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Original Article

Combination Therapy of Anti-PD-1 Immunotherapy and Taxanes in Relapsed and/or Metastatic Head and Neck Squamous Cell Carcinoma: A Real-world Single-center Retrospective Study

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Abstract

Background: Recurrent/metastatic head and neck squamous cell carcinoma (R/M-HNSCC) carries a poor prognosis despite the current standard of care. This study aimed to investigate the efficacy and safety of a novel non-cisplatin-containing chemo-immunotherapy regimen combining a programmed cell death protein 1 (PD-1) inhibitor and a taxane, in platinum-ineligible or platinum-refractory R/M-HNSCC patients. **Materials and Methods:** This retrospective analysis of medical charts included 24 patients aged ≥18 with unresectable R/M-HNSCC, eastern cooperative oncology group performance status ≤2, no prior immune checkpoint inhibitor (ICI) therapy, and adequate follow-up. All patients received a PD-1 inhibitor and a taxane. The primary endpoints were progression-free survival (PFS) and objective response rate (ORR), and the secondary endpoints were overall survival (OS) and toxicity. **Results:** The ORR was 50%, the disease control rate was 66.7%, the median PFS was 6.4 months, and the median OS was 11.6 months. The average time to response was 3.3 months, with a median duration of response of 5.0 months. Common adverse events included anemia (58.3%), hypothyroidism (29.2%), and dermatitis (25%). Grade ≥ 3 adverse events occurred in 20.8% (5/24) of the patients, with one ICI discontinuation due to severe dermatitis; others were manageable. **Conclusion:** The results of this real-world retrospective analysis showed satisfactory efficacy including ORR, PFS, and OS, and manageable toxicity for PD-1 inhibitor/taxane combination therapy as first-or later-line treatment in ICI-naïve R/M-HNSCC patients. Larger prospective studies are warranted.

Keywords: Chemotherapy, immunotherapy, locally advanced head-and-neck cancer, medical oncology, taxane

Introduction

Head and neck squamous cell carcinoma (HNSCC) is a common type of cancer with approximately 745,000 new cases and 364,000 cancer-related deaths annually worldwide.[1] In Taiwan, HNSCC is fifth among the top ten cancers and also the third most common cancer among men, with an age-standardized annual incidence of 40.4 cases per 100,000 people; oral cavity cancer alone led to 16.8 deaths per 100,000 people in men in 2024.[2]

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About 60%–80% of patients present with nonmetastatic locally advanced disease (American Joint Committee on Cancer 8th edition clinical stage III, IVA or IVB) at first diagnosis and receive definitive treatment consisting of surgical resection, radiotherapy (RT), and systemic therapies. Despite treatment, recurrence ranges from 14% to 47%, and 20% of patients also develop metachronous distant metastasis, with an average 5-year overall survival (OS) rate of <50%.[3-5]

During the past few decades, traditional platinum-based chemotherapy, mostly in combination with fluorouracil (PF regimen) or sometimes with taxanes for locally advanced, unresectable, recurrent or metastatic HNSCC (R/M-HNSCC), has been the common practice in induction, neoadjuvant, or palliative settings.[6,7] With the advent of cancer cell targeted therapies, both anti-epidermal growth factor receptor (EGFR) monoclonal antibodies and immune checkpoint inhibitors (ICIs) with or without chemotherapy have shown improved survival results for R/M-HNSCC and have thus become the current standard of care.[8]

Despite efforts to improve local and systemic treatments, prognosis remains poor for R/M-HNSCC. This is mainly due to the high recurrence rate, with over 50% of patients developing early recurrence within 6 months, and also a high incidence of treatment failure of up to 89% within 2 years.[9] A median OS (mOS) ranging from 10 to 15 months has been reported under current standard of care treatment, which includes either an anti-EGFR antibody or programmed cell death protein 1 (PD-1) ICI with or without platinum-based chemotherapy.[10,11] Nevertheless, chemo-immunotherapy (IO), especially ICI-based, has gained increasing attention in R/M-HNSCC treatment as a forward-looking strategy by targeting multiple pathways in the cancer cell cycle and immunology pathways to overcome the limitations of monotherapies. Numerous chemotherapy, targeting agents or immunotherapies of different mechanisms have been investigated in combination therapy with ICIs.[12]

