SERUM LAG-3 IS ASSOCIATED WITH IMPROVED PATIENT PROGNOSIS IN HIGH GRADE SEROUS OVARIAN CANCER

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Background High grade serous ovarian cancer (HGSOC) is a lethal gynecologic malignancy with a five-year survival rate of only 39 percent.¹ Despite the fact that ovarian tumors are considered immunologic, HGSOC patients respond poorly to PD-1 based immunotherapy. Hence, the need to identify novel prognostic and therapeutic immunologic factors is crucial. Our previous investigation uncovered intratumoral levels of immune co-inhibitory receptor LAG-3 as a marker of improved HGSOC patient survival. For this current study we sought to evaluate the prognostic utility of serum-based LAG-3, as well as determine how these circulating levels change in response to HGSOC standard of care therapy.

Methods This study was approved by the Women and Infants Institutional Review Board; approval number 1057626. HGSOC serum samples were obtained from the Department of Special Testing and the Program in Women's Oncology Gynecologic Tissue Bank at Women and Infants Hospital. A total of 43 HGSOC treatment naïve serum samples were tested for serum LAG-3 and in 20 of these patients, samples from on- and post- frontline platinum-based chemotherapy were also analyzed. A commercially available ELISA kit was employed to detect serum LAG-3.

Results There was no statistically significant change in pre-, on-, and post- serum LAG-3 levels following frontline chemotherapy, however median levels of LAG-3 decreased once patients initiated therapy and remained stable post-treatment. Spearman Rank Correlation analysis revealed a significant relationship between progression-free survival (PFS) and pre-treatment serum LAG-3 levels ($r=0.36$, $p=0.017$). Furthermore, it was found that patients with a PFS of 6 months or less exhibited a significantly ($p=0.0031$) lower mean rank of pre-treatment serum LAG-3 levels, compared to patients with a PFS of 18 months or longer. Finally, Kaplan Meier curve analysis revealed a statistically significant association between longer patient PFS and higher pre-treatment LAG-3 concentrations, when stratified by both median ($HR=0.4916$, $\log\text{-rank } p=0.022$) and quartile LAG-3 serum levels ($HR=0.2679$, $\log\text{-rank } p=0.0031$).

Conclusions This study demonstrates for the first time that circulating immune checkpoint receptors have prognostic capabilities in ovarian cancer. Our findings suggest that LAG-3 is a marker for improved patient PFS. Future directions include an expansion of this original cohort in order to validate and further assess the clinical prognostic utility of serum LAG-3 in HGSOC.

REFERENCE

1. Survival Rates for Ovarian Cancer, American Cancer Society, [https://www.cancer.org/cancer/ovarian-cancer/detection-diagnosis-staging/survival-rates.html]

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