immunoSEQ®

HEMATOLOGY/ONCOLOGY

CASE STUDY

Contribution of systemic and somatic factors to clinical response and resistance to PD-L1 blockade in urothelial cancer: An exploratory multi-omic analysis

Snyder A, et al. *PLOS Medicine*. 2017; 14(5): e1002309.
MAY 2017

WHY IMMUNOSEQ?

The quantitative nature allows clone tracking and evaluation of clonal expansion

Allows the calculation of TIL density and clonality using the same assay

Flexible requirements allows direct comparison of fresh and FFPE samples

amplify **discovery**™

CASE STUDY: Contribution of systemic and somatic factors to clinical response and resistance to PD-L1 blockade in urothelial cancer: An exploratory multi-omic analysis—*Snyder A, et al. PLOS Medicine. 2017; 14(5): e1002309.*

BACKGROUND

Immune checkpoint blockade therapy for treating solid tumors is rising in popularity. Atezolizumab (anti-PD-L1) has demonstrated responses in 15-25% of patients with advanced urothelial carcinoma. Previous studies have correlated mutational burden and response to atezolizumab, and shown that the tumor-infiltrating lymphocyte (TIL) repertoire can be associated with outcomes in immune checkpoint blockade therapy in a variety of tumor types. In this paper, the authors combine a variety of methods to further evaluate the role and interaction of tumor, peripheral and clinical factors in urothelial carcinoma patients' responses to atezolizumab.

AIM

- Characterize predicted neoantigen load in tumors and evaluate its correlation with clinical response to atezolizumab treatment.
- Explore if tumor and/or blood TCRB repertoire clonality in treated patients aligns with clinical benefit.
- Evaluate the relationship of TCRB data with whole exome sequencing and RNA-seq as potential biomarkers of durable clinical benefit (DCB).

METHODS

29 patients with urothelial carcinoma in a single arm, phase II clinical trial were evaluated.

1. Pre-treatment tumor → whole exome sequencing, RNA-seq and **immunoSEQ hsTCRB Assay**
2. Pre-treatment and serially collected post-treatment blood → **immunoSEQ hsTCRB Assay**

RESULTS

- Increased pre-treatment TIL density corresponded to DCB, but not continuous progression free survival (PFS).
- High diversity in pre-treatment blood is associated with improved PFS and overall survival (OS).
- Expansion of TIL clones (at 3 weeks after initiation of treatment) was pronounced in the post-treatment blood of patients with DCB.
- All patients with high diversity blood repertoires and increased TIL clonality survived over 1 year following treatment.
- No significant association between mutation burden or predicted neoantigen load with DCB or OS.

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Figure 1.

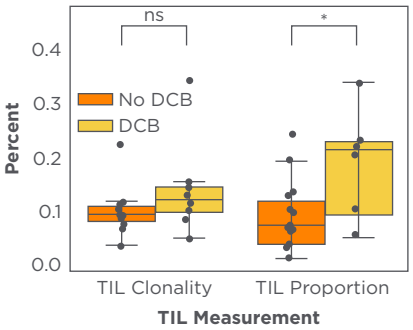

Figure 2.

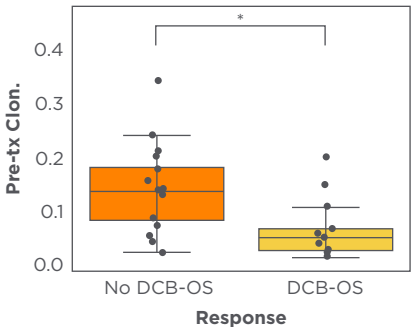

Figure 1. TIL proportion alone was associated with durable clinical benefit in tumors from patients who had DCB while TIL clonality alone was not significantly associated with DCB in tumors.

Figure 2. There was a significant association between TCR clonality in the peripheral blood prior to initiating treatment and overall survival greater than 12 months.

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CONCLUSIONS

- It is important to consider the complex interaction of somatic, immune and clinical factors when evaluating patient response to checkpoint inhibitor therapy.
- Additional research is needed to determine how to best identify patients that will benefit from such treatment.

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