First-line programmed cell death 1 inhibitor plus chemotherapy vs. standard treatment in patients with recurrent or metastatic oral squamous cell carcinoma: A retrospective cohort study

LEI CHENG[1], CONGNA CHAI[2], YINGQI LIU[1] and JIANJUN JIAO[2]

[1]Department of Stomatology, Handan Central Hospital, Handan, Hebei 056001, P.R. China;
[2]Department of Oral and Maxillofacial Surgery, Handan Central Hospital, Handan, Hebei 056001, P.R. China

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Abstract. Programmed cell death 1 (PD-1) inhibitor revives the killing effect of immune cells to prevent tumor progression. The present study aimed to evaluate the efficacy and safety of first-line PD-1 inhibitor + chemotherapy vs. standard treatment in recurrent or metastatic (R/M) oral squamous cell carcinoma (OSCC). A total of 51 patients with R/M OSCC were reviewed and divided into the PD-1 inhibitor + chemotherapy (n=21) and standard treatment (n=30) groups based on their actual treatments. The results of the present study demonstrated that the objective response rate (52.4 vs. 36.7%, P=0.265) and disease control rate (81.0 vs. 70.0%, P=0.377) were numerically elevated in the PD-1 inhibitor + chemotherapy group compared with those in the standard treatment group; however, the results did not reach statistical significance. The progression-free survival (PFS) was numerically increased (without statistical significance) in the PD-1 inhibitor + chemotherapy group compared with that of the standard treatment group (P=0.057). Specifically, the PD-1 inhibitor + chemotherapy group and the standard treatment group exhibited a median [95% confidence interval (CI)] PFS duration of 6.7 (1.6-11.8) and 5.2 (3.4-7.0) months, respectively. In addition, the PD-1 inhibitor + chemotherapy group demonstrated increased overall survival (OS) compared with that of the standard treatment group (P=0.032). Specifically, the PD-1 inhibitor + chemotherapy group and the standard treatment group exhibited a median (95% CI) OS duration of 18.3 (11.9-24.7) and 10.3 (7.9-12.7) months, respectively. Furthermore, multivariate Cox regression analysis indicated that PD-1 inhibitor + chemotherapy was independently associated with improved PFS [hazard ratio (HR)=0.308, P=0.002] and OS (HR=0.252, P=0.003). In addition, the incidence of grade 3-5 adverse events (AEs) was relatively low in both groups and the incidence of any grade of each AE was not significantly different between groups (all P>0.050). In conclusion, the first-line PD-1 inhibitor + chemotherapy group had improved efficacy and comparable safety compared with those of the standard treatment in patients with R/M OSCC.

Correspondence to: Dr Congna Chai, Department of Oral and Maxillofacial Surgery, Handan Central Hospital, 59 North Congtai Road, Handan, Hebei 056001, P.R. China
E-mail: nagangguanlil@163.com

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Introduction

Oral cavity cancer ranks sixth among the most commonly diagnosed cancer types; the most prevalent pathological subtype is oral squamous cell carcinoma (OSCC), accounting for >90% of all reported diagnoses (1-3). OSCC is associated with various factors, including tobacco consumption, alcohol abuse, exposure to human papillomavirus and genetic predisposition (4). Surgery is the preferred radical treatment option for OSCC. However, surgery in patients with recurrent/metastatic (R/M) OSCC has limited feasibility, and systemic therapy for palliation with active drugs, such as cetuximab, platinum, 5-fluorouracil and paclitaxel, is recognized as the standard treatment (5-7). Despite the use of standard treatment, a proportion of patients with R/M OSCC develop further tumor progression, resulting in a dismal prognosis of the disease (5). Therefore, the exploration of certain different treatment options with the potency to improve the treatment response or survival of patients with R/M OSCC is urgent.

Programmed cell death 1 (PD-1) inhibitor binds to the PD-1 checkpoint receptor to avoid its interaction with the programmed cell death ligand 1 (PD-L1), which restores the recognition and cytotoxic effect of immune cells, preventing the immune escape of tumor cells and inhibiting tumor progression (8,9). Available evidence suggests that the use of PD-1 inhibitors is effective for certain tumor types. In recent years, the efficacy of the PD-(L)1 inhibitors (including camrelizumab, nivolumab, pembrolizumab and durvalumab) in OSCC has been reported in several studies (10-14). For instance, a previous study has shown that nearly 60% of patients with recurrent/unresectable/metastatic OSCC treated with pembrolizumab achieve objective response (10). An

additional study has revealed that the 1-year progression-free survival (PFS) rate is 25.4% in nivolumab-treated patients with R/M OSCC (11). Another study showed that durvalumab was able to achieve numerically higher 12-, 18- and 24-month survival rates compared to standard of care in R/M head and neck squamous cell carcinoma (HNSCC) (lacking statistical significance) (13). However, certain patients do not have a durable clinical benefit and the efficacy of the PD-1 inhibitors can be improved by rational combination with other therapies, which results in overcoming potential resistance (10,11,15-18). To date, only one study has suggested that PD-1 inhibitor combined with concurrent chemoradiotherapy treatment is able to achieve satisfactory efficacy [median overall survival (OS), 19 months] for Chinese patients with R/M HNSCC (19). However, the previous study is single-arm and the potential of PD-1 inhibitor + chemotherapy in Chinese patients with R/M OSCC requires further exploration (19).

