

p16 is a prognostic biomarker in anti-PD-1 immunotherapy-treated recurrent/metastatic oropharyngeal squamous cell carcinoma patients

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INTRODUCTION

Despite the utilization of multi-disciplinary treatment modalities, ~50% of patients with Head and Neck Squamous cell carcinoma (HNSCC) develop recurrence or metastatic (R/M) disease within 3 years from initial diagnosis. Traditional treatment options included salvage surgery, re-irradiation, and/or chemotherapy. Anti-PD-1 immunotherapies, nivolumab and pembrolizumab, have recently been approved as treatment options for platinum-refractory and/or unresectable R/M HNSCC patients.

HPV+ HNSCC, which predominantly originates in the oropharynx, are biologically and clinically distinct from HPV- HNSCC and is associated with superior treatment responses and outcomes than p16- HNSCC patients. However, this did not appear to be the case with anti-PD-1 immunotherapies where recent landmark trials showed equivalent activity in p16+ and p16- patients (1,2). Results from clinical trials may not translate to real-world practice; therefore, in this study, we assessed the utility of p16 as a prognostic biomarker in R/M HNSCC patients treated with anti-PD-1 immunotherapies at our institution.

METHODS

Following IRB approval, we queried the University Hospitals Seidman Cancer Center composite clinical database and identified R/M HNSCC patients treated with anti-PD-1 immunotherapies, nivolumab and pembrolizumab, from December 2015 to October 2019.

METHODS

Patient chart review was performed to include patients' clinical and treatment histories. All statistical analyses were performed using R (version 4.0.2). Survival analysis was performed with Kaplan-Meier (KM) curves and log-rank tests using the R package *survival* and plotted by *ggplot2*. Multivariate logistic regression analysis was utilized to create a forest plot. A p-value of <0.05 was considered to be statistically significant.

