88 GENETIC ASSOCIATION BETWEEN VITILIGO GENETIC SUSCEPTIBILITY AND RESPONSE TO IMMUNE-CHECKPOINT INHIBITORTHERAPY IN ADVANCED MELANOMA PATIENTS

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Background Only ~50% of advanced melanoma patients show objective responses to immune checkpoint inhibitor (ICI) therapy. Currently, there are still no reliable predictive biomarkers explaining ICI response heterogeneity. Vitiligo development during ICI therapy is associated with a better prognosis in melanoma patients. Genetic susceptibility to vitiligo has been well-characterized using multiple large GWAS studies, and includes genes that are also associated to other autoimmune diseases.

Objective To test if the germline genetic association to vitiligo is able to predict response to ICI in patients with advanced melanoma.

Methods Data from >1,000 patients from 6 melanoma centers in the Netherlands participating in the international IO-GEM melanoma consortium were analyzed in this study. DNA was extracted from blood or saliva and genotyped by Illumina GSA MD v3.0. Clinical data was obtained from the Dutch Melanoma Treatment Registry. We developed a polygenetic vitiligo-susceptibility score using a pre-defined set of 54 vitiligo-associated single nucleotide polymorphisms (SNPs) predicting overall survival.

Results We found a significant protective relation of the unweighted vitiligo-susceptibility score to all-cause mortality. Weighted for the association to vitiligo, the vitiligo-susceptibility score outperformed the unweighted score in predicting all-cause mortality.

Conclusions These results suggest that genetic susceptibility to vitiligo may be associated with more favorable survival outcome in melanoma patients upon ICI treatment. The risk scores will be validated in the remaining part of IO-GEM.

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