In this light, the present study intended to assess the efficacy and safety of PD-1 inhibitors (pembrolizumab, camrelizumab and nivolumab) + chemotherapy as first-line treatment compared with the standard treatment in Chinese patients with R/M OSCC.

Materials and methods

Study population and treatment. In the present retrospective cohort study, 51 patients with R/M OSCC who were treated with PD-1 inhibitor + chemotherapy or standard treatment as the first-line treatment from August 2020 to February 2023 were included. The inclusion criteria were the following: i) Patients diagnosed as R/M OSCC by histopathology; ii) age >18 years; iii) patients who received PD-1 inhibitor + chemotherapy or standard treatment as the first-line treatment; iv) patients who had at least one clinical response result and follow-up data. If the patients had active autoimmune disease with serious lesions in important organs, such as the heart, lungs and kidneys, they were excluded. Females during pregnancy or lactation were also excluded. All patients received first-line PD-1 inhibitor + chemotherapy or standard treatment. The regimen details of PD-1 inhibitor + chemotherapy included the following: Pembrolizumab (200 mg per cycle) + platinum + 5-fluorouracil (5-FU); camrelizumab (200 mg per cycle) + platinum + 5-FU; and nivolumab (3 mg/kg every 2 weeks) + platinum + 5-FU. PD-1 inhibitors were continued until disease progression, death or toxicity-based intolerance. The chemotherapy lasted 4 to 6 cycles with a 3-week cycle and the conventional doses used were identical to those reported in a previous study (18). The regimen of standard treatment involved the following: Cetuximab + platinum + 5-FU; cetuximab + cisplatin + docetaxel; platinum + 5-FU; and cetuximab + paclitaxel. The doses of the drugs used were based on the Chinese Society of Clinical Oncology diagnosis and treatment guidelines for head and neck cancer 2018 (7).

Data collection and assessment. Age, gender, current or former smoking status, Eastern Cooperative Oncology Group performance status (ECOG PS) score (20), primary tumor location according to the 4th edition of the World Health Organization Classification of Head and Neck Tumors (21), disease status and PD-L1 combined positive score (CPS) were collected. PD-L1 expression was determined by immunohistochemical staining (22), and the staining was performed according to the manufacturer's protocol. Antibodies used included PD-L1 polyclonal antibody (cat. no. PA5-88105; dilution, 1:100; Thermo Fisher Scientific, Inc.) and goat anti-rabbit IgG (H+L) secondary antibody, HRP (cat. no. 31460; dilution, 1:100; Thermo Fisher Scientific, Inc.). The PD-L1 CPS was calculated via the following formula (23):

$$\text{PD-L1 CPS} = \frac{\text{No. PD-L1-stained cells}}{\text{(tumor cells, lymphocytes, macrophages)}} \text{x100}$$
$$\text{Total No. of viable tumor cells}$$

PD-L1 CPS <1 was defined as PD-L1-negative (Fig. S1A), while PD-L1 CPS ≥1 was defined as PD-L1-positive (Fig. S1B). In addition, the clinical response results were collected and assessed via the response evaluation criteria in solid tumors version 1.1 (24). The disease progression or death statuses were obtained as well. In addition, adverse events (AEs) were recorded.

The objective response rate (ORR) and disease control rate (DCR) were calculated according to the clinical response results after 4 cycles (~2.8 months) of treatment. The PFS and OS rates were calculated based on the disease statuses and survival durations. PFS was defined as the time from the start of treatment in the study until disease progression or death of any cause; OS was defined as the time from the start of treatment in the study until any-cause death of any cause. AEs were graded via the Common Terminology Criteria for Adverse Events (v.5.0) (25).

Statistical analysis. SPSS v.26.0 (IBM Corp.) was used for data analyses. Student's t-test, the χ^2 test or Fisher's exact test were applied for comparisons as appropriate. Kaplan-Meier curves were plotted to illustrate PFS and OS of the groups and the log-rank test was used for statistical comparison. Enter-method multi-variable Cox regression analyses were performed to identify factors affecting PFS and OS in patients with OSCC, in which PD-1 inhibitor plus chemotherapy, age, male sex, current or former smoking, ECOG PS score, primary tumor location, and disease status were included in the analyses. $P<0.05$ was considered to indicate a statistically significant difference.