In real-world practice, a substantial proportion of R/M-HNSCC patients are considered to be ineligible for platinum-based therapy either due to comorbidities, poor performance status, intolerable side effects, or treatment refractoriness. In the treatment of HNSCC, the reported resistance rate to cisplatin ranges from 20% to 33%.[13,14] In addition, re-irradiation can be challenging in R/M-HNSCC due to constraints of cumulative dosage, normal organs at risk, and toxicity.[15] Accordingly, an increasing number of trials on cisplatin-sparing chemo-IO regimens have also been conducted.[12]

The aim of this study was to investigate the efficacy and safety of a noncisplatin-containing chemo-IO regimens that incorporate a PD-1 inhibitor and a taxane in R/M-HNSCC patients who were either platinum-ineligible at diagnosis or had platinum-refractory disease.

Materials and Methods

Study cohort

This retrospective analysis was performed on patients with locoregional relapse or metastatic HNSCC treated with combination therapy of an anti-PD-1 ICI and a taxane between December 2016 and November 2023 at a single center in Taiwan. The study was conducted in accordance with the Declaration of Helsinki and was approved by the Institutional Review Board (IRB) of MacKay Memorial Hospital (No. 25MMHIS278e 2025-08-15). The need for informed consent was waived by the IRB.

The main inclusion criteria were patients: (1) who met the diagnosis mentioned above; (2) with unresectable tumor status or could not be cured by local therapy alone; (3) aged ≥18 years; (4) with an Eastern cooperative oncology group (ECOG) performance status ≤2; and (5) with adequate follow-up information in their medical records that met the purposes of this study. Patients with documented autoimmune diseases or other synchronous malignancies, and those previously exposed to ICI-containing therapies were excluded. The patients received therapeutic regimens with the physician's choice of an ICI (either nivolumab 3 mg/kg every 2 weeks[8] or pembrolizumab 200 mg every 3 weeks[16]) and a taxane (either paclitaxel at a dose of 80 mg/m^2 once weekly[17] or 90 mg/m^2 biweekly,[18] or docetaxel 75 mg/m^2 every 3 weeks).[6,7] Local therapies with palliative intent via surgical resection or RT were performed according to the physicians' judgement.

Evaluation of treatment efficacy

Imaging studies using either computed tomography, magnetic resonance imaging, or positron emission tomography were performed at least every 3 months to assess the response. Repeated assessments used the same imaging tool for each patient. Treatment response was assessed mainly according to the revised RECIST guidelines (version 1.1)[19] or by a physician if it could not be evaluated otherwise.

The primary endpoints were progression free survival (PFS) and objective response rate (ORR). The secondary endpoints were OS, disease control rate (DCR), time to response (TTR), duration of response (DOR), toxicity, and tolerability. Data were censored at the last valid assessment date for patients who were still alive or the last seen date for patients who were lost to follow-up without a documented death event before cutoff.

Evaluation of adverse events

As a retrospective study, data collection may have limitations. Data of adverse events were retrieved retrospectively from our institution's standardized documentation system, which was developed based on National Cancer Institute (NCI)-common terminology criteria for adverse events (CTCAE) version 5.0.7[20] and drug-specific package insert guidelines.

Statistical methods

All data were expressed as mean and a 95% confidence interval (CI). Categorical data were compared using the

Chi-square test or Fisher's exact test. The Student's *t*-test was used to compare the mean values of continuous variables. All reported *P* values were based on two-sided tests and considered statistically significant if <0.05. Data were analyzed using SPSS version 25.0.2.0 (IBM Inc., Armonk, NY, USA).

Results

Baseline demographics and disease characteristics of the patients

We reviewed the medical charts of 24 patients retrospectively, all of whom had previously been treated with platinum-based chemotherapy with or without cetuximab. Twenty-one (87.5%) patients were male, and the median age was 58.4 years (range: 45–72 years, 95% CI: 54.8–62.0). The demographics and disease characteristics of the patients are shown in Table 1. All of the patients had recurrent or metastatic diseases from previous early stage or locally advanced HNSCC, except for one patient who presented initially with newly diagnosed metastatic HNSCC (nasal cavity SCC with spinal column metastasis).

The key baseline variables including comorbidities, performance status distribution (ECOG performance status), and prior lines of systemic therapy are detailed below.

