ANALYZING THE GENOMIC, TRANSCRIPTOMIC AND IMMUNE LANDSCAPES ASSOCIATED WITH SURFACE SOMATOSTATIN RECEPTOR 2 (SSTR2) GENE EXPRESSION IN NASOPHARYNGEAL CARCINOMA (NPC)

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Background NPC is a highly invasive squamous-differentiated carcinoma, more common in east and southeast Asia, and the Epstein-Barr virus (EBV) plays a key role in its pathogenesis. Recurrent and metastatic NPC is treated with cisplatin-based chemotherapy regimens, with poor survival. SSTR2 is expressed by a spectrum of neuroendocrine neoplasms and has diagnostic and therapeutic utility as a pharmaceutical target. Many NPCs express SSTR2 on the cell surface, linked to EBV positivity. In this study, we investigated the association of SSTR2 expression and EBV status with the genomic and immune landscape of NPC.

Methods 198 NPC specimens were tested at Caris Life Sciences (Phoenix, AZ) with NextGen Sequencing of DNA (592-gene panel or whole exome [WES]) and RNA (whole transcriptome). EBV status (EBV+/−) was defined using WES and EBER ISH. 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 (dMMR/MSI). Tumors were stratified as SSTR2-High (H) and -Low (L) per top and bottom quartile expression of SSTR2, respectively; or by EBV positivity. Transcriptome data were analyzed for a signature predictive of response to immunotherapy (T-cell inflamed score). Immune cell fractions were estimated using quanTIseq. Mann-Whitney U, Fisher’s Exact and χ² tests were applied as appropriate with p-values adjusted for multiple comparisons (p < 0.05).

Results 60.4% of NPC were EBV+ (98/165) and the prevalence of SSTR2-H status was significantly associated with EBV+ compared to SSTR2-L status (90.5% vs 7.3%, p < 0.05). PD-L1 positivity was highly prevalent in NPC, without significant difference observed between SSTR2-H vs -L tumors (97.9% vs 86.5%). dMMR/MSI-H was observed in 0.38% (1/261) of tumors. A significantly higher fraction of SSTR2-H vs SSTR2-L tumors were T-cell inflamed (75% vs 6%, p < 0.05; figure 1). SSTR2-H tumors (vs SSTR2-L) also had significantly elevated M1 macrophages (8.1% vs 3.5%), B-cells (13.0% vs 5.4%) and Tregs (7.3% vs 2.2%) infiltrate and significantly reduced neutrophil infiltrate (2.4% vs 4.9%) (all p < 0.05). When segmenting NPC by EBV status, EBV- NPC had a higher prevalence of pathogenic PIK3CA mutations compared to EBV+ NPC (16.9% vs 0%, p < 0.05).

Conclusions In NPC, SSTR2 expression was positively associated with EBV positivity and with an inflamed, immunogenic tumor microenvironment. Thus, in SSTR2-H NPC, immunotherapy and also SSTR2-directed strategies may be appropriate therapeutic strategies. In EBV NPC, PIK3CA-directed therapy merits further investigation.