Tumor mutation burden (TMB) in immune checkpoint inhibitor (ICI)-naïve and -experienced patients with metastatic melanoma treated with lifileucel, a tumor-infiltrating lymphocyte (TIL) cell therapy

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Background

- Tumor neoantigen burden (TNB) is a key driver of ICI response. In melanoma, a high TMB genotype is also associated with increased response rate to ICI
- PD-1, programmed cell death protein-1; PD-L1, programmed death ligand-1; Q3W, once every 3 weeks; Q6W, once every 6 weeks.

Methods

- Baseline characteristics of cohorts are presented in Table 1
- In ICI-naive patients, TMB was higher in TIL responders compared to ICI-naïve patients in Cohort 1A (ICI-Experienced)
- In ICI-experienced patients, 8% of patients with high TMB (≥20 mut/Mb) did not respond to lifileucel

Results

- Baseline characteristics of the patients included in each matched cohort are presented in Table 1
- In ICI-naive patients, TMB was higher in TIL responders compared to ICI-naïve patients in Cohort 1A (ICI-Experienced)
- In ICI-experienced patients, 8% of patients with high TMB (≥20 mut/Mb) did not respond to lifileucel

Conclusions

- Lifileucel TIL cell therapy produced clinical responses across the TMB spectrum, regardless of prior ICI exposure
- A higher proportion of patients who were ICI-naive had high TMB than those who were ICI-experienced
- In ICI-naïve patients, TMB was associated with response to lifileucel
- TMB correlated with predicted TNB and NEOPS scores in ICI-naïve and -experienced patients
- No association was observed between single-gene mutations and response
- Response to lifileucel was seen in patients with inflamed and non-inflamed tumors in both cohorts
- After TIL infusion, TCR repertoires persisted and shifted to be composed of more tumor-associated clonotypes, regardless of TMB

References

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