SMALL CELL LUNG CANCER MOLECULAR SUBTYPES AND VULNERABILITY TO IMMUNE CHECKPOINT BLOCKADE


Methods We analyzed pre-treatment RNA-sequencing (RNA-seq) from 271 patient tumors from IMpower133. We applied nonnegative matrix factorization (NMF) to define SCLC classes within this dataset and correlated these new subtypes with clinical outcomes to atezolizumab+CE versus placebo+CE (OS HR, 0.26 [0.12-0.57]).

Conclusions We further refine SCLC subtypes and describe a spectrum of heterogeneity. We identify two inflamed subtypes with distinct clinical outcomes to atezolizumab+CE therapy dependent on the balance of T-effector to TAM infiltration. These results demonstrate the potential for personalization of therapy for SCLC patients based on molecular subtypes.

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REFERENCES

Ethics Approval The study protocol for IMpower133 was approved by the institutional review board or independent ethics committee for each study site and was performed in full accordance with the Guideline for Good Clinical Practice and the Declaration of Helsinki. All human tumor specimens in this study, and subsequent evaluations, were used in accordance with the informed consent agreements obtained from all subjects.