Comorbidities

The distribution of baseline comorbidities was as follows: chronic kidney disease, stage 3 ($n = 4$); type 2 diabetes mellitus ($n = 2$). Child-Pugh A liver cirrhosis ($n = 2$), metachronous early stage hepatocellular carcinoma ($n = 2$), chronic obstructive pulmonary disease ($n = 1$), subclinical hypothyroidism ($n = 1$); heart failure, New York Heart Association Class I ($n = 1$).

Eastern cooperative oncology group performance status

Fifteen patients had a performance status of 1, and the other 9 patients had a score of 2.

Prior lines of systemic therapy

Except for one patient who presented with de novo metastatic HNSCC, the other 23 patients had been heavily pretreated with one (9/23), two (12/23), or three (2/23) lines of prior platinum-based therapies. Five patients had been pretreated with cetuximab, three as second line and two as third line, all were refractory. All 23 patients completed one RT course and six patients (6/23) completed two RT courses.

After enrollment, four patients received a surgical intervention. Of these patients, one received resection of the recurrence tumor, two received unilateral radical lymph node dissection, and the other one underwent metastasectomy for oligo metastases in the lungs. Five patients received additional palliative RT concurrently or subsequently for a locoregional main tumor (3 patients) and metastatic sites (2 patients with lung and brain metastasis, respectively).

The efficacy of treatment

Figure 1 shows the Kaplan–Meier plots for median PFS (mPFS) and mOS. The mPFS was 6.4 months (range: 1.8–39.3 months, 95% CI: 4.3–11.2) (A) and the mOS was 11.6 months (range: 2.1–39.3 months, 95% CI: 6.3–22.3) (B).

Figure 2 shows a swimmer plot demonstrating events in each patient during the observation period, including treatment regimen and duration, death or data censorship, and timing of treatment response. The follow-up duration ranged from 3 to 40 months. The average TTR was 3.3 months (range: 0.3–8.0 months, 95% CI: 2.6–4.0), and the median DOR was 5.0 months (range: 0.7–36.6 months, 95% CI: 1.8–16.5). The average number of treatment cycles received (including

Table 1: The demographics and disease characteristics of the patients

Patients with relapsed and/or metastatic head and neck SCC ($n = 24$[§])	Number of patients (%)
Gender	
Male	21 (87.5)
Female	3 (12.5)
Primary anatomical tumor sites*	
Sinonasal	2 (8.3)
Oropharynx	5 (20.8)
Oral cavity	9 (37.5)
Larynx	2 (8.3)
Hypopharynx	7 (29.2)
Histology	
SCC	21 (87.5)
Adenosquamous cell carcinoma	1 (4.2)
Sarcomatoid SCC	2 (8.3)
Histological grade[†]	14 evaluable patients
Grade 1	6 (42.9)
Grade 2	6 (42.9)
Grade 3	2 (14.3)
Disease status at the time of enrollment	
Locoregional recurrence	8 (33.3)
Distant metastasis	8 (33.3)
Locoregional recurrence and distant metastasis	8 (33.3)
Local therapy after enrollment	
No	19 (79.2)
Palliative radiotherapy or tomotherapy	5 (20.8)
Prior systemic treatment for recurrent and metastatic disease	23 evaluable patients[‡]
1	9 (37.5)
2	12 (50)
≥3	2 (8.3)
Time to progression/recurrence after platinum-based treatment before enrollment	23 evaluable patients[‡]
<6 months	13 (56.5)
6~12 months	6 (26.1)
>12 months	4 (17.4)

*One patient had synchronous oral cavity (left maxillary gingiva) and oropharyngeal cancer, [†]Histological grade assessed by pathologist from resection or biopsy specimen of primary tumor: 10 patients had biopsy or aspiration specimen which showed inadequate information to determine the histological grade, [‡]1 out of 24 patients presented with *de novo* metastatic HNSCC, [§]20 patients received anti-PD-1 immunotherapy and paclitaxel therapy, 4 patients received anti-PD-1 immunotherapy and docetaxel therapy. SCC: Squamous cell carcinomas, HNSCC: Head and neck squamous cell carcinoma

