COMBINATION OF IGF1R INHIBITION WITH PD-1 BLOCKADE RESULTS IN SIGNIFICANT ANTI-TUMORAL ACTIVITY IN EPITHELIAL OVARIAN CANCER

Lina Somri-Gannam, Shiilav Meisel Sharon, Shay Hantisteau, Hallak Mordechai, Haim Werner, Ilan Bruchim*. Hillel Yaffe Medical Center, Obstetrics and Gynecology, Hadera, Israel

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Objectives The insulin-like growth factor (IGF) system plays a key role in regulating growth and invasiveness in epithelial ovarian cancer (EOC), therefore, is regarded as a promising therapeutic target. Recently, it has been shown that the IGF1 axis can regulate dendritic cells (DC) maturation and T cell activation. Our study aims to investigate the combination effect of IGF1 receptor (IGF1R) inhibition along with anti-PD-1 on EOC. We believe that this combination may reverse immune escape in EOC patients.

Methods EOC cell lines were co-cultured with IGF1R inhibitor (AEW-541)-treated-DCs. DC differentiation and EOC proliferation levels were evaluated by Flow Cytometry Assay (FACS). C57BL/6 mice with established peritoneal ID8 OC were injected with single or combined anti-PD-1 and AEW-541, and their survival was evaluated. Myeloid DCs and T-cell population levels were analyzed by FACS. Finally, RNA from tumors was extracted and submitted for RNAseq analysis (results are pending).

Results IGF1R inhibitor treatment induced DC differentiation. In addition, (AEW-541)-treated-DCs significantly decreased EOC cell proliferation. Combined anti-PD-1/IGF1R treatment decreased tumor weight compared to single treatments. Moreover, the anti-PD-1/IGF1R treatment significantly increased the Myeloid DC1 frequencies by 34% and 40%, and DC2 frequencies by 10% and 24% compared to AEW-541 and anti-PD-1 treatments, respectively. Additionally, the combined treatment increased CD8+ T-cells levels (115%) compared to AEW-541 treatment.

Conclusions IGF1R pathway inhibition in differentiated DCs suppressed EOC cell proliferation. IGF1R inhibitor combined with anti-PD-1 may result in enhanced anti-tumor activity. Thus, restoring the anti-tumor immune response by IGF1R targeting in combination with immunotherapy may be an effective therapy for EOC.
Methods Patients who underwent second-look surgery either with or without consolidation HIPEC after having a complete or partial response to primary cytoreductive surgery and adjuvant platinum-based chemotherapy between January 1991 and December 2003 were identified. The 10-year progression-free survival (PFS), overall survival (OS), and toxicity within postoperative 28 days were investigated.

Results The 10-year PFS and OS were significantly longer in the HIPEC group compared with the control group (PFS, 53.6% vs. 34.9%, \( p = 0.009 \); OS, 57.0% vs. 34.5%, \( p = 0.025 \)). In a subgroup of patients with stage III, the HIPEC group showed significantly longer 10-year PFS and OS compared with the control group (PFS, 42.6% vs. 14.8%, log-rank \( p < 0.001 \); OS, 46.7% vs. 19.6%, \( p = 0.036 \)). Patients who underwent HIPEC with paclitaxel showed a longer PFS and OS trend compared with subjects who underwent HIPEC with carboplatin. The more common adverse events in the HIPEC group were thrombocytopenia, elevated liver enzymes, and wound complications.

Conclusions The consolidation HIPEC demonstrated a significant improvement in 10-year PFS and OS with acceptable toxicity in patients with primary epithelial ovarian cancer. Further randomized controlled trials are warranted to confirm these results.

EP211/#794 Optimism selection criteria for secondary cytoreductive surgery in patients with recurrent ovarian cancer: A multicenter study

1Joo-Hyuk Son, 2Tae-Wook Kang, 2Soon Jin Park, 3Eun Ji Lee, 3Hee Seung Kim, 3Nam Kyong Kim, 4Yeoh Kim, 2Woo Yeon Hwang, 4Dong Hoon Suh, 5Tae Hun Kim, 4Eun Jung Yang, 5Seung Hyuk Shim, 5Suk-Joon Chang. 1Ajou University School of Medicine, Department of Obstetrics and Gynecology, Suwon, Korea, Republic of; 2Seoul National University College of Medicine, Department of Obstetrics and Gynecology, Seoul, Korea, Republic of; 3Seoul National University Bundang Hospital, Department of Obstetrics and Gynecology, Seongnam, Korea, Republic of; 4National University Boramae Medical Center, Department of Obstetrics and Gynecology, Seoul, Korea, Republic of; 5Konkuk University School of Medicine, Department of Obstetrics and Gynaecology, Seoul, Korea, Republic of

Objectives Optimum selection criteria for secondary cytoreductive surgery (SCS) in recurrent ovarian cancer is often dependent on the multiple confounding factors. This study aimed to evaluate the survival outcomes of recurrent ovarian cancer and investigated the factors identifying patients most likely benefit from the SCS.

Methods We retrospectively reviewed medical records of recurrent ovarian cancer patients from 5 referral hospitals in Korea from 2010 to 2021. Recurrent characteristics, treatment methods and potential factors for survivals were evaluated between the chemotherapy and surgery groups.

Results A total of 670 patients with recurrent ovarian cancer were identified. The patient’s median age was 55 (24 – 83) and 88.1% of patients had initial stage III/IV disease. Of all patients, 215 (32.1%) patients received SCS for the disease recurrence and others received 2nd line chemotherapy. The median survival was 85 months (95% CI, 65.0 – 105.0) in chemotherapy group and the median survival time was not reached in SCS group (p < 0.001). Among the patients received SCS, only patients received complete resection showed improved survival. Patients with any gross residual disease after SCS had no survival benefit compared to patients received chemotherapy (p = 0.942). In multivariate cox analysis, residual disease at primary surgery, PFI, recurrent sites, ascites and SCS was significant prognostic factors for the survival. Meanwhile, predicting factor for complete resection after SCS was only recurrent sites (≤ 3 lesions or regional carcinomatosis, P < 0.001).

Conclusions Platinum-sensitive recurrence with limited regional diseases (< 3 regions or limited carcinomatosis without ascites) can be considered as optimum criteria for SCS in recurrent ovarian cancer.