Von Willebrand factor predicts response to immunotherapy in patients with metastatic melanoma

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Background & objectives

An increased incidence of thrombotic events associated with increased mortality has been observed in cancer patients during treatment with immune checkpoint inhibitors (ICI). Recent studies on coagulation pathways have also revealed the direct role of important coagulation proteins and platelets in carcinogenesis, angiogenesis and progression. The aim of this study was to assess the prognostic value of VWF and its regulatory enzyme ADAMTS13, D-dimers and platelets in a cohort of patients with metastatic melanoma receiving ICI therapy.

Methods

In a prospective cohort of 57 patients with metastatic melanoma, we measured systemic levels of VWF-Ag, ADAMTS13 activity, D-dimers and platelets at baseline and 6, 12 and 24 weeks after the initiation of treatment. In parallel, we recorded standard clinical parameters (LDH, S100, NLR, CRP). Subsequently, single- and multivariable Cox proportional models were used to investigate a possible association between these parameters and clinical progression (PFS and OS). Baseline values of VWF were compared between primary responders and resistant patients according to the patients' response status to therapy. Changes during the course of therapy were also compared according to the patients' response to therapy.

Results

Melanoma patients had dysregulated levels of VWF-Ag and ADAMTS13 activity, LDH, S100 and CRP at baseline. At a median clinical follow-up of 31 months, vWF-Ag was the only parameter significantly associated with PFS in univariate analysis (HR:1.1 (1-1.1, p=0.005)). When comparing primary responders and resistant patients, VWF-Ag was the only parameter that differed between the two patient groups, with lower levels observed in the primary responder group (median: 29.3µg/ml vs. 33.3µg/ml; p=0.02). Regarding OS, we found an

association with vWF-Ag and ADAMTS13 activity in univariate analysis and with D-dimers in multivariate analysis. A follow-up over the course of treatment showed different developmental profiles for vWF-Ag between the primary response and resistance groups.

Conclusion

In this prospective cohort, the vWF-Ag level at baseline were identified to be a relevant parameter associated with response to ICI therapy, suggesting a new aspect of the role of coagulation in response to ICI therapy.