

435 INTRATUMORAL PLASMA CELLS PREDICT OUTCOMES TO PD-L1 BLOCKADE IN NON-SMALL CELL LUNG CANCER

Namrata Patil*, Barzin Nabet, Sören Müller, Hartmut Koeppen, Wei Zou, Jennifer Giltane, Jason Cheng, Chikara Takahashi, Avantika Chitre, Linda Rangell, Sangeeta Jayakar, William O’Gorman, Marcus Ballinger, Romain Banchereau, David Shames. *Genentech Inc., South San Francisco, CA, United States*

Background Inhibitors of the programmed cell death-1 (PD-1/PD-L1) signaling axis are approved to treat non-small cell lung cancer (NSCLC) patients, based on their significant overall survival (OS) benefit. However, the mechanisms behind this efficacy are not completely understood and there remains a significant unmet need for patients who do not respond to these therapies.

Methods To better understand the mechanisms behind the survival benefit associated with atezolizumab, we performed transcriptomic analysis of 891 NSCLC tumors from patients treated with either the PD-L1 inhibitor atezolizumab or chemotherapy from two large randomized clinical trials.

Results We found a significant B cell association with extended OS with PD-L1 blockade, independent of CD8+ T cell signals. We then derived gene signatures corresponding to the dominant B cell subsets present in NSCLC from single-cell RNA-seq data. Importantly, increased plasma cell signatures were predictive of OS in patients treated with atezolizumab, but not chemotherapy. B cells were also associated with the presence of tertiary lymphoid structures (TLS) and organized lymphoid aggregates.

Conclusions Our results suggest an important contribution of B and plasma cells to PD-L1 blockade efficacy in NSCLC. The association of plasma cells and TLS with improved outcomes suggests that novel therapeutics targeting these mechanisms that can be combined with PD-(L)1 blockade to improve their overall efficacy.

Acknowledgements This study was performed using tissue samples from the open-label, randomized Phase 2 POPLAR (NCT01903993) and Phase 3 OAK trials (NCT02008227).

Trial Registration NCT01903993, NCT02008227

Ethics Approval Both the POPLAR and OAK studies were performed in full accordance with the guidelines for Good Clinical Practice and the Declaration of Helsinki, and all patients gave written informed consent. Protocol approval was obtained from independent ethics committees for each participating site for both studies and an independent data monitoring committee reviewed the safety data.

Consent Both the POPLAR and OAK studies were performed in full accordance with the guidelines for Good Clinical Practice and the Declaration of Helsinki, and all patients gave written informed consent.

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