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. 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 pretreatment 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-rank p=0.022) and quartile LAG-3 serum levels (HR=0.2679, log-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

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