CD8 stained sections were first analyzed in a primary compartmental analysis that identifies CD8+ T cells within tumor, tumor margin, and stromal compartments.

**Preclinical data revealed that combination of SRK-181 and anti-PD1 overcame tumor shrinkage also experienced CD8+ infiltration into the tumor compartment across multiple tumor types.**

**A biomarker strategy to validate SRK-181’s mechanism in patients and evaluate treatment response was based on our proof-of-concept for SRK-181 in preclinical models. Here we present biomarker data validating SRK-181’s mechanism of action in patients.**

**Methods**

- **Blood for flow cytometry analysis of myeloid derived suppressor cells (MDSC) was originally collected at baseline and pre-infusion on Cycle 1.**
- **Myeloid-derived suppressor cell (MDSC) levels were quantified in patients.**
- **Infiltrated vs. desert vs. excluded tumor types, including UC, melanoma, and NSCLC, consistent with established MOA observed in preclinical studies.**
- **Dose Escalation**
  - Part A: SRK-181 Single Agent (50-300mg q3w)
  - Part B: SRK-181 (1500mg q3w) + Pembrolizumab (200mg q3w)
- **Expanded solid tumor non responders to anti-PD-L1 (n=15)**
- **Primary Compartmental Analysis**
  - % CD8+ T cells per compartment: 5% CD8+ in tumor nest, >1% CD8+ in peripheral interface (Excluded), < 5% CD8+ in tumor nest, <1% CD8+ in peripheral interface (Desert).

**Summary**

- **SRK-181 leads to a decrease in immunosuppressive MDSCs which may be linked to responses.**
- **SRK-181 treatment leads to an increase in CD8+ T-cell infiltration into the tumor compartment across multiple tumor types.**
- **Collection of paired biopsies from ccrCC patients has been challenging.**
- **Exclusion of CD8+ T cells from the tumor has been proposed as a mechanism underlying immunosuppression contributing to CPI resistance.**
- **Brain metastatic melanoma patients were analyzed for FDA approval.**
- **CD8+ T cells from the tumor has been proposed as a mechanism underlying immunosuppression contributing to CPI resistance.**

**Abbreviations:** Anti-FDL, anti-programmed death ligand 1 antibody/anti-programmed death protein 1 antibody; BOR, best overall response; ccrCC, clear cell renal cell carcinoma; CPI, checkpoint inhibitor; gMDSC, granulocytic monocyte derived suppressor cell; MDSC, monocyte derived suppressor cell; NSCLC, non-small cell lung cancer; PD, partial responsive; q3w, every 3 weeks; TGFβ1, transforming growth factor beta 1; UC, urothelial carcinoma.

**References:**