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

¹Lina Somri-Gannam, ¹Shihav Meisel-Sharon, ¹Shay Hantisteanu, ¹Mordechai Hallak, ²Haim Werner, ¹Ilan Bruchim*. ¹Hillel Yaffe Medical Center, Obstetrics and Gynecology Division, Hadera, Israel; ²Tel Aviv University, Department of Human Molecular Genetics and Biochemistry, Sackler School of Medicine, Tel Aviv, Israel

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Introduction The insulin-like growth factor 1 receptor (IGF1R) 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 IGF1 can regulate dendritic cell (DC) maturation and T cell activation. Our study aims to investigate the combination effect of IGF1R inhibition and anti-PD-1 treatment on EOC.

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 ovarian cancer were injected with single or combined anti-PD-1 and AEW-541 treatment, and their survival was evaluated. Conventional DCs and T-cell population levels were analyzed by FACS. Finally, RNA was extracted from tumors and RNA sequencing was performed.

Results IGF1R inhibitor treatment significantly induced DC differentiation in AEW-541 pre-treated-DCs compared to control after 24 h. In addition, Differentiated AEW-541-treated-DCs significantly decreased EOC cell proliferation. In vivo experiment showed that combined anti-PD-1/IGF1R treatment decreased tumor weight compared to single treatments. Moreover, the anti-PD-1/IGF1R treatment significantly increased the conventional DCs compared to AEW-541 and anti-PD-1 treatments. The Gene Ontology (GO) analysis indicate that the most significant differential biological process terms were immune response by increased lymphocytes cells activation.

Conclusion/Implications 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.

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DISPARITIES IN TREATMENT MODALITIES AND SURVIVAL AMONG ELDERLY HIGH GRADE SEROUS OVARIAN CANCER PATIENTS

Tong Shu, Yan Cai*, Hong Zheng. Peking University Cancer Hospital and Institute, Gynecologic Oncology, Beijing, China

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Introduction Elderly women with ovarian cancer are often undertreated. We aimed to evaluate the treatment modalities of elderly patients and its impact on overall survival.

Methods A total of 5,055 high grade serous ovarian cancer patients and 3584 advanced stage (IIIC+IV) patients aged 65

years or older were hereby identified, all from the Surveillance, Epidemiology, and EndResults (SEER) database from January 1, 2010 to December 31, 2017. Overall survival (OS) and ovarian cancer-specific survival (OCSS) was compared across age and Cox proportional-hazards model was created to adjust for case-mix.

Results The very elderly patients (≥ 75 years old) had significantly: less surgical complexity like undone lymphadenectomy (59.7% vs 48.6%; $p < 0.001$), less chemotherapy (78.2% vs 89.4%; $P < 0.001$), less standard treatment (70.6% vs. 85%; $p < 0.001$) and less optimal debulking surgery (44.0% vs 52.7%; $p < 0.001$). The very elderly and elderly patients all had a high use of NACT, but no significant difference was found (38.7% vs 36.2%; $P = 0.212$). Patients ≥ 75 had significantly worse OS and OCSS.

Conclusion/Implications The survival of women with EOC strongly decreases with increasing age, EOC patients over 75 years old received less standard treatment and more elderly patients were treated with NACT.

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PROGNOSTIC NUTRITIONAL INDEX AS A PROGNOSTIC BIOMARKER IN ADVANCED OVARIAN CANCER

¹Jairo Rubio, ¹Guillermo Moreno Flores, ²David Cantú De León*, ³Armando Monroy, ¹Abraham Osuna, ¹Pamlea Martínez, ¹Lenny Gallardo, ³Salim Barquet, ³Rosa Salcedo. ¹Instituto Nacional de Cancerología, Clinical Research, TLALPAN, Mexico; ²Instituto Nacional de Cancerología, Direction of Research, cdmx, Mexico; ³Instituto Nacional de Cancerología, Gynecologic Oncology, cdmx, Mexico

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Introduction The prognostic nutritional index (PNI) is a biomarker of nutritional and immunological status that has been validated as a prognostic factor in cancer. In ovarian cancer (OC) it has been studied in the Asian population. The aim of our study was to evaluate the association of PNI in Mexican patients with advanced ovarian cancer treated with neoadjuvant chemotherapy followed by debulking surgery.

Methods Retrospective cohort study of 220 patients with OC. PNI was calculated with de formula: albumin (g/L) + 0.005 X lymphocyte count (mm³). The cut-off point was obtained using ROC curves. Categorical variables were analyzed with Chi square and multivariate analysis with logistic regression. DFS was obtained with Kaplan Meier. P value 0.05 was considered significant.

Results The PNI cut-off values at diagnosis and post chemotherapy to predict complete and optimal surgery were 40.5 (AUC 0.62, OR: 1.07; $p = 0.0023$) and 44.5 (AUC 0.67, OR: 1.16; $p = 0.00014$), with significant association with high levels of PNI ($p = 0.003$ and $p = 0.000$), respectively. In logistic regression high levels of PNI were protective for residual disease (OR: 0.349, $p = 0.005$) and (OR: 0.168, $p = 0.001$). Median DFS was 15 ($p = 0.054$) and 13 ($p = 0.640$) months, respectively for cut-off points.

Conclusion/Implications In our study PNI behaves as an independent prognostic factor in advanced OC. High levels are associated with complete and optimal surgery and may be a predictor of DFS.