Background Immune checkpoint inhibitor (ICI)-based immunotherapy has become standard of care in a growing number of advanced cancer indications. Recently, its use has been extended to the adjuvant and even neoadjuvant settings in a few solid tumor types. Despite this tremendous progress, however, a significant proportion of patients across cancer types fail to achieve clinical benefit. For metastatic melanoma (MM), the response rate is 40–60%. Redirecting non-responding patients to other therapeutic options is desired to avoid unnecessary side effects and improve patient outcomes. Whole blood transcriptome has been successfully applied to ICI response monitoring in metastatic urothelial cancer and shows great potential for MM.

Methods Whole blood samples from 29 patients with BRAF+ and high lactate dehydrogenase MM were collected before and after 6 or 12 weeks of anti-PD-1/CTLA-4 combination treatment. Nineteen were classified as responders (R) (progression-free survival (PFS) ≥ 6 months) and 10 as non-responders (NR). Transcriptome profiles were generated by RNA-seq and Differential Expression Genes (DEG) were identified by combining differential expression analysis (DEA) and advanced multivariate machine learning analysis (MLA). Biological relevance was assessed by over representation and gene network analysis.

Results DEA and MLA between baseline and on-treatment samples from responders (R) identified 141 DEGs associated with early response to the treatment. Functional analysis of the 141 DEGs revealed upregulated cell proliferation, immune checkpoint proteins and interferon-regulated genes. These results are in line with theoretical expectations from the therapy. Interestingly, similar pathway enrichments were observed in our previous analysis of a mUC ICI-treated cohort, suggesting a common modulation of immune programming upon immunotherapy, independent of the targeted disease.

Conclusions In conclusion, whole blood immuno-transcriptome profiling combined with proprietary advanced data analytics identified biomarkers for the monitoring of ICI response in MM and mUC and offers new insights that may help understanding the underlying processes and mechanism of action.

REFERENCE