Department of Obstetrics and Gynecology, Incheon St. Mary’s Hospital, College of Medicine, the Catholic University of Korea, Seoul, Incheon, Korea. Republic of; 2Department of Obstetrics and Gynecology, St. Vincent Hospital, College of Medicine, the Catholic University of Korea, Seoul, Suwon, Korea, Republic of.

Introduction/Background This study aimed to review multicenter real-world data for BRCA1/2 gene test and clinical outcomes in epithelial ovarian, peritoneal, fallopian tube cancer.

Methodology We reviewed the patients who underwent primary surgery and adjuvant treatment between January 2009 and December 2021 in Seoul, Yeouido, and Incheon St. Mary’s Hospital, College of Medicine, the Catholic University of Korea. The following data were retrospectively obtained for analysis: clinical factors such as patient age, levels of tumor markers (CA 125, CA 19–9); stage (International Federation of Gynecology and Obstetrics) at diagnosis, histopathology, and the results of BRCA1/2 gene test.

Results In total, 652 patients were evaluated and 237 patients (36.3%) underwent BRCA1/2 gene test. Among all patients who received BRCA1/2 gene test, BRCA1/2 mutations were noted in 62 patients (26.2%). In BRCA1/2 mutation group, 53 had high-grade serous ovarian cancer (HGSOC), and 9 had non-HGSOC consisting of endometrioid carcinoma (n=5), clear cell carcinoma (n=2), and mixed carcinoma (n=2). The portion of HGSOC in BRCA1/2 mutation group was significantly higher than that in BRCA1/2 wild-type group (85.8% versus 61.0%, p<0.001). Progression free survival (PFS) of BRCA1/2 mutation group was significantly worse than that of BRCA1/2 wild-type group (30.4 versus 36.6 month, p=0.003).

Overall survival of mutation group was better than that of wild-type group without significant differences (64.4 versus 48.8 month, p=0.807). The 26 patients in BRCA1/2 mutation group were treated by poly ADP ribose polymerase (PARP) inhibitor for maintenance therapy.

Conclusion BRCA1/2 mutations were reported in epithelial ovarian, peritoneal, and fallopian tube cancer. In contrast to other studies that reported better PFS in BRCA1/2 mutation group than in BRCA1/2 wild-type group, BRCA1/2 mutation group showed worse PFS in this study. Further studies are needed on the effect of BRCA1/2 mutation on prognosis.

REPROGRAMMING OF PATIENT-DERIVED HGSOC ORGANOID TREATMENT LINKS STEMNESS POTENTIAL AND MECHANISMS OF RESISTANCE

Anca Chelaru-Raicu, Nemanja Vasovic, Aarushi Devkumar Dawesar, Eduardo Beltran, Benedikt Obermayer, Alexander Burges, Fabian Kraus, Fabian Tillsch, Sven Mahner, Mirjana Kesler, Department of Obstetrics and Gynecology, LMU University Hospital, Munich, Germany; 1Department of Clinical Neuramunology, LMU University Hospital, Munich, Germany; 2Core Unit Bioinformatics, Berlin Institute of Health, Charité-Universitätsmedizin, Berlin, Germany.

Methods Phenotypically and genotypically validated PDOs from primary tumor deposits of HGSOC were used to study biological changes after carboplatin exposure by combining single-cell RNA sequencing, and functional in vitro assays. Organoid formation efficiency assay (OFE) was developed to quantify the growth capacity of PDOs following 48 hours of carboplatin and analyse the long-term expansion of platinum pretreated lines. Changes in organoid cellular architecture were investigated by FACS sorting of progenitor populations, confocal imaging, and qPCR of key developmental regulators.

Results Overall, 4 organoid lines with known clinical response to carboplatin was investigated by sc RNA sequencing providing insight into tumor heterogeneity and key cellular pathways activated in PDOs resistant to carboplatin. The expression profile of the acute response (48 h) revealed candidate pathways behind incomplete drug response and tumor survival,