Abstract #6851: The genomic, transcriptomic, and immunologic landscape of TEM8 (*ANTXR1*) in neuroendocrine neoplasms (NENs)

Samuel A. Kareff, MD, MPH[1]; Harris Krause, PhD[2]; Andrew Elliott, PhD[2]; Peter Hosein, MD[3]; Emil Lou, MD, PhD[4]; Heloisa Soares, MD[5]; Matthew Oberley, MD[2]; Aman Chauhan, MD[3]

[1]University of Miami Sylvester Comprehensive Cancer Center/Jackson Memorial Hospital, [2]Caris Life Sciences, [3]University of Miami Sylvester Comprehensive Cancer Center, [4]Uniersity of Minnesota Masonic Cancer Center; [5]Univeristy of Utah Huntsman Cancer Center

Take-home points: 1) The increased immune infiltrate and prevalence of T-cell inflamed status among *ANTXR1*^{H} NENs suggests increased response to ICIs. 2) Further investigation of the clinical and molecular associations with *ANTXR1* expression is warranted and underway.

Introduction

- The TEM8 receptor (*ANTXR1*) is overexpressed in malignant tissues, with novel oncolytic viruses such as SVV-01 uniquely binding to this receptor 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 (TME) into "hot" milieu more amenable to treatment with immune checkpoint inhibitors (ICIs).

Methods

- NextGen sequencing of DNA (592 genes or WES) and RNA (WTS) was performed on neuroendocrine neoplasms (NENs; *N* = 1724), excluding small-cell lung cancer, submitted to Caris Life Sciences (Phoenix, AZ).
- *ANTXR1* expression was divided by *ANTXR1*-expression quartiles (transcripts per million [TPM]; Q4: ^{H}, Q1: ^{L}).
- PD-L1 expression (SP142; Positive (+): ≥2+, ≥%5) was assessed by IHC.
- High tumor mutational burden (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 (MPAS).
- Real-world overall survival (OS) data was obtained from insurance claims, and Kaplan-Meier estimates were calculated for molecularly defined subpopulations of patients.
- Mann-Whitney U and X^2/Fisher-Exact tests were applied where appropriate, with *p*-values adjusted for multiple comparisons ($p < 0.05$).

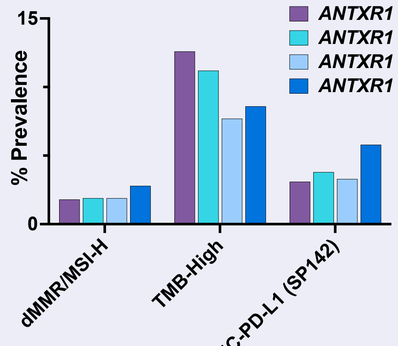

Figure 1: No pathogenic mutations were associated with *ANTXR1*^{H} vs ^{L} tumors ($p > 0.05$ for all tested), along with no differences in the prevalence of dMMR (2.8% vs 1.8%) TMB-H (8.6% vs 12.6%) or PD-L1+ (5.8%: vs 3.1%) ($p > 0.05$).

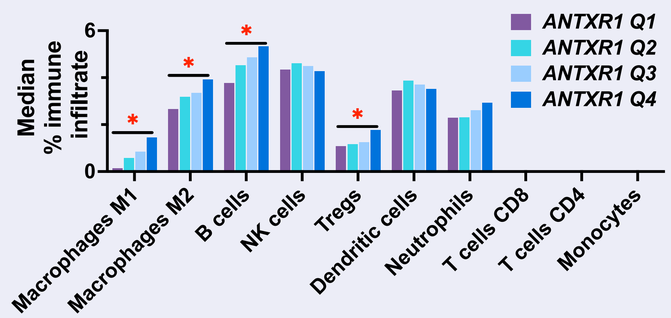

Figure 2: A greater proportion of B cell (5.34 % vs 3.78%, $p < 0.001$), M1 (1.46% vs 0.15%, $p < 0.001$) and M2 macrophages (3.92% vs 2.67%, $p < 0.001$), and T-regulatory cell (1.77% vs 1.08%, $p < 0.001$) immune infiltrate was observed in ANTXR1^{H} tumors.

SUMMARY: There were no genes or biomarkers of ICI response that varied with *ANTXR1* expression. There was a significant increase in the prevalence of B cells, M1 and M2 macrophages, and T_{regs} with increased *ANTXR1* expression. Finally, MPAS and T-cell inflamed tumor scores increased with *ANTXR1* expression. There was no difference in OS.

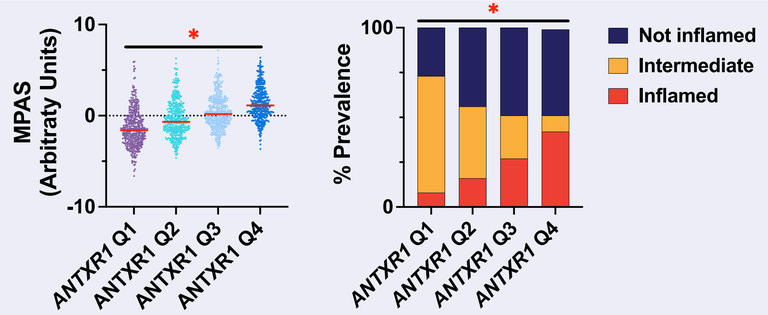

Figure 3: *ANTXR1*^{H} tumors had higher MPAS compared to *ANTXR1*^{L} (1.16 vs -1.61 arbitrary units, $p < 0.001$), which were also more frequently classified as T cell-inflamed compared to *ANTXR1*^{L} (42% vs 8%, $p < 0.001$).

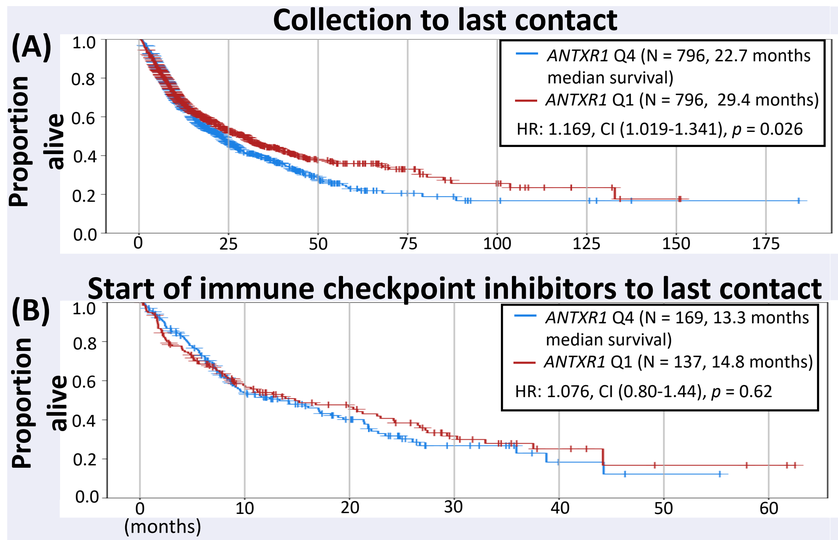

Figure 4: There was a significant difference in median OS between *ANTXR1*^{H} vs ^{L} tumors (A) but this difference was not observed for survival since start of immune checkpoint inhibitors (B).