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Immune checkpoint inhibitors in sinonasal squamous cell carcinoma

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Introduction

Sinonasal squamous cell carcinoma (SNSCC) comprises of 3–5% of all head and neck cancers (HNSCC) [1]. Prognosis of recurrent or metastatic (R/M) SNSCC remains poor [2]. Anti-PD-1 immune checkpoint inhibitors (ICI) have revolutionized treatment of R/M HNSCC, however, the pivotal trials of ICI in HNSCC did not include SNSCC [3–5]. Because of this, limited data exists on the efficacy of ICI in SNSCC. Here, we present, to our knowledge, the first series describing the clinical outcomes of patients with SNSCC treated with ICI, and their molecular characteristics.

Methods

Clinicopathologic data were retrospectively collected on patients diagnosed with R/M SNSCC who received anti-PD-1 antibody ICI treatment between 2015 and 2019 at the Massachusetts General Hospital. Archived tissues were prospectively analyzed for PD-L1 expression and human papillomavirus (HPV) status by p16, RNA in situ hybridization or PCR, when sufficient tissue was available. Overall survival (OS) was defined as the time from initiation of ICI to the date of death from any cause. Progression-free survival (PFS) was defined as the time elapsed between initiation of ICI and tumor progression or death from any cause. Objective response rate (ORR) was assessed according to RECISTv1.1. The Kaplan–Meier method was used to estimate PFS and OS.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Results

A total of 11 consecutive patients who met the study criteria were included. The median (range) age was 65 (26–92). Three tumors (27.3%) were both p16 and high-risk HPV positive. PD-L1 expression (defined as combined positive score (CPS) > 1) was observed in three cases (27.3%) with a median CPS of 0.2 (0–16). Five patients received ICI as first line therapy and six received ICI as second/beyond line therapy. Additional clinicopathologic characteristics are summarized in Table 1. With a median follow-up of 14.2 months (range 1.8–40.0 months), the median (m)PFS was 4.2 months (95% CI, 0.3–8.1). Both PD-L1 status and line of treatment (first line) showed a trend toward longer PFS (Table 2). PFS rate and disease control rate at 6 months were 36.4% and 36.4%, respectively. The median OS was not reached at the time of data analysis and the 6-month OS rate was 63.6%. Three patients achieved partial response (ORR 27.2%) with 2 responses lasting over 6 months. One responder had prior platinum and cetuximab therapy. Responses were observed regardless of PD-L1 expression (2 responses in CPS 0 and 1 response in CPS 16) (Table 2).

Discussion

We report our single institution retrospective analysis of patients with SNSCC treated with ICI. Notably, the ORR was 27.2% and mPFS was 4.2 months. Reported ORRs to anti-PD-1 therapy in landmark R/M HNSCC trials have been 13.3–16.9% and mPFS 2.3–3.4 months [3–5]. Thus, while a direct comparison is not possible, SNSCC appears to have a favorable response to ICI when benchmarked against historic non-SNSCC HNSCC cohorts, without controlling for additional variables. PD-L1 expression and first vs. subsequent line therapy both trended toward improved outcomes, which is in line with HNSCC data, although the study is not powered to assess statistical significance of differences between these subgroups. This study is limited by inherent biases of retrospective analysis of uncontrolled groups, small sample sizes, short follow-up time, and lack of multivariate analyses. However, it serves as the first case series in the literature of SNSCC ICI response outcomes. In summary, R/M SNSCC appears to have a favorable ICI response, regardless of PD-L1 expression or previous treatment history. Considering the dearth of information regarding SNSCC and ICI, this case series should serve to encourage inclusion of SNSCC in future prospective ICI trials.

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Table 1

Baseline clinicopathologic characteristics.

Characteristic	No.
Median (range) age, years	65 (27–75)
Sex	
Male	6 (54.5%)
Female	5 (45.5%)
Race	
White	11 (100%)
Primary site	
Nasal cavity	7 (63.6%)
Maxillary sinus	3 (27.3%)
Other/unknown	1 (9.1%)
Smoking (> 10 PY)	
Yes	4 (36.4%)
No	7 (63.6%)
Anti-PD-1 inhibitor	
Pembrolizumab	8 (72.7%)
Nivolumab	3 (27.3%)
Line of anti-PD-1 inhibitor	
First-line	5 (45.5%)
Second/beyond line	6 (54.5%)
HPV status	
Positive	3 (27.3%)
Negative	7 (63.6%)
Unknown	1 (9.1%)
PD-L1 status (CPS > 1)	
Positive	3 (27.3%)
Negative	7 (63.6%)
Unknown	1 (9.1%)

Table 2

Characteristics and response outcomes.

Characteristics	mPFS	95% CI	ORR	95% CI
Total	4.2 months	0.3, 8.1	27.2%	6.0, 61.0
PD-L1				
PD-L1 +	5.7 months	0.3, 11.1	33.3%	8.0, 90.6
PD-L1 −	2.1 months	0.1, 5.4	25.0%	3.2, 65.1
Line of anti-PD-1 inhibitor				
First-line	5.7 months	0.1, 26.7	40.0%	5.3, 85.3
Second/beyond line	2.1 months	1.5, 2.7	16.7%	0.4, 64.1
HPV status				
HPV +	1.8 months	0.7, 2.9	0%	N/A
HPV −	5.7 months	0.1, 13.4	37.5%	8.5, 75.5