Survival Association of PIK3CA in HPV-driven Head and Neck Squamous Cell Carcinoma (HNSCC)

Kelly Bridgham MD[1] ,Tolulope Adeyelu[2], Andrew Elliott[2], Hani Samrah BS[1], Farah Abdulla[2], Trisha Wise-Draper[3], Ammar Sukari[4], Matthew Oberley[2], Jennifer Johnson MD PhD[1], Joseph M Curry[1].

[1]Department of Otolaryngology- Head and Neck Surgery, Thomas Jefferson University Hospital, Philadelphia, PA ; [2]Caris Life Sciences, Phoenix, AZ

[3]University of Cincinnat;i[4]Karmanos Cancer Institute, MI

Contact: Kelly.Bridgham@Jefferson.edu

Introduction

- PD1 Immune Checkpoint Inhibitors (ICIs) have been integrated into treatment algorithms for a variety of solid tumor malignancies, including head and neck squamous cell carcinoma (HNSCC)
- Durable response to single agent therapy occurs in only a fraction of patients.
- There is a great need to understand the molecular underpinnings of response and resistance mechanisms.
- PIK3CA mutation is a common driver of HPV+ mediated malignancy
- We sought to understand the prevalence and clinical impact of PIK3CA mutation in HPV+ and HPV- cancer by applying a multi-omics approach to a large, clinically appended dataset.

Methods and Materials

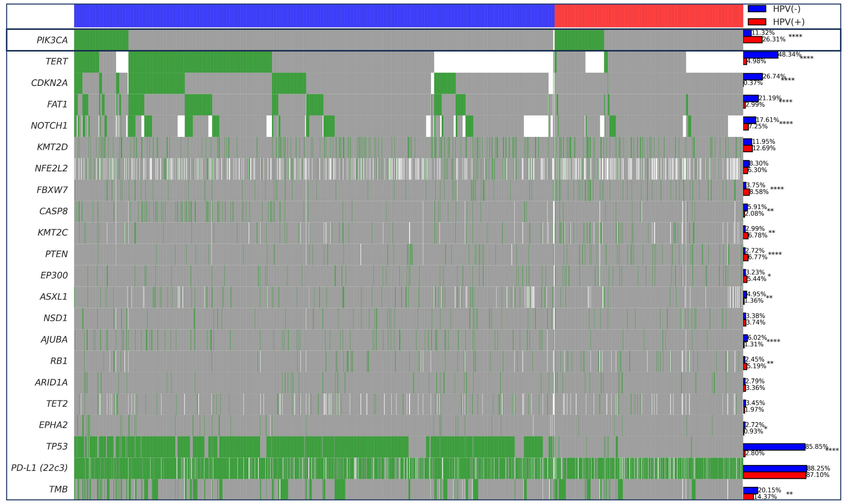
- HNSCC (N = 1901) patients who underwent DNA (592-gene or whole exome) and RNA (whole transcriptome) sequencing at Caris Life Sciences (Phoenix, AZ) were queried to identify HPV+ and HPV- HNSCC cohorts.
- Tumor mutational burden (TMB) was measured by totaling all somatic mutations (mt) per tumor (TMB-H: > 10 mt/MB).
- Differentially regulated pathways was obtained using Gene Set Enrichment Analysis (GSEA).
- Real-world overall survival (rwOS) was obtained from insurance claims data, calculated from either time of biopsy (OS) or start of immunotherapy ($_{IO}$OS) to last contact, or time on ICI ($_{IO}$TOT). Mann-Whitney U and X^2/Fisher-Exact tests were applied, with *p*-values adjusted ($p < .05$).

Results

Table 1.0: Sample Demographic Information

	HPV+ HNSCC	HPV- HNSCC	P-value
Counts	536	1365	
Median Age [Range]	65 [21 – 89]	65 [22 – 89]	0.132
Male	485 (90.5%)	973 (71.3%)	<0.001
Female	51 (9.5%)	392 (28.7%)	
PIK3CA Status			
Mutated	141 (26.3%)	154 (11.3%)	<0.001
WT	395 (73.7%)	1207 (88.7%)	
Smoking Status			
Smokers	47 (8.7%)	166 (12.2%)	0.066
Not Reported	489 (91.2%)	1199 (87.8%)	
Met Status			
Primary	280 (52.2%)	978 (71.7%)	<0.001
Local Mets	88 (16.4%)	123 (9.0%)	
Distant Mets	168 (31.3%)	263 (19.3%)	

Figure 1: Oncoprint showing the top mutated genes in HNSCC



- Compared to HPV- samples, PIK3CA mutation was highly associated with HPV+ primary (28.6% vs 11.4%, p <0.01) and metastatic (23.8% vs 11.2%, p<0.01) lesions.
- The prevalence of TMB-H was significantly higher in both HPV+ (30.7% vs 7.9%, p<0.01) and HPV- (30.7% vs 18.2%, p<0.01) with PIK3CA mutation compared to WT.

Figure 2: Gene Set Enrichment Analysis for Hallmark Pathways in comparison to HPV+/PIK3CA Mutated Cohorts

- Immune related pathways (Interferon gamma/alpha) are significantly enriched in PIK3CA mutated HPV negative HNSCC.
- Similar pathways observed based on the HPV status irrespective of the PIK3CA status

Figure 3: OS from Start of IO Based on HPV Status and PIK3CA Mut/WT

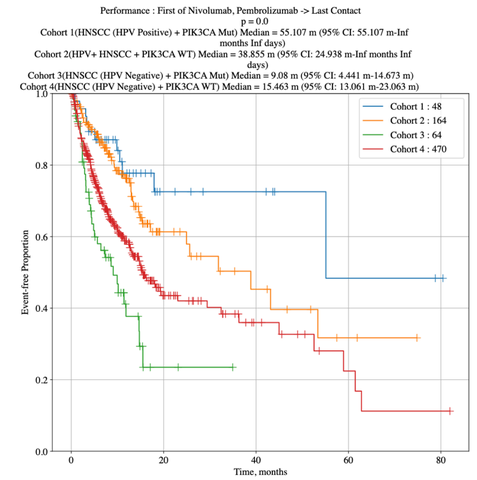
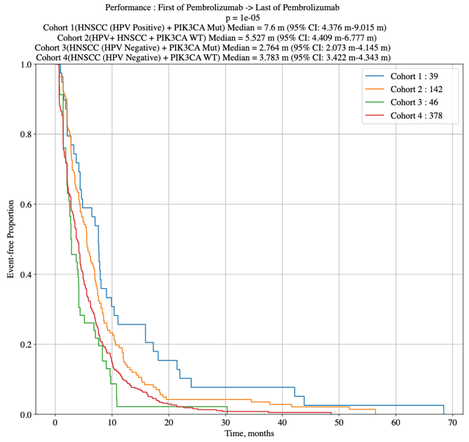


Figure 4: TOT Based on HPV Status and PIK3CA Mut/WT



Conclusions

- HPV+ HNSCC shows prolonged survival compared to HPV- while those with PIK3CA mutation are enriched with better survival compared to wild type
- In contrast, survival tends to be prolonged in HPV- with PIK3CA WT as compared to PIK3CA Mut
- Further research is needed to explore the mechanism underlying these findings and identify other molecular factors that might contribute to the observed outcomes