Abstract **3128**: The genomic, transcriptomic, and immunologic landscape of TEM8 (*ANTXR1*) in Small Cell Lung Cancer (SCLC)

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Background:

- The **TEM8 receptor** (*ANTXR1*) is overexpressed in malignant tissues, with novel oncolytic viruses such as SVV-001 uniquely binding on tumor-associated angiogenic endothelial cells, pericytes, fibroblasts, and immune inflammatory cells
- Recent pre-clinical data suggest that TEM8-targeting therapies may convert immunologically "cold" tumor microenvironments (TMEs) into "hot" milieu more amenable to treatment with immune checkpoint inhibitors (ICIs)

Methods:

- **NextGen Sequencing** of DNA (NGS; 592 genes or WES) and RNA (WTS) was performed on 1,404 SCLC tumor samples submitted to Caris Life Sciences (Phoenix, AZ, USA)
- *ANTXR1* expression was **divided by quartiles** (transcripts per million; Q4: ^{H}; Q1: ^{L})
- PD-L1 expression (22c3; positive TPS ≥1%) was assessed by IHC
- TMB-H was defined as ≥10 mutations per mB
- Cell infiltration in the TME was estimated by QuantiSEQ. Gene expression profiles were analyzed for transcriptional signatures predictive of response to immunotherapy (T-cell inflamed) and MAPK pathway activation score (MAPS)
- Overall survival **(OS) data** were obtained from insurance claims
- Mann-Whitney U and χ2/Fisher-exact tests were applied as appropriate, with *p*-values adjusted for multiple comparisons ($p < 0.05$).

The increased immune infiltrate and T-cell inflamed status among *ANTXR1*^{H} SCLC suggests responsiveness to simultaneous ICI and TEM8 therapies.

A Phase 1 trial is soon to open!

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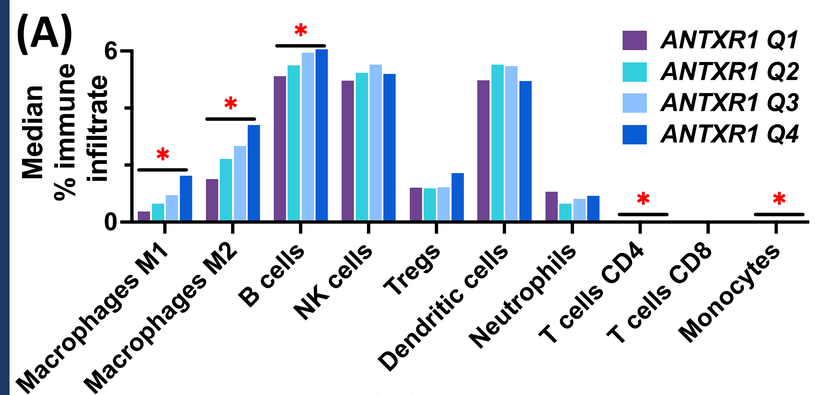
Results/Graphs/Data:



(A) No pathogenic mutations were associated with *ANTXR1*^{H} vs ^{L} tumors, along with no differences in the prevalence of dMMR, TMB-H, or PD-L1+ ($p > 0.05$). **(B)** Immune cell infiltrate or **(C)** the prevalence of T cell inflamed tumors across ANTXR1 expression quartiles (red asterisk indicate $p < 0.05$). **(D)** OS from start of immune check point inhibitors (ICI) to last contact for indicated subgroups.