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CHARACTERIZING SOMATOSTATIN RECEPTOR 2 (*SSTR2*) EXPRESSION AND THE IMMUNE LANDSCAPE OF OLFACTORY NEUROBLASTOMA (ONB), SINONASAL NEUROENDOCRINE CARCINOMA (SNEC), AND SINONASAL UNDIFFERENTIATED CARCINOMA (SNUC)

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Background ONB, SNEC and SNUC are rare sinonasal neoplasms demonstrating varying neuroendocrine characteristics, with limited systemic treatment options. ONB expresses *SSTR2*, diagnostically and therapeutically actionable; SNUC is heterogeneous and a diagnosis of exclusion. We examined the gene expression of *SSTR2* and the immune landscape in ONB, SNUC and SNECs.

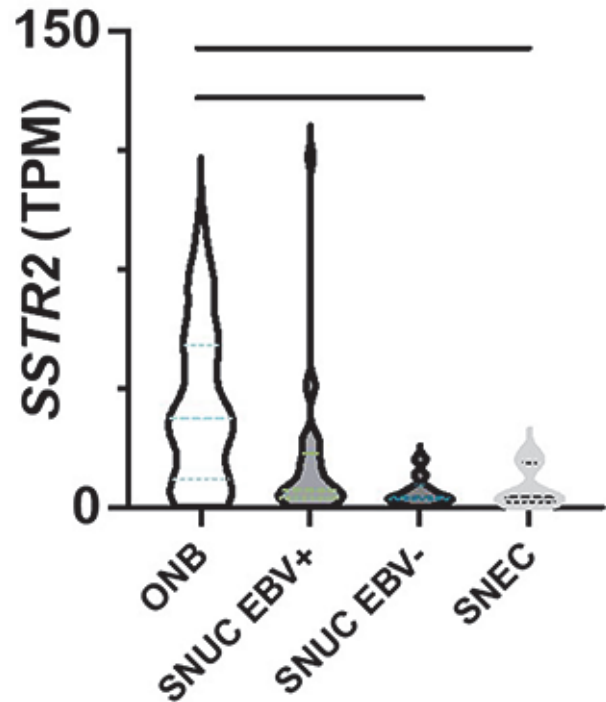
Methods ONB (N = 26), SNUC (N = 25), and SNEC (N = 7) tumors (all histologies per referring clinician, not internally validated) were tested at Caris Life Sciences (Phoenix, AZ) with NextGen Sequencing of DNA (592-gene or whole exome [WES]) and RNA (whole transcriptome). Tumors were defined as HPV 16/18⁺ using WES and Epstein Barr Virus⁺ (EBV⁺) using WES and *EBER* ISH. SNUC was further stratified into EBV⁺/EBV⁻ cohorts. PD-L1 expression (22C3; Positive (+): TPS ≥1%) was assessed by IHC. A combination of IHC, NGS, and fragment analysis was used to assess deficient mismatch repair status and microsatellite instability (dMMR/MSI). RNA-Seq data were analyzed for a transcriptomic signature predictive of immunotherapy response (T-cell inflamed score) and immune cell fractions were estimated using quanTIseq. Mann-Whitney U, Fisher's Exact and χ^2 tests were applied as appropriate with p-values adjusted for multiple comparisons ($p < 0.05$).

Results All ONB and SNEC were EBV⁻, while 60% (15/25) of SNUC were EBV⁺. Only 10% (1/10) of EBV⁻ SNUCs were HPV16⁺ with all other tumors being HPV 16/18⁻. The median expression of *SSTR2* was highest in ONB followed by EBV⁺ SNUC, EBV⁻ SNUC and SNEC (27.9, 8.4, 3.1, 3.1 (transcripts/million [TPM])) (figure 1, asterisk indicates $p < 0.05$). 18.75% (3/16) of ONB, 10% (1/10) of EBV⁻ SNUC, and 100% (13/13) of EBV⁺ SNUC were PD-L1⁺ ($p < 0.05$, no data for SNEC). T cell-inflamed tumors were significantly more prevalent in EBV⁺ SNUC (67%) compared to EBV⁻ SNUC (49%), ONB (9%) and SNEC (0%, $p < 0.001$). EBV⁺ SNUC had significantly higher median estimates (%) of immune cell infiltrates, including B cells (15.1, 8.2, 7.1 and 8.8), CD8⁺ T cells (5.2, 0.2, 0.5, 0.0), M1 macrophages (6.0, 1.3, 0.4, 0.6), and T_{regs} (7.2, 1.0, 0.0, 0.0) compared to EBV⁻ SNUC, ONB and SNEC (all $p < 0.05$).

Conclusions In this real-world dataset, the highest expression of *SSTR2* was found in ONB and EBV⁺ SNUC, suggesting a role for *SSTR2*-directed strategies. Additionally, all EBV⁺ SNUCs were PD⁻, immunogenic, and predominantly T-cell inflamed suggesting potential for immunotherapeutic strategies. For SNUC, validation of these results in additional cohorts is important.

Consent This study was conducted in accordance with the guidelines of the Declaration of Helsinki, Belmont Report, and US Common Rule. In keeping with 45 CFR 46.101 (b),

this study was performed utilizing retrospective, deidentified clinical data. Therefore, this study was deemed Institutional Review Board exempt, and no patient consent was necessary from the subjects.



Abstract 1509 Figure 1 *SSTR2* expression across rare sinonasal malignancies

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