The results of this large-scale study suggest that pathogenic variants in BRCA1 and BRCA2 were associated with the type of mutation, however larger studies are warranted.

### EP172/#350 INTEGRATED MOLECULAR PROFILE OF PLATINUM RESISTANT EPITHELIAL OVARIAN CARCINOMA

1. Karolina Seborova, 1,2 Viktor Hlavac, 1,2 Petr Holy, 3 Suniva Bjerkund, 4 Thomas Fleischer, 1,3 Albeta Spalenkova, 5 Lukas Rob, 6 Martin Hrudia, 4 Petr Ceraj, 7 Jiří Bouda, 5,6 Vessela N Kristens, 1,2 Pavel Soucek, 7 Radka Vlachkova, 1 National Institute of Public Health, Toxicogenomics Unit, Praha, Czech Republic; 2 Biomedical Center, Laboratory of Pharmacogenomics, Pilsen, Czech Republic; 3 Institute of Clinical Medicine, Faculty of Medicine, University of Oslo, Department of Medical Genetics, Oslo, Norway; 4 Institute of Cancer Research, Norwegian Radium Hospital Oslo University Hospital, Department of Cancer Genetics, Oslo, Norway; 5 University Hospital Kralovske Vinohrady and Third Faculty of Medicine, Department of Gynecology and Obstetrics, Prague, Czech Republic; 6 University Hospital in Pilsen, Department of Gynecology and Obstetrics, Pilsen, Czech Republic; 7 National Institute of Public Health, Toxicogenomics Unit, Praha, Czech Republic

Objectives Epithelial ovarian carcinoma (EOC) is a serious malignancy with high mortality due to late diagnosis and drug resistance development. Drug resistance is one of the major obstacles to successful anticancer therapy. The main aim of our study was to analyze molecular profile based on gene expression, DNA methylation level, and genetic variability in EOC patients stratified by the platinum therapy resistance status.

Methods For the present study, we selected 72 EOC patients with sensitive (N=43) or resistant (N=30) status. Whole genome expression of protein-coding genes was profiled by mRNA sequencing technology (N=60), lncRNA expression by whole transcriptome RNA sequencing (N=23), global methylation by DNA microarrays (N=50), and somatic mutation rate by whole exome sequencing (N=50).

Results Molecular profile of platinum resistant EOC patients differed from sensitive EOC patients in upregulation of five protein-coding genes (NEURL1, FGCBP, MMP11, NCAM1, and ARMC3) and five lncRNA (ADAMTS9A1, TCF21A1, ARMC3A1, LINC-HIST2H3PS2-35, and LINC-BCR-4), higher methylation of seven protein-coding genes (ABCC4, ABCB10, SLC1A7, SLC19A2, SLC50A1, XPC, and FOXO1) and three lncRNA (LINC00263, LINC00460, NEAT1) and higher frequency of mutations in TP53 gene. On the other hand, three protein-coding genes (LPL, CD36, FABP4) and three lncRNA (LINC-IGGL5, LINC-TEEM121-12, CHST6-AS1) were downregulated, lower methylation was observed for ATP1A1 gene, and the Hippo pathway genes were less mutated in resistant patients.

Conclusions Our study shows a complex network of dysregulated genes and gene expression products connected with the resistance status of EOC patients which should be further characterized. Supported by INTER-ACTION LTAUSA19032, GACR no. 21–140825, AZV no. NU20–09–00174 and GAUK no.1074120.