Results

Patient characteristics. The mean age of the PD-1 inhibitor + chemotherapy group and the standard treatment group was 59.9±11.9 years and 61.8±10.0 years (P=0.524), respectively. There were 17 (81.0%) males in the PD-1 inhibitor + chemotherapy group and 21 (70.0%) males in the standard treatment group (P=0.377). A total of 10 (47.6%), 1 (4.8%) and 5 (23.8%) patients in the PD-1 inhibitor + chemotherapy group had a history of surgery, chemotherapy and radiotherapy, respectively. In comparison, in the standard treatment group, 13 (43.3%), 8 (26.7%) and 12 (40.0%) patients had a history of surgery, chemotherapy and radiotherapy, respectively. In the PD-1 inhibitor + chemotherapy group, all 21 (100%) patients were rated as PD-L1 CPS ≥1, while in the standard treatment group, 8 (26.7%) and 9 (30.0%) patients were classified as PD-L1 CPS <1 and ≥1, respectively; the PD-L1 CPS status of the remaining 13 (43.3%) patients in that group was unknown (P<0.001). In addition, current or former smoking, primary tumor location, disease status and ECOG PS score did not

Table I. Clinical features of patients with oral squamous cell carcinoma.

Item	PD-1 inhibitor plus chemotherapy (n=21)	Standard treatment (n=30)	P-value
Age, years	59.9±11.9	61.8±10.0	0.524
Male sex	17 (81.0)	21 (70.0)	0.377
Current or former smoker	16 (76.2)	20 (66.7)	0.463
History of surgery	10 (47.6)	13 (43.3)	0.783
History of chemotherapy	1 (4.8)	8 (26.7)	0.064
History of radiotherapy	5 (23.8)	12 (40.0)	0.366
ECOG PS score			0.530
0	6 (28.6)	11 (36.7)	
1	14 (66.7)	19 (63.3)	
2	1 (4.8)	0 (0.0)	
Differentiation			0.604
Poor	4 (19.0)	9 (30.0)	
Moderate	13 (61.9)	18 (60.0)	
Well	4 (19.0)	3 (10.0)	
Primary tumor location			0.672
Tongue	8 (38.1)	16 (53.3)	
Gingiva	8 (38.1)	9 (30.0)	
Mouth floor	3 (14.3)	4 (13.3)	
Others	2 (9.5)	1 (3.3)	
Disease status			0.568
Metastatic disease only	11 (52.4)	14 (46.7)	
Recurrent disease only	4 (19.0)	10 (33.3)	
Recurrent metastatic disease	6 (28.6)	6 (20.0)	
Metastatic site			
Lymph nodes	7 (33.3)	16 (53.3)	0.253
Lung	9 (42.9)	11 (36.7)	0.773
Bone	7 (33.3)	5 (16.7)	0.196
Liver	1 (4.8)	6 (20.0)	0.217
Other	5 (23.8)	7 (23.3)	>0.999
Recurrence site			0.886
Tongue	5 (50.0)	7 (43.8)	
Gingiva	3 (30.0)	4 (25.0)	
Mouth floor	2 (20.0)	5 (31.3)	
PD-L1 CPS			<0.001
<1	0 (0.0)	8 (26.7)	
≥1	21 (100.0)	9 (30.0)	
Unknown	0 (0.0)	13 (43.3)	

Values are expressed as the mean ± standard deviation or n (%). PD-1, programmed cell death 1; ECOG PS, Eastern Cooperative Oncology Group performance status; PD-L1 CPS, programmed death-ligand 1 combined positive score.

exhibit any differences between the two groups (all P>0.050). The specific information is displayed in Table I.

Treatment information. In the PD-1 inhibitor + chemotherapy group, 14 (66.7%) patients, 4 (19.0%) patients and 3 (14.3%) patients received pembrolizumab + platinum + 5-FU, nivolumab + platinum + 5-FU and camrelizumab + platinum + 5-FU, respectively. In the standard treatment group, 20 (66.7%), 4 (13.3%), 5 (16.7%) patients and 1 (3.3%) patient were treated with cetuximab + platinum + 5-FU, cetuximab + cisplatin + docetaxel, platinum + 5-FU and cetuximab + paclitaxel, respectively (Table II).

ORR and DCR. The ORR was numerically elevated (without statistical significance) in the PD-1 inhibitor + chemotherapy group compared with that in the standard treatment group

Table II. Treatment regimens for patients with oral squamous cell carcinoma.