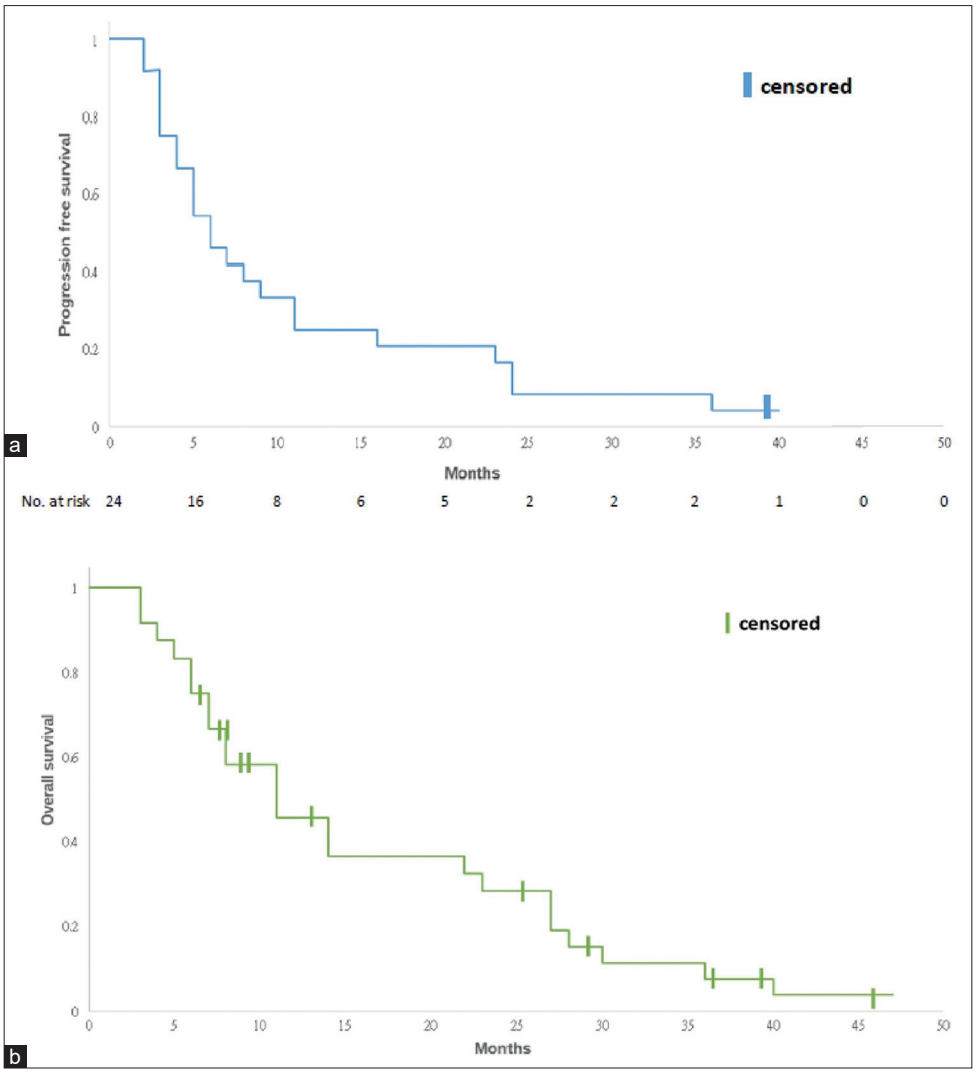

Figure 1: The Kaplan-Meier curves depict the progression-free (a) and overall (b) survival of anti-PD-1 immunotherapy and taxanes combination therapy. The median progression free survival was 6.4 months and the median overall survival was 11.6 months

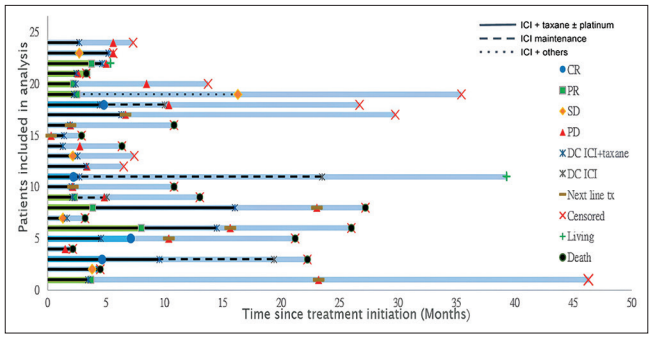

Figure 2: Swimmer plot demonstrating events of each patient during the observation period, including: treatment regimen and each duration, death or data censorship, and timing of treatment responses. ICI: Immune checkpoint inhibitors

