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CLINICAL AND PATHOLOGICAL FEATURES IN CPS POSITIVE RECURRENT/METASTATIC HEAD AND NECK CANCER PATIENTS TREATED WITH IMMUNOTHERAPY

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OBJECTIVES

Head and neck squamous cell carcinoma (HNSCC) comprises a heterogeneous spectrum of diseases originating predominantly from the oral cavity, oropharynx, hypopharynx, and larynx (1). Despite the multimodality treatment for early-stage tumours, disease recurrence and/or metastasis (R/M) are frequent and commonly associated with poor prognosis (2). The advent of immune checkpoint inhibitors (ICIs) has remarkably changed the management of R/M HNSCC. However, only a small percentage of patients achieves long-term benefit in terms of overall response and survival (3). For this reason, the identification of novel biomarkers correlated to tumorigenesis and neoplastic progression is a possible strategy to stratify patients' prognosis in this therapeutic setting.

The aim of our study is to investigate the role of different clinico-pathological features in predicting anti-PD-1 immunotherapy response in R/M HNSCC.

METHODS

We reviewed data from 95 patients with R/M HNSCC receiving between May 2020 and January 2023 first line immunotherapy with or without chemotherapy based on a combined positive score (CPS) ≥1. Slides for PD-L1 evaluation were immunostained with SP263 clone on a Ventana BenchMark Ultra (4).

Anonymized data including age, sex, ECOG PS, comorbidities, history of tobacco smoking, alcohol abuse and primary tumour sites were collected. Tumour response was assessed every 12 weeks using Immune Response Evaluation Criteria in Solid Tumors (iRECIST) guidelines. Progression-free survival (PFS) was defined as the time from the administration of treatment until the first progression or death. The overall survival (OS) was defined as the time from patient registration to death from any cause.

Histological features were retrieved from pathological report. Hematoxylin-eosin-stained slides were evaluated independently by 2 pathologists with an expertise in HNSCC in a blind manner for the presence and percentage of stromal TILs (sTILs) based on the standardized method proposed by the International TILs Working Group 2014 (5).

GRAPHS & TABLES

Table 1. **Baseline characteristics.**

Characteristic	N = 95
Age	71 (60, 78)
Sex	
male	62 (65%)
female	33 (35%)
Primary tumour site	
oral cavity	58 (61%)
larynx	21 (22,1%)
oropharynx	8 (8,4%)
hypopharynx	5 (5,3%)
nasal cavity	3 (3,2%)
Primary/Metastatic tumour	
primary tumour	82 (86,3%)
metastasis	13 (13,7%)
Sample type	
biopsy	74 (78%)
surgical sample	21 (22%)
Tumor grade	
1	6 (6.3%)
2	63 (66%)
3	26 (27%)
Stromal TILs	30 (15, 68)
CPS	
H-CPS	56 (59%)
L-CPS	39 (41%)

Figure 1. **Distribution of sTILs in different sub-sites of HNSCC primary tumour.**

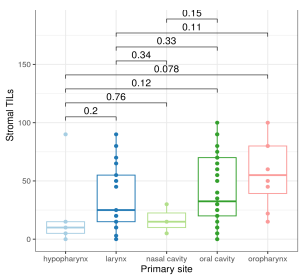
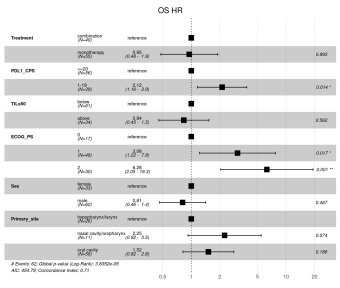


Figure 2. **Multivariable Cox regression model.**



RESULTS

Clinical and pathological features of the study population are listed in Table 1. Briefly, 62 patients were male and 33 female and median age was 71 years. Fifty-five patients received Pembrolizumab in monotherapy while 40 patients received immunotherapy with chemotherapy (combo group). The median PFS was 3 and 5 months in the monotherapy and combo group, respectively; on the other hand, median OS was 5 and 14 months in the monotherapy and combo group, respectively.

Sections representative of the paraffin-embedded tissue from 74 core biopsies (78%) and 21 surgical samples (22%) were evaluated. Tissue samples were obtained from the primary tumour in 82 cases (86,3%), being the oral cavity the most common site (n= 58, 61%) and from metastatic lesions in the remaining 13 (13,7%). All cases were scored as CPS ≥1. According to clinically relevant cut-off, we further stratified our study sample in two groups: "low-CPS" (L-CPS), and "high-CPS" (H-CPS), with CPS expression <20 or ≥20, respectively. Based on this criterion, 39 patients (41%) were classified as L-CPS and 56 cases (59%) as H-CPS.

The median value of sTILs was 30 (range: 15-68) associated with tertiary follicles in 9 patients. Oropharynx was characterized by the numerically higher TILs median value (55), followed by oral cavity (35), larynx (25), nasal cavity (15) and hypopharynx (10). Stromal TILs were higher in: i) primary tumor samples when compared to sites of local recurrence or metastatic localization (p=0.045); ii) in tumor with H-CPS (p=0.05); in samples with tertiary follicles (p=0.063). Sex, HPV status, primary site and tumor grade did not show differences in sTILs distribution. We did not find an association between sTILs (both as continuous parameter, per 5% increase and with a cutoff of 50%) and OS in a univariable and multivariable Cox regression model. In multivariable Cox regression model with treatment, CPS and ECOG PS were the only variables significantly associated with OS.

REFERENCES

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CONCLUSIONS

Our results confirm the role of Combined Positive Score and Performance Status in predicting outcome in R/M head and neck cancer patients. In particular, patients with a cut-off value of CPS≥20 are characterized by a better overall survival.

As concerning the overall assessment of TILs in HE-stained sections, our study confirm that different subsites of head and neck cancer were characterized by different TILs level being the oropharynx the most inflamed. Stromal TILs were higher in the primary tumor samples compared to metastatic localization confirming the transition from hot tumor to cold tumor in the evolution of disease while the percentage of sTILS doesn't seem to affect the response to immunotherapy. This data highlights the need in the scenario of head and neck cancer of a deeper characterization of immune infiltrate with cell-specific immune markers and the opportunity of using immunotherapy strategies in earlier settings.