153 HIGH EXPRESSION OF TERTIARY LYMPHOID STRUCTURE GENE SIGNATURES IS ASSOCIATED WITH IMPROVED SURVIVAL IN HEAD AND NECK SQUAMOUS CELL CARCINOMA PATIENTS TREATED WITH IMMUNE CHECKPOINT BLOCKADE

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Background The presence of tertiary lymphoid structures (TLS) has been associated with improved response to immune checkpoint blockade (ICB) treatment in several indications including non-small cell lung and bladder cancers, sarcomas, and melanoma. While ICB therapies have been approved for treatment of squamous cell head and neck cancers (HNSCC), biomarkers associated with response to ICB are being assessed.
Methods Six published TLS signatures[1–3] were assessed in HNSCC (n = 500, 69/412 HPV+/-) data from TCGA (treatment naïve) and in pre-treatment samples from a real-world (RW) cohort from a Tempus Labs dataset (ICB monotherapy, n = 17, chemotherapy, n = 112, and ICB+chemo, n = 47). The RW cohort primarily consisted of stage 3 and 4 (~71%) cancers. Time-to-event analysis was conducted using the Kaplan-Meier and Cox proportional hazards models. K-means clustering in TCGA and RW samples using the 6 TLS signatures identified patients over-expressing TLS signatures. In both cohorts, associations between TLS signatures and median overall survival (mOS) were assessed. In the RW cohort, correlation between TLS-signature levels in treatment groups and mOS was examined.
Results In the TCGA cohort, high expression of 5/6 TLS signatures was associated with better mOS. The TLS signatures were correlated across the TCGA (R = 0.60 – 0.86) and RW (R = 0.61 – 0.83) cohorts. TCGA HPV+ patients had higher expression of 5/6 TLS signatures compared to HPV- patients. Two clusters of patients were identified based on expression of the 6 TLS signatures. TLS-high patients had significantly higher mOS compared to TLS-low patients (24.2 vs. 19.1 months). The median survival for the entire cohort was 21.3 months. In ICB monotherapy-treated RW patients, elevated levels of 2/6 TLS signatures were associated with better mOS ($p < 0.1$). In TLS-high patients (based on clustering of 6 signatures), mOS was highest in ICB monotherapy treated patients (15.6 vs. 2.6 months). TLS-high patients did not have better OS compared to TLS-low patients in the chemo treated group (7.7 vs. 8.2 months). No association was observed between TLS-high vs. TLS-low expression and survival in ICB +chemo-treated patients (11.6 vs. 12.5 months respectively). HPV+ RW patients (12/23) had higher expression of 4/6 TLS signatures.
Conclusions TLS signatures were prognostic in treatment naïve HNSCC patients, but associations between high TLS signatures and improved OS in ICB treated patients were observed in later stage HNSCC patients. These results suggest that the presence of TLS in HNSCC may indicate an improved response to ICB therapy.

REFERENCES

1. Cabrita R, Lauss M, Sanna A, *et al*. Tertiary lymphoid structures improve immunotherapy and survival in melanoma. *Nature* 2020;**577**:561–565. https://doi.org/10.1038/s41586-019-1914-8
2. Helmink BA, Reddy SM, Gao J, *et al*. B cells and tertiary lymphoid structures promote immunotherapy response. *Nature* 2020;**577**:549–555. https://doi.org/10.1038/s41586-019-1922-8
3. Sautès-Fridman C, Petitprez F, Calderaro J, *et al*. Tertiary lymphoid structures in the era of cancer immunotherapy. *Nat Rev Cancer* 2019;**19**:307–325. https://doi.org/10.1038/s41568-019-0144-6

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