Treatment	N (%)
Programmed cell death 1 inhibitor plus chemotherapy	
Pembrolizumab + platinum + 5-FU	14 (66.7)
Nivolumab + platinum + 5-FU	4 (19.0)
Camrelizumab + platinum + 5-FU	3 (14.3)
Standard treatment	
Cetuximab + platinum + 5-FU	20 (66.7)
Cetuximab + cisplatin + docetaxel	4 (13.3)
Platinum + 5-FU	5 (16.7)
Cetuximab + paclitaxel	1 (3.3)

5-FU, 5-fluorouracil.

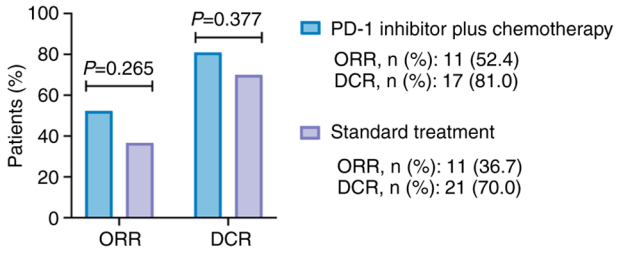


Figure 1. Clinical response in patients with recurrent or metastatic oral squamous cell carcinoma. DCR, disease control rate; ORR, objective response rate; PD-1, programmed cell death 1.

(52.4 vs. 36.7%, P=0.265). In addition, the DCR exhibited an elevated trend (lacking statistical significance) in the PD-1 inhibitor + chemotherapy group compared with that in the standard treatment group (81.0 vs. 70.0%, P=0.377; Fig. 1).

PFS and OS. The PFS exhibited a prolonged trend (lacking statistical significance) in the PD-1 inhibitor + chemotherapy group compared with that in the standard treatment group (P=0.057). In detail, the median [95% confidence interval (CI)] PFS duration of the PD-1 inhibitor + chemotherapy group and the standard treatment group was 6.7 (1.6-11.8) months and 5.2 (3.4-7.0) months, respectively. The 12-month PFS rate in the PD-1 inhibitor + chemotherapy group and in the standard treatment group was 38.5 and 8.1%, respectively. Furthermore, the 24-month PFS rate in the two groups was 14.4 and 4.0%, respectively (Fig. 2A).

The OS was prolonged in the PD-1 inhibitor + chemotherapy group compared with that in the standard treatment group (P=0.032). Specifically, the median (95% CI) OS duration of the PD-1 inhibitor + chemotherapy group and that of the standard treatment group was 18.3 (11.9-24.7) months and 10.3 (7.9-12.7) months, respectively. Furthermore, the 12-month OS rate of the PD-1 inhibitor + chemotherapy group and that of the standard treatment group was 68.2 and 30.6%, respectively, while the 24-month OS rate was 34.1 and 10.9% in the corresponding groups (Fig. 2B).

In addition, neither PFS (P=0.869; Fig. S2A) nor OS (P=0.834; Fig. S2B) was different among R/M OSCC patients with different primary tumor locations.

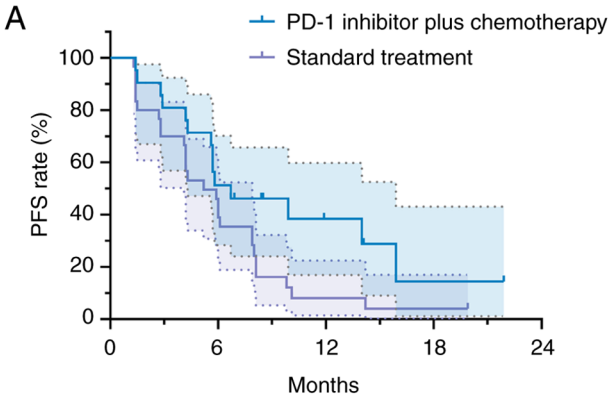
Subgroup analysis. In patients who received treatment between 2020 and 2022, PFS exhibited a prolonged trend (without statistical significance) in the PD-1 inhibitor + chemotherapy group in comparison with that in the standard treatment group (P=0.054; Fig. S3A). OS was prolonged in the PD-1 inhibitor + chemotherapy group compared to the standard treatment group (P=0.031; Fig. S3B). However, in patients who received treatment in 2023, neither PFS (P=0.918; Fig. S3C) nor OS (P=0.705; Fig. S3D) was different between the two groups.