I/O + taxane ± platinum) was 7.9 cycles (range: 3–29, 95% CI: 2.8–5.8). Treatment duration of the above regimens ranged from 1.3 to 16.0 months. The treatment regimens were primarily built upon a backbone of anti-PD-1 therapy combined with a taxane. The most common regimen was nivolumab plus paclitaxel, administered to 17 out of the 24 patients. Two patients received nivolumab and docetaxel, while two other patients were treated with pembrolizumab and docetaxel. Three patients with a relatively higher tumor burden received platinum-based cytoreduction treatment in addition to IO/taxane combination: two received carboplatin (area under the curve [AUC] 2) biweekly along with nivolumab/paclitaxel for 3 cycles, and the other patient received cisplatin 60 mg/m^2 every 3 weeks for 2 cycles along with pembrolizumab/paclitaxel. Twelve of the patients died, with the main causes of death being pneumonia in seven patients and sepsis in the other five.

As shown in Table 2, the ORR was 50% (12/24) and the DCR during the observation period was 66.7% (16/24).

Treatment-related adverse events during the study period were graded in accordance with the NCI-CTCAEs version 5.0,[20] as listed below [Table 3]. The most common adverse event

Table 2: Treatment responses of anti-PD-1 immunotherapy and taxane combination therapy

Best response	Number of patients ($n=24$)	Percentage (95% CI)
CR/PR (ORR)	12	50.0 (49.2–50.6)
SD	4	16.7 (4.5–42.7)
PD	8	33.3 (14.4–65.7)
DCR	16	66.7 (38.1–100.8)

CR: Complete response, PR: Partial response, ORR: Objective response rate, SD: Stable disease, PD: Progress disease, DCR: Disease control rate, CI: Confidence interval

Table 3: All grades of observed adverse events of anti-PD-1 immunotherapy and taxane combination therapy

Adverse events	Any grade ($n=24$)	Grade 3–4
Anemia	14 (58.3)	0
Neutropenia	3 (12.5)	1 (4.2)
Lymphocytopenia	5 (20.8)	2 (8.3)
Dermatitis	6 (25.0)	1 (4.2)
Oral mucositis	2 (8.3)	0
Hypothyroidism	7 (29.2)	0
Elevated creatinine level	1 (4.2)	0
Diarrhea	2 (8.3)	0
Cough	3 (12.5)	0
Pneumonitis	1 (4.2)	1 (4.2)
Fatigue	2 (8.3)	0
Alopecia	2 (8.3)	0
Peripheral neuropathy	1 (4.2)	0
Arthralgia	1 (4.2)	0
Hyperkalemia	1 (4.2)	0
Hyponatremia	2 (8.3)	0
Hypocalcemia	1 (4.2)	0

Data are presented as *n* (%)

was anemia (58.3%, 14/24), followed by hypothyroidism (29.2%, 7/24) and dermatitis (25%, 6/24). A total of 20.8% (5/24) grade 3 or more adverse events were noted. One severe dermatitis event led to the discontinuation of ICI treatment, while the others were manageable under proper supportive care.

Discussion

A wide range of tumor cells including head and neck cancer cells express PD-ligand 1 (PD-L1) or PD-L2. PD-1 is expressed on most immune cells, and the PD-1/PD-L1 axis promotes the inhibition of host immune response and is also responsible for the development of immune escape of cancer cells, leading to an undesirable outcome in many anti-cancer therapies.[21,22] Consequently, ICIs have been widely studied as a cancer treatment and investigated in numerous preclinical and clinical studies.

Before the advent of ICIs, platinum-based palliative poly-chemotherapy was the first-line option for R/M-HNSCC. At the beginning of the 1990s, a combination of 5-fluorouracil (5-FU) plus a platinum salt (either cisplatin or carboplatin) was shown to lead to a better overall response rate compared to single agents (5-FU or platinum alone).[23] In 2008, the EXTREME trial demonstrated that adding cetuximab (an EGFR monoclonal antibody) to the former regimen led to a significantly improved PFS, OS, and ORR (from 20% to 36%, $P < 0.001$) compared to fluorouracil-platinum alone.[10,24] However, for patients with platinum-refractory R/M-HNSCC, which is often considered to have a poor prognosis with an average survival of < 6 months, treatments were confined mainly to the EXTREME regimen, taxanes, and methotrexate.[25]

