Clinical correlates and multiplatform molecular analysis of response to anti-PD-1/PD-L1 in renal cell carcinoma (RCC)

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Introduction

• Immune checkpoint inhibitors, such as antibodies against PD-1, PD-L1, and CTLA-4, enhance the T cell response and have become a mainstay of treatment against cancer (NCI, cancer.gov)

• RCC is historically immune responsive
• However, molecular factors often associated with response to immune checkpoint inhibitor therapy in other cancers, like tumor mutation burden in lung cancer, have not been predictive in RCC

Patient Cohorts

212 confirmed patients with RCC and exposure to anti-PD-1/PD-L1

118 patients excluded for:
• Only one dose of ICI
• Anti-PD-1/PD-L1 in combination with another agent
• Insufficient EMR to assess response

94 patients with sufficient exposure to single-agent anti-PD-1/PD-L1 and EMR documentation to assess response (primary cohort)

26 patients with tissue for molecular analysis (biomarker cohort)

Results

Figure 1. Clinical characteristics of primary cohort

Figure 2. Laboratory evaluation and response to anti-PD-1/PD-L1 in primary cohort

Figure 3. PD-L1 expression is associated with response

Figure 4. Tumor gene expression patterns suggest response

Figure 5. TCR clonal diversity does not correlate with response but impacts survival

Conclusions

• Further validation of findings in a larger, prospective cohort
• Cross-platform analysis of multiple molecular parameters to improve predictive biomarker selection
• Identify antigens recognized by the TCR clones expanded in responders

Future Directions