Independent factors affecting PFS and OS. PD-1 inhibitor in addition to chemotherapy was independently associated with longer PFS [hazard ratio (HR): 0.308, P=0.002]. In addition, male sex (HR: 4.309, P=0.005) and a higher ECOG PS score (HR: 4.040, P=0.002) were independently related to reduced PFS. Whereas higher age, current or former smoking, primary tumor location in the gingiva (vs. tongue), mouth floor (vs. tongue), other locations (vs. tongue), metastatic disease only (vs. recurrent metastatic disease) and recurrent disease only (vs. recurrent metastatic disease) were not independently associated with PFS (all P>0.050) (Fig. 3). Furthermore, PD-1 inhibitor in addition to chemotherapy (HR: 0.252, P=0.003) and recurrent disease only (vs. recurrent metastatic disease; HR: 0.232, P=0.019) were independently associated with longer OS, whereas male sex (HR: 6.502, P=0.004) and higher ECOG PS score (HR: 4.871, P=0.003) were independently associated with reduced OS. However, higher age, current or former smoking, primary tumor location in gingiva (vs. tongue), mouth floor (vs. tongue), other locations (vs. tongue) and metastatic disease only (vs. recurrent metastatic disease) were not independent related factors for OS (Fig. 4).

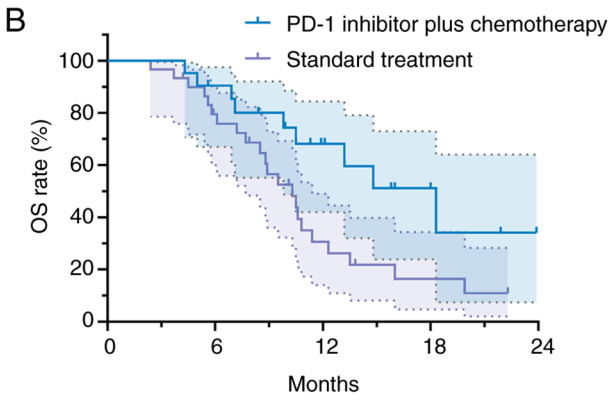
AEs. The most common AEs of any grade in the PD-1 inhibitor + chemotherapy group were fatigue (42.9%), anemia (28.6%), neutropenia (28.6%), nausea (28.6%), leukopenia (23.8%) and liver dysfunction (23.8%). In addition, the incidence of grade 3-5 AEs in the PD-1 inhibitor + chemotherapy group was relatively low, including neutropenia (9.5%), fatigue (4.8%), anemia (4.8%), nausea (4.8%), leukopenia (4.8%) and liver dysfunction (4.8%). In the standard treatment group, fatigue (36.7%), nausea (33.3%), anemia (26.7%), diarrhea (26.7%), rash (26.7%), thrombocytopenia (23.3%), neutropenia (20%), leukopenia (20.0%), liver dysfunction (20.0%) and vomiting (20.0%) were common AEs of any grade. Grade 3-5 AEs in the standard treatment group included neutropenia (6.7%), fatigue (3.3%), nausea (3.3%), leukopenia (3.3%), liver dysfunction (3.3%), diarrhea (3.3%) and vomiting (3.3%). Overall, the incidence of each AE of any grade was not significantly different between the PD-1 inhibitor + chemotherapy and the standard treatment group (all P>0.050; Table III).

Discussion

Various studies have reported on the utilization of PD-1 inhibitors in patients with R/M HNSCC (26-28). For instance, a previous study revealed that patients with R/M HNSCC



	PD-1 inhibitor plus chemotherapy	Standard treatment
Log-rank test	*P*=0.057	
Median (95% CI), (month)	6.7 (1.6–11.8)	5.2 (3.4–7.0)
12-months PFS (%)	38.5	8.1
24-months PFS (%)	14.4	4.0



	PD-1 inhibitor plus chemotherapy	Standard treatment
Log-rank test	*P*=0.032	
Median (95% CI), (month)	18.3 (11.9–24.7)	10.3 (7.9–12.7)
12-months OS (%)	68.2	30.6
24-months OS (%)	34.1	10.9

Figure 2. Survival of patients with R/M OSCC. (A) The PFS indicated a numerically elevated trend (lacking statistical significance) in patients with R/M OSCC receiving PD-1 inhibitor + chemotherapy compared with those receiving standard treatment. (B) Patients with R/M OSCC who were treated with PD-1 inhibitor + chemotherapy exhibited better OS compared with those who were treated with standard treatment. R/M, recurrent or metastatic; OSCC, oral squamous cell carcinoma. PFS, progression-free survival; PD-1, programmed cell death 1; OS, overall survival.

