Background The availability of immune checkpoint inhibitors (ICI) has radically changed the prognosis of patients (pts) with metastatic melanoma. More recently, PD-1 inhibitors have also become the standard of care as adjuvant therapy in high-risk and resected melanoma.1–7 However, 65–80% of patients treated with ICI experience immune-related adverse events (irAEs)8 causing morbidity and a potential decrease in clinical benefit. Currently, there are no biomarkers that can predict which patients are at risk of developing irAEs. Aim of this study is to recognize patients who will develop toxicity to anti-PD1 treatment.

Methods Gene profiling analysis was performed using NanoString IO360 panel from basal PBMCs of patients treated with anti-PD1 in both setting (adjuvant and first line therapy). Patient’s characteristics are reported in (table 1). To identify the best genes signature the Sparse Partial Least Squares Discriminant Analysis (sPLS-DA) was applied. Differences in characteristics of patients with and without toxicity were tested by t-test or Wilcoxon test (according to their distribution) and Pearson chi-squared test for continuous and categorical variables, respectively. ROC curves were used to determine the best cut off which defines the border line between absence and presence of toxicity (table 2).

Results Among 161 pts included, 75 received anti-PD1 as adjuvant therapy (AT) and 86 as first line therapy (FLT). Arthralgia and fever were observed in the 27% and 14% of total population (12% and 9% respectively in AT; 15% and 4% respectively in FLT). A specific gene signature for predicting the onset of arthralgia has been identified and characterized by the most representative genes such as: ZEB2, TGF513, RPTOR, NEKBE, GNL1, CCNB1. In particular, we observed that genes involved in the mTORC/NF-kB pathway correlate with arthralgia. Differently, the gene signature for predicting the onset of fever is mainly characterized by humoral immunity genes such as: HLA-F, CD8B, CD45RA, CD27. In both cases, the increase of signature value is associated with a greater probability of toxicity onset.

Conclusions In this retrospective study, we found a gene signature model able to predict the onset of toxicities (arthralgia and fever) related to anti-PD1 treatment. Further investigations are needed to get additional information.

REFERENCES