RESULTS

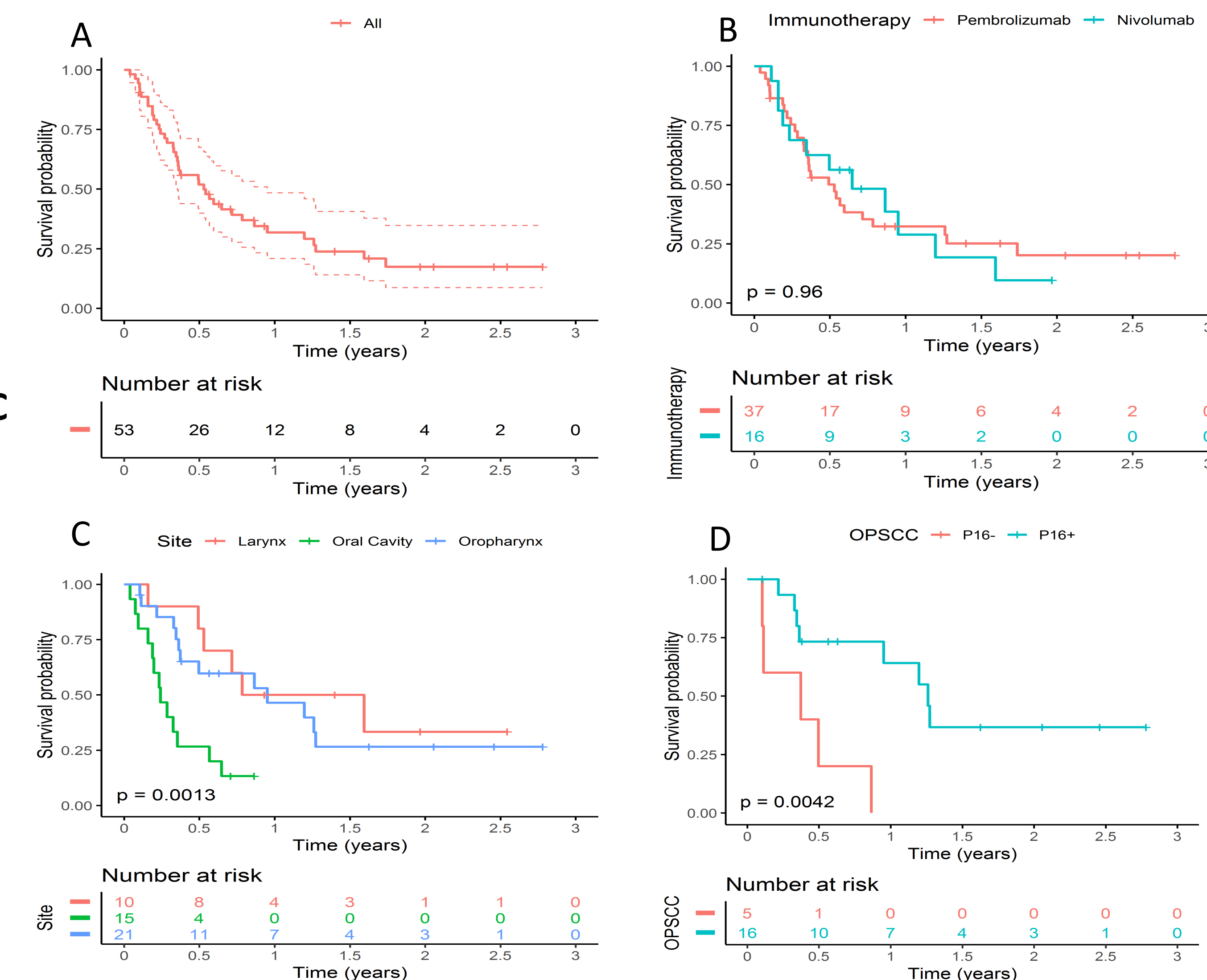
Fifty-three R/M HNSCC patients were treated with anti-PD-1 immunotherapy, nivolumab (n=37), pembrolizumab (n=15), or both (n=1), and had a median overall survival (OS) of 6.3 months (Figure A). Details of the clinicopathologic characteristics of our cohort are shown in Table 1. The average age of patient in our cohort was 63.4, and 75% (n=40) of patients were male. Nivolumab and pembrolizumab showed equivalent efficacy (log-rank, p=0.9) (Figure B). Anatomical site was associated with distinct OS; oropharyngeal and laryngeal SCC patients have superior OS compared to oral cavity SCC patients, where median OS was 2.9, 11.4, and 14.2 months in oral cavity, oropharynx, and larynx SCC, respectively. A multivariate model adjusting for smoking, anatomical site, recurrence pattern, and immunotherapy choice revealed that anatomic site is an independent prognostic biomarker. (Figure C).

Median OS was 15.1 months and 4.5 months for p16+ and p16- oropharyngeal SCC patients, respectively. Cox regression revealed p16 status as an independent prognostic biomarker in this cohort; p16- patients had a 7.67-fold (95% CI: 1.23 to 47.8; p=0.029) increase in risk of death compared to p16+ patients. (Figure D)

Table 1. Clinicopathologic characteristics of R/M HNSCC patients treated with anti-PD-1 immunotherapy.

Smoking history	
Yes	83% (n=44)
No	17% (n=9)
Anatomical Site	
Oropharynx	40% (n=21)
Oral Cavity	28% (n=15)
Larynx	19% (n=10)
Other	13% (n=7)
Definitive treatment	
Non-Surgical	55% (n=29)
Surgical	45% (n=24)
Time to recurrence (months)	7 (1-57)
Recurrence	
Local/Regional	21% (n=11)
Distant	79% (n=42)

RESULTS



CONCLUSIONS

Tumor p16 status is strongly associated with anti-PD-1 treatment outcome and should be considered as a variable in the design of future immunotherapy clinical trials in the R/M oropharyngeal SCC setting

References:

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