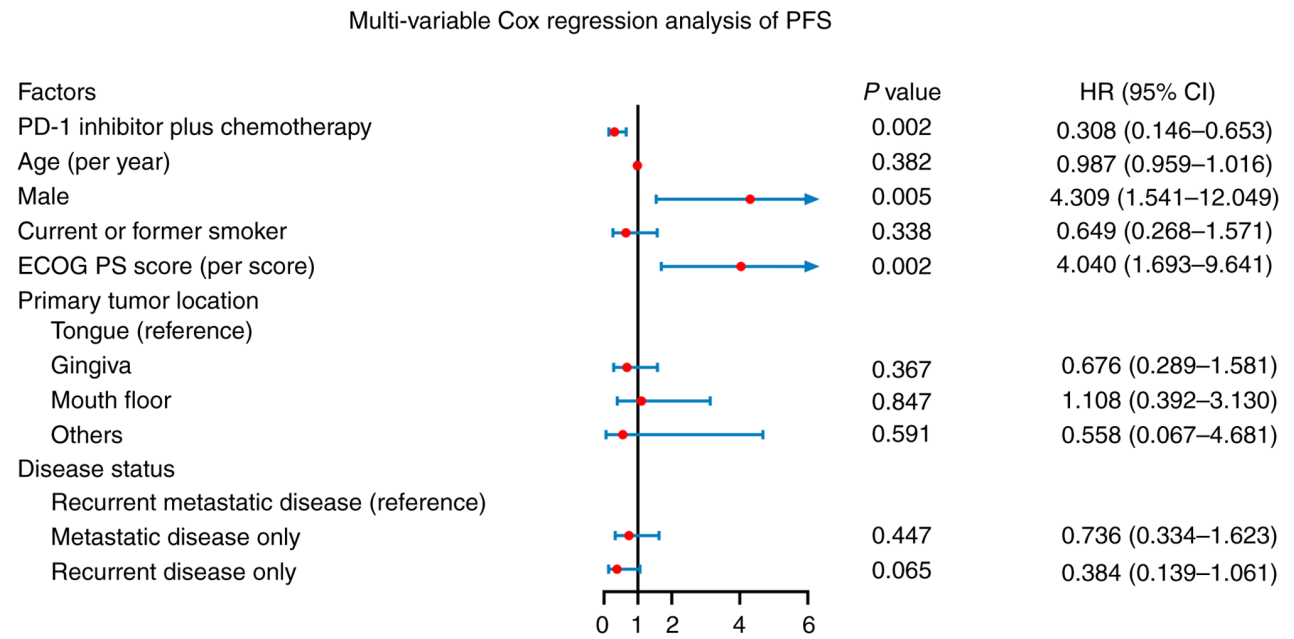


Figure 3. Independent factors for PFS of patients with recurrent or metastatic oral squamous cell carcinoma. PFS, progression-free survival; PD-1, programmed cell death 1; ECOG PS, Eastern Cooperative Oncology Group performance status; HR, hazard ratio.

receiving nivolumab exhibited an ORR of 13.3%, which was superior to that noted in the standard therapy group (5.8%) (26). An additional study demonstrated that pembrolizumab caused a numerical elevation in the ORR (14.6 vs. 10.1%) compared with methotrexate, docetaxel or cetuximab following platinum drug treatment in patients with R/M HNSCC (28). However, the

Table III. AEs [n (%)].

	Programmed cell death 1 inhibitor plus chemotherapy (n=21)			Standard treatment (n=30)			
AE	Any grade	Grade 1-2	Grade 3-5	Any grade	Grade 1-2	Grade 3-5	P-value
Fatigue	9 (42.9)	8 (38.1)	1 (4.8)	11 (36.7)	10 (33.3)	1 (3.3)	0.656
Anemia	6 (28.6)	5 (23.8)	1 (4.8)	8 (26.7)	8 (26.7)	0 (0.0)	0.881
Neutropenia	6 (28.6)	4 (19.0)	2 (9.5)	6 (20.0)	4 (13.3)	2 (6.7)	0.518
Nausea	6 (28.6)	5 (23.8)	1 (4.8)	10 (33.3)	9 (30.0)	1 (3.3)	0.718
Leukopenia	5 (23.8)	4 (19.0)	1 (4.8)	6 (20.0)	5 (16.7)	1 (3.3)	0.744
Liver dysfunction	5 (23.8)	4 (19.0)	1 (4.8)	6 (20.0)	5 (16.7)	1 (3.3)	0.744
Thrombocytopenia	4 (19.0)	4 (19.0)	0 (0.0)	7 (23.3)	7 (23.3)	0 (0.0)	>0.999
Stomatitis	4 (19.0)	4 (19.0)	0 (0.0)	5 (16.7)	5 (16.7)	0 (0.0)	>0.999
Diarrhea	4 (19.0)	4 (19.0)	0 (0.0)	8 (26.7)	7 (23.3)	1 (3.3)	0.739
Hypothyroidism	3 (14.3)	3 (14.3)	0 (0.0)	1 (3.3)	1 (3.3)	0 (0.0)	0.293
Vomiting	3 (14.3)	3 (14.3)	0 (0.0)	6 (20.0)	5 (16.7)	1 (3.3)	0.720
Pyrexia	2 (9.5)	2 (9.5)	0 (0.0)	3 (10.0)	3 (10.0)	0 (0.0)	>0.999
Rash	2 (9.5)	2 (9.5)	0 (0.0)	8 (26.7)	8 (26.7)	0 (0.0)	0.167
Pneumonitis	1 (4.8)	1 (4.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.412
Renal dysfunction	1 (4.8)	1 (4.8)	0 (0.0)	2 (6.7)	2 (6.7)	0 (0.0)	>0.999

