Abstract #10587: Distinct immunogenomic features of cancers arising in solid organ transplant recipients (SOTRs)

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Background

- SOTRs require chronic immunosuppression, to prevent rejection, which increases cancer risk.
- The molecular and immunologic landscape of cancers in SOTRs remains poorly defined.
- Tumors in SOTRs develop with reduced immune selective pressure, potentially leading to distinct immunogenomic features and altered responses to immunotherapy.
- This study characterizes the tumor microenvironment and immunotherapy biomarkers in cancer arising in SOTRs vs non-SOTRs

Methods

- Retrospective analysis of patients who underwent molecular profiling at Caris Life Sciences using NGS (592-gene panel, DNA WES, or RNA WTS).
- SOTRs identified via ICD codes matched 1:10 to non-SOTRs by age, sex, and cancer type.
- Immune cell fractions estimated using QuanTIseq.
- Gene expression profiles for transcriptomic signatures (IFN-γ and T-cell–inflamed [TCI] scores) predictive of response to immune checkpoint inhibitors (ICI).
- Tumor mutational burden (TMB), microsatellite instability (MSI), and PD-L1 expression (IHC) were analyzed.
- Real-world overall survival from initiation of ICI to last contact while hazard ratio (HR) was calculated by Cox proportional hazard method.
- Mann-Whitney U and χ^2/Fisher exact tests were applied with adjustment for multiple comparisons

- **Cancers in SOTRs have an immune-desert phenotype with high TMB.**
- **TMB is a potential predictor of response to ICI therapy in SOTRs.**

Results

Cancers in SOTRs exhibited reduced adaptive immune cell infiltration, including fewer CD8+ T-cells, regulatory T-cells, and B-cells, along with myeloid dendritic cells with no other differences in innate immune cell fractions (**Figure 1**).

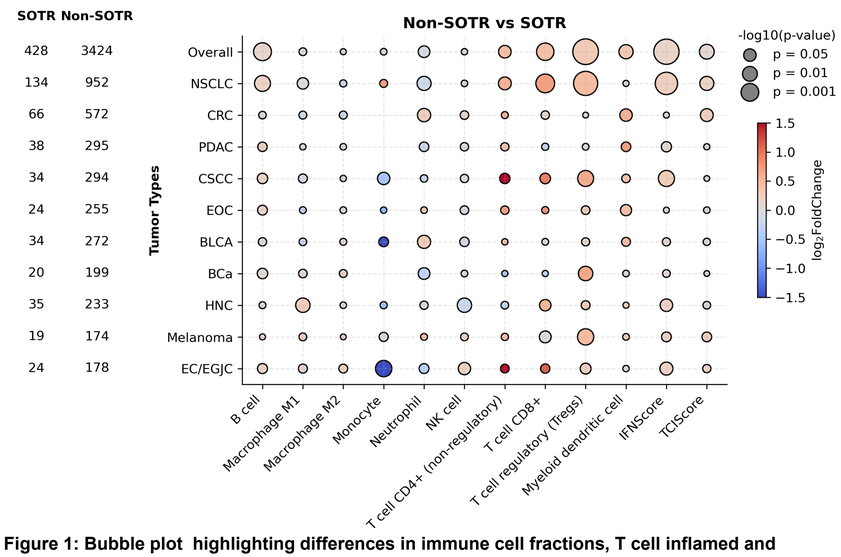
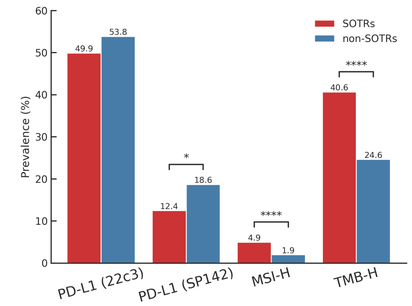


Figure 1: Bubble plot highlighting differences in immune cell fractions, T cell inflamed and interferon gamma score between SOTRs and non-SOTRs among different cancer types.

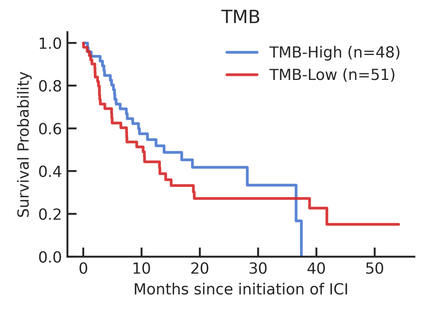
NSCLC Non-small cell lung cancer; CRC colorectal adenocarcinoma; PDAC pancreatic adenocarcinoma; cSCC squamous cell skin Cancer; EOC ovarian surface epithelial cancer; BLCA bladder cancer; BCa breast cancer; HNC Head and neck cancer; EC/EGJC esophageal and esophagogastric junction cancer

Also shown in **Figure 1**: cancers in SOTRs demonstrated reduced immune gene expression signatures (IFN-γ and TCI scores).

- Higher prevalence of TMB-high (≥10 mut/Mb) and MSI-high was observed in cancers from SOTRs compared to non-SOTRs.
- PD-L1 positivity was less frequent in cancers from SOTRs – **Figure 2A**



- Among SOTRs treated with ICIs, those with TMB-high tumors had lower mortality (adjusted hazard ratio 0.47 95%CI 0.22-0.98, p=0.046) – **Figure 2B**



Conclusions

- Cancers in SOTRs have unique immunogenomic features (immune desert, high TMB).
- ICI treatment in SOTRs should be individualized based on tumor features (including TMB) and must be carefully monitored for allograft rejection.

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