Abstract

Epithelial ovarian cancer is the sixth most common tumor disease among women and it is the leading cause of death from all types of gynecologic malignancies. The current standart of care consist of debulking surgery followed by platinum-taxane chemotherapy. Althought some patients benefit from the treatment, most eventually experience platinum-resistance and die from this disease. Immunotherapy based on application of immune checkpoint blockers represents a new treatment strategy in different cancer malignancies. However, emerging clinical data show only limited clinical efficacy of these agents in ovarian cancer patients with objective response rates of 10-15%. Therefore there is a strong need to identify a potential biomarkers, which allows to identify the group of patients, who will benefit the most from this costly treatment. The aim of my diploma thesis was to characterize the prognostic and predictive role of the immune checkpoints within the retrospective and prospective cohort of patients with high-grade serous ovarian cancer (HGSOC). Our study follows, that the expression of PD-L1 molecule and high frequencies of PD-1^+ tumor infiltrating lymphocytes (TILs) in tumor microenviroment is significantly correlated with a better prognosis of patients with HGSOC. Moreover, PD-L1 and PD-1 expression correlates with a strong anti-tumor immune response in the tumor microenvironment, as documented using immunohistochemical and cytometric analysis. In our work, we also identified the key positive prognostic role of CTLA-4^+ and LAG-3^+ TILs in the tumor microenvironment of patients with HGSOC. Importantly, the concomitant high densities of PD-1^+, LAG-3^+, CTLA-4^+ TILs and high expression of PD-L1 in tumor microenvironment allowed a distinction of HGSOC patients with the most favorable prognosis. Altogether, our results indicite that the presence of immune checkpoints in TME correlate with the enhanced anti-tumor immune response and clinical benefits of HGSOC.

Keywords: anti-tumor immunotherapy, immune checkpoints, ovarian HGSC, inhibitors of immune checkpoints, PD-1, PD-L1, LAG-3, CTLA-4