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ORAL ABSTRACT

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Ovarian cancer proteomic biomarkers for pembrolizumab response

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Objectives
To identify biomarkers in ovarian cancer that predict response to immune checkpoint inhibitors (ICI) that could be developed to guide future patient management.

Methods
A two-institutional retrospective study that analyzed pretreatment tumor samples from 32 patients with recurrent or metastatic ovarian cancer that received ≥ 2 cycles of anti-Programmed Death 1 (anti-PD-1) monoclonal antibody, pembrolizumab, and their respective survival data. Laser capture microdissection and reverse phase protein microarray (LCM-RPPA) were performed to quantify tumor cell-specific expression of (phospho)proteins. Univariate categorical Cox proportional hazard (PH) regression analysis of progression free survival (PFS) was performed. Proteins that showed a significant ($p < 0.05$) association with survival were dichotomized by median expression levels for Kaplan-Meier survival analyses. Association between proteins was calculated pairwise using z-score normalized values in the Pearson correlation.

Results
Pretreatment ovarian tumors were obtained from 32 patients with a median age 64 (range 29-83) and a majority showing stage III (68.8%) high grade (87.5%) serous histology (71.9%). Median PFS was 7 months (range 0-74). Of 194 (phospho)proteins measured by LCM-RPPA, four proteins showed a significant association with reduced PFS on ICI: Histone H3 trimethyl K27 (HR 1.86, 95% CI 1.21-2.85, p=0.005), immune checkpoint ligand B7-H3 (HR 1.6, 95% CI 1.06-2.53, p=0.025), mesenchymal transcriptional factors SNAIL (HR 1.7, 95% CI 1.06-2.83, p=0.029) and N cadherin (HR 1.50, 95% 1.01-2.22, p=0.041). Three proteins were significantly associated with better PFS on ICI: MHC-I (HR 0.38, 95% CI 0.15-0.96, p=0.040), translation initiation factor eIF4E S209 (HR 0.60, 95% CI 0.37-0.98, p=0.40), and acetyl CoA carboxylase S79 (HR 0.54, 95% CI 0.30-0.97, p=0.040). SNAIL and N cadherin were found to be interrelated, as expected, given their function in driving mesenchymal transition.

Conclusions
These data show promising proteomic biomarkers to prognosticate ICI benefit and possibly to inform additional therapeutic targets. Our findings underscore the significance of understanding the molecular profile of ovarian cancer in the era of immunotherapy.

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