D-Dimers as a liquid prognostic biomarker in melanoma patients treated with immune-checkpoint inhibitors

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Background & objectives

Immune-checkpoint inhibition (ICI) has become a valuable cancer treatment option, replacing chemotherapy as the therapeutic gold standard for melanoma patients. While prognosis can be greatly improved under ICI, patients still experience a variety of treatment- or disease-related adverse events, including deep vein thrombosis and pulmonary embolism. Several studies suggest a negative prognostic role of the activation of coagulatory pathways in cancer patients. D-Dimers are biomolecules that are generated by the fibrinolytic degradation of blood clots in the body and are well established as sensitive biomarkers for the early detection and diagnosis of thromboembolic events. However, D-Dimers are not routinely measured in melanoma patients yet, as their role as potential prognostic markers for ICI therapy outcome and patient survival remains unclear. For that reason, we aimed to investigate the potential role of D-Dimers as a prognostic marker for progression free survival and overall survival in Melanoma patients who receive ICI.

Methods

A prospective cohort study including 203 patients with AJCC stage III or IV melanoma who received ICI treatment (anti-PD-1 with or without anti-CTLA-4 antibodies) was conducted between April 2018 and September 2022 at the University Medical Center Hamburg-Eppendorf. Blood was drawn at baseline and before every therapy cycle. Cutoff values were calculated using the ROC method. Anticoagulation and platelet aggregation inhibitors (PAI) were considered.

Results

Out of 203 patients, D-Dimer levels were measured in 179 patients. In patients with elevated D-Dimer levels, both, OS (n=192, cutoff=0.62 mg/L, hazard ratio: 4.55 (95% CI: 2.22-9.09, p<0.001)), as well as PFS (n=131, cutoff=0.38 mg/L, hazard ratio: 2.08 (95% CI: 1.19-3.57, p=0.01)), were significantly impaired in the elevated D-Dimer group regardless of ICI treatment regimen. An increased OS was detected in patients receiving ICI with platelet aggregation inhibitors as co-medication.

Conclusion

D-Dimers have been demonstrated as a strong prognostic blood-based biomarker for OS and PFS in melanoma patients receiving ICI. As the measurement of D-Dimers is widely available and cost-effective, they may be used in Liquid Biopsy to stratify the prognosis and identify melanoma patients who may benefit from PAI treatment.