AE, adverse event. The P-values pertain to the comparison of 'any grade' AEs between the two groups.

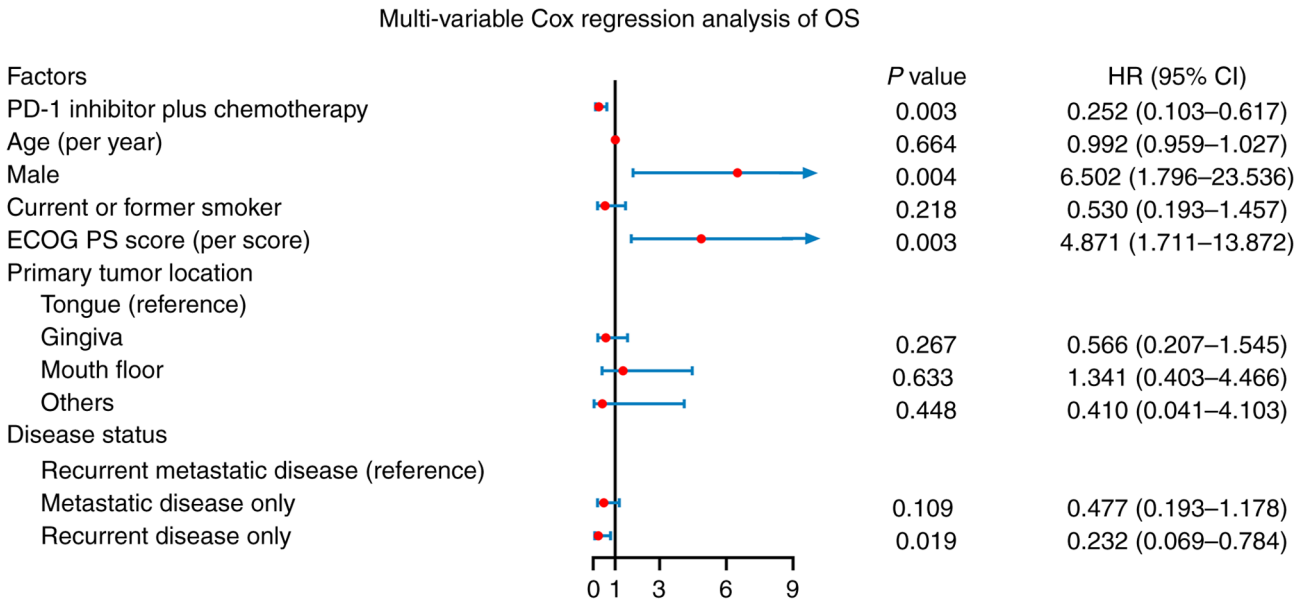


Figure 4. Independent factors for OS of patients with recurrent or metastatic oral squamous cell carcinoma. OS, overall survival; PD-1, programmed cell death 1; ECOG PS, Eastern Cooperative Oncology Group performance status; HR, hazard ratio.

efficacy of the application of PD-1 inhibitor + chemotherapy lacked sufficient evidence. In the present study, the results did not demonstrate a statistically significant benefit of treatment response in patients with PD-1 inhibitor + chemotherapy compared to standard treatment as the first-line treatment in patients with R/M OSCC, which may be due to the relatively small sample size. However, the ORR (52.4 vs. 36.7%) and DCR (81.0 vs. 70.0%) were numerically elevated in patients with R/M OSCC treated with PD-1 inhibitor + chemotherapy compared with those receiving standard treatment. The potential explanations may be as follows: PD-1 inhibitor was assumed to potentiate the cytotoxic effect of chemotherapy on tumor cells by altering the tumor microenvironment (29-31), and to facilitate death of tumor cells through reviving the cytotoxic activity of T lymphocytes (32). Therefore, PD-1 inhibitor + chemotherapy achieved a numerically higher ORR and DCR in patients with R/M OSCC compared with those on standard treatment; however, the findings require

further validation in large-scale studies. In addition, it is worth mentioning that although the salvage operation was an optimal choice for locally recurrent OSCC, certain patients were not suitable for salvage operation due to overload tumor burden or rejection of salvage operation for various reasons. Thus, for this population in the present study, conservative treatment was chosen. Furthermore, the treatment decision is made by the oncological board, which is based on the Chinese Society of Clinical Oncology guidelines (7) combined with the patient's condition and choice.

