

malignant germ cell tumors have no complete intra peritoneal surgical staging.

EPV195/#37

VEGF-A INHIBITOR INDUCED TUMOR-ASSOCIATED MACROPHAGE REPROGRAMMING AND PD-L1 OVEREXPRESSION VIA A DUAL ROLE OF IFN- γ IN OVARIAN CANCER

^{1,2}C Li*, ^{1,2}J Peng, ³Y Li, ^{1,2}C Sun, ⁴Z Zhang, ^{1,2}L Liu, ^{1,3}S Yao, ^{1,2}Y Li, ^{1,2}K Song. ¹Qilu Hospital of Shandong University, Gynecology Oncology Key Laboratory, Jinan, China; ²Qilu Hospital, Cheoloo College of Medicine, Shandong University, Obstetrics and Gynecology, Jinan, China; ³School of Medicine, Cheoloo College of Medicine, Shandong University, Obstetrics and Gynecology, Jinan, China; ⁴Beijing Chao-Yang Hospital, Capital Medical University, Obstetrics and Gynecology, Beijing, China

10.1136/ijgc-2021-IGCS.266

Objectives The beneficial effects of vascular endothelial growth factor A (VEGF-A) inhibitor are only observed in a subset of patients with advanced ovarian cancer. The lack of response of VEGF-A inhibitors is thought to be related with the immunosuppressive microenvironment; however, this is still controversial. A better understanding of the underlying mechanism of VEGF-A inhibitor (Bevacizumab)-mediated the immune escape could benefit the development of therapeutic regimens for patients with ovarian cancer.

Methods The polarization of tumor-associated macrophages (TAMs), IFN- γ secretion of macrophages and ovarian cancer cells, PD-L1 expression in ovarian cancer cells, and phagocytic function of macrophages after Bevacizumab intervention were examined. In addition, the efficacy of combined Bevacizumab with anti-PD-1 antibody (aPD-1) was evaluated in a murine ovarian cancer model.

Results We first identified that Bevacizumab stimulated IFN- γ secretion from macrophages and ovarian cancer cells. Moreover, we demonstrated that Bevacizumab upregulated PD-L1 expression in an IFN- γ -PI3K-NF- κ B-dependent manner in ovarian cancer. Interestingly, although Bevacizumab elicited antitumor immunity by inducing macrophage polarization to an M1 phenotype via elevated IFN- γ secretion, the phagocytic function of macrophages was suppressed by upregulated PD-1 expression in macrophages. Furthermore, Bevacizumab combined with an aPD-1 significantly decreased the tumor burden and prolonged survival time in mice with ovarian cancer.

Conclusions Here, we demonstrated a dual role of IFN- γ induced by Bevacizumab in ovarian cancer. Specifically, IFN- γ promoted immune activation in terms of M1 polarization and immune suppression through PD-L1/PD-1 upregulation. The combination of Bevacizumab and aPD-1 improved the local immune status and provided a promising novel therapeutic regimen against ovarian cancer.

EPV196/#377

PROGESTERONE TRIGGERS CARCINOGENESIS IN A MOUSE MODEL THAT PHENOPIES HIGH GRADE SEROUS CARCINOMA HARBORING A GERMLINE BRCA MUTATION

¹C-H Cho*, ²SY Kwon, ¹S-J Shin, ¹S Lee, ³J Kim. ¹Keimyung University Dongsan Hospital, Department of Obstetrics and Gynecology, Daegu, Korea, Republic of; ²Keimyung University Dongsan Hospital, Department of Pathology, Daegu, Korea, Republic of; ³Indiana University Melvin and Bren Simon Comprehensive Cancer Center, Department of Biochemistry and Molecular Biology, Indianapolis, USA

10.1136/ijgc-2021-IGCS.267

Objectives The purpose of this study is elucidating the role of ovarian hormones in the development of ovarian cancer.

Methods To evaluate the effects of steroid hormones on HGSC development, upon ovariectomy at 5–6 weeks of age, DKO mice were implanted subcutaneously with a pellet of 17- β estradiol (E2) (0.72 mg/90days/mouse), progesterone (P4) (25 mg/90 days/mouse), or combined E2 (0.72 mg) & P4 (25 mg). Also, for shorter periods of P4 exposure, ovariectomized DKO mice were treated with a P4 pellet of 2 mg (1 week) or 6 mg (3 weeks). Another set of ovariectomized DKO mice implanted with a placebo served as controls. To examine whether mifepristone (RU486) inhibits HGSC development in DKO mice by blocking PR, DKO mice with intact ovaries were implanted with a mifepristone pellet once at 9 mg/90 days (3 months) or three times at 33.3 mg/60 days. For a control group, DKO mice received a placebo pellet for mifepristone.

Results We show that ovarian progesterone is a crucial endogenous factor inducing the development of primary tumors progressing to metastatic ovarian cancer in a mouse model of high-grade serous carcinoma (HGSC), the most common and deadliest ovarian cancer type. Blocking progesterone signaling by the pharmacologic inhibitor mifepristone or by genetic deletion of the progesterone receptor (PR) effectively suppressed HGSC development and its peritoneal metastases. Strikingly, mifepristone treatment profoundly improved mouse survival (~18 human years).

Conclusions Targeting progesterone/PR signaling could offer an effective chemopreventive strategy, particularly in high-risk populations of women carrying a deleterious mutation in the BRCA gene.

EPV197/#394

BCARE- FUNCTIONALLY ASSESSING TREATMENT RESPONSE IN OVARIAN CANCER PATIENTS

^{1,2}F Geissler*, ²R Coelho, ^{1,2}T Zwimpfer, ²A Fedier, ²F Jacob, ^{1,2}V Heinzelmann-Schwarz. ¹University Hospital Basel, Department of Gynaecology and Obstetrics, Basel, Switzerland; ²University of Basel, Department of Biomedicine, Basel, Switzerland

10.1136/ijgc-2021-IGCS.268

Objectives Treatment regimens in oncology frequently become personalized and multimodal. Therefore, reliable biomarkers to predict drug responses are needed. Here, we establish a functional assay reflecting response to DNA damage-based treatment approaches.

Methods Our Bimodal prediction of ovarian CANcer treatment REsponse (BCARE) score combines irradiation-induced DNA damage with functional assessment of homologous recombination (HR) DNA repair visualized by immunofluorescence detection of γ H2AX and cyclinA2/RAD51 positive cells. BCARE is quantified by automated image analysis using Image J and R/Bioconductor. Treatment response of cancer cells to PARP inhibition, radiotherapy, and chemotherapy is analyzed by colony formation and MTT cell viability assays.

Results BCARE reflects the percentage of RAD51/cyclinA2 double positive cells. It significantly correlated with response to various drugs tested in 6 ovarian cancer cell lines: olaparib (R=0.92, p=0.0095), radiotherapy (R=0.78, p=0.0374), cisplatin (R=0.85, p=0.0325), doxorubicin (R=0.92, p=0.0095), and carboplatin (R=0.77, p=0.0738). Additionally, we show that the BCARE coincides with the