The application of PD-1 inhibitors has improved the survival profile of patients with HNSCC, including cancer of the hypopharynx, larynx, oral cavity and oropharynx (18,33,34). For instance, a previous study indicated that the OS was increased in patients with R/M HNSCC receiving pembrolizumab + chemotherapy (13.0 months) compared with those receiving cetuximab + chemotherapy (10.7 months) (18). An additional study suggested that nivolumab effectively improved the 24-month OS rate of patients with R/M HNSCC compared with that of patients treated with methotrexate, docetaxel or cetuximab (16.9 vs. 6.0%) (33). Another study found that PD-1 inhibitor in combination with paclitaxel and cisplatin achieved a 12-month PFS rate of 80.4% and 12-month OS rate of 94.1% in patients with locally advanced laryngeal and hypopharyngeal squamous cell carcinoma (34). In the current study, PFS indicated a numerically elevated trend and OS was prolonged in patients with R/M OSCC who underwent PD-1 inhibitor + chemotherapy compared with those who underwent standard treatment. In addition, PD-1 inhibitor + chemotherapy was independently related to higher PFS and OS of patients with R/M OSCC. The possible explanation may be as follows: Inhibition of PD-1 had a favorable anti-tumor effect and its combination with chemotherapy further impeded the progression of OSCC, contributing to improved survival (16). Consequently, the PD-1 inhibitor + chemotherapy combination was an independent factor for prolonged PFS and OS (vs. standard treatment) of patients with R/M OSCC. Of note, in comparison with previous studies (18,33), patients administered with PD-1 inhibitor + chemotherapy in the current study achieved a relatively longer OS, which may be explained by the following etiology: Clinically, PD-1 inhibitors are recommended for patients with PD-L1 CPS≥1 (35); in addition, all of the patients receiving PD-1 inhibitor + chemotherapy in the present study were classified as PD-L1 CPS≥1 and thus benefited more from the immunotherapy. It is interesting to note that male sex was independently associated with worse PFS and OS in the present study, which was consistent with a previous study (36).

In line with previous studies (18,37), fatigue, nausea, neutropenia and anemia were the most common AEs associated with PD-1 inhibitor + chemotherapy in the present study. Furthermore, fatigue, nausea, anemia, diarrhea and rush were the most common AEs in the standard treatment group of the current study, which was similar to the results noted in previous studies (18,38). More importantly, the incidences of all AEs did not vary between patients who received PD-1 inhibitor + chemotherapy and standard treatment. In addition, the majority of AEs in the present study were of grade 1-2; the incidence of grade 3-5 AEs was relatively low, indicating that the systematic toxicity of both PD-1 inhibitor + chemotherapy and standard treatment in patients with R/M OSCC was controllable.

Certain limitations were inevitable in the present study: First, the current retrospective study was conducted at a single center and it was difficult to avoid selection bias. Furthermore, this was a retrospective study; therefore, the documentation of AEs may have been inadequate, which may have potentially led to an underestimation of AEs in both groups. In addition, the present study had a relatively small number of enrolled patients and it was difficult to summarize useful information, such as the association of various tumor localizations with treatment response. Finally, the follow-up duration of the present study was not adequate and the findings required more verification in studies with a longer follow-up period.

In conclusion, the present study indicated that PD-1 inhibitor + chemotherapy achieved numerically elevated treatment response and was an independent factor for prolonged PFS and OS with comparable safety compared to standard treatment in patients with R/M OSCC. The findings suggest that PD-1 inhibitor + chemotherapy may serve as a potential first-line therapeutic regimen for patients with R/M OSCC. Further validation through multi-center randomized, controlled studies with a large sample size is necessary.

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Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

LC, CC, YL and JJ contributed to the study conception and design. Material preparation, data collection and analysis were performed by LC, CC and YL. The first draft of the manuscript was written by LC. LC, CC, YL and JJ commented on previous versions of the manuscript. YL and JJ confirm the authenticity of all the raw data. All authors have read and approved the final manuscript.

Ethics approval and consent to participate

The Ethics Committee of Handan Central Hospital (Handan, China) gave approval for this study (approval date, 2023/02/10; no approval number was provided). Oral informed consent for analysis and publication of personal information was obtained from each patient via telephone. Besides, the PD-L1 IHC staining was performed for treatment purposes.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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