The introduction of ICIs has increased the therapeutic options for R/M-HNSCC. Anti-PD-1 ICIs such as nivolumab and pembrolizumab were the first immunotherapies approved by the US FDA in 2016 and also the European Commission in 2017 for R/M-HNSCC as second-or later-line treatment.[8,26] The Phase Ib KEYNOTE-012 study of 192 patients treated with pembrolizumab as monotherapy at two different dosages and frequencies showed an encouraging 12-month OS rate of 38%.[27] Subsequently, the CheckMate-141 phase 3 trial of 361 patients with R/M-HNSCC and early relapse or disease progression with platinum-based therapy within 6 months revealed a nearly 3-fold improvement in 24-month OS rate and also better tolerability over standard regimens of the investigators choice (24-month OS: 16.9% vs. 6.0%).[28] Subsequently, in a similar setting of R/M-HNSCC, the Keynote-040 study of 495 patients receiving pembrolizumab monotherapy also showed survival benefits and favorable safety outcomes compared to chemotherapy agents (OS: 8.4 vs. 6.9 months, hazard ratio: 0.80 [95% CI: 0.65–0.98]).[29]

Despite current evidence showing notable results and survival benefits, the response rate of single-agent ICIs in the overall population seems to be limited between a range of 13%–18%, indicating the development of primary or secondary treatment resistance.[8,27,29] To overcome this problem, ICIs in combination with other therapeutic regimens have been widely studied and trialed across all cancer types.[30] In R/M-HNSCC, the Keynote-048 phase 3 trial investigated the role of pembrolizumab as first-line treatment and also in combination with traditional PF regimens (5-fluorouracil plus a platinum) in 882 patients, and the results demonstrated superior PFS and OS rates in both pembrolizumab study arms, which included pembrolizumab monotherapy and in combination with PF, compared with the standard of care EXTREME regimen in the control arm.[11,31]

Several combination immunotherapies in patients with R/M-HNSCC have been reported to have promising results. One cohort of a phase 2 study using pembrolizumab and cetuximab for platinum-refractory or ineligible patients, and reported an ORR of 45% (95% CI 28–62).[32] The LEAP-010 phase 3 randomized controlled trial also reported that adding the multikinase inhibitor lenvatinib to pembrolizumab as first-line therapy for patients with R/M-HNSCC and a PD-L1 combined positive score (CPS) ≥1 led to a significantly better

ORR compared to pembrolizumab alone (ORR: 46.1% vs. 25.4%, $P < 0.00001$) and a net prolonged PFS of 6.4 months after a median 11.5 months of follow-up.[33] Therapeutic approaches of dual ICIs have also been studied widely. For example, anti-cytotoxic T-lymphocyte-associated protein 4 antibodies such as ipilimumab or tremelimumab in combination with an anti-PD-1 or anti-PD-L1 have been shown to lead to a durable response and fewer treatment-related adverse effects.[34-36] Other ICI therapy combinations include oncolytic virus,[37] human papillomavirus 16 (HPV-16) vaccine for HPV-16-positive cancers including oropharyngeal cancer (OPC),[38] and histone deacetylase inhibitors[39] have demonstrated modest increases in ORRs in phase 2 studies.

On the other hand, taxane, an anti-cancer drug classified as "anti-microtubule," disturbs microtubules by binding to β-tubulin to stabilize and stop them from disassembling, thus inhibiting cell division and causing the cell cycle to arrest at the G2/M phase, ultimately inducing cell death. Other anti-neoplastic mechanisms include inducing the expressions of tumor suppressor genes and downregulating anti-apoptotic proteins.[40,41] Before the ICI era, clinical studies of docetaxel administered in addition to the standard fluorouracil plus platinum (PF) regimen as induction chemotherapy reported improvements in both PFS and OS for nonmetastatic stage III or IV HNSCC.[9-11] Following the advent of cetuximab, Guigay *et al*. investigated the first-line use of docetaxel added to a modified EXTREME regimen (TPExtreme) for R/M-HNSCC. Although it failed to demonstrate superiority over the EXTREME regimen, the authors concluded that it may be an alternative to EXTREME due to a more favorable safety profile.[42]

A few literature reviews have reported higher response rates of chemotherapeutic agents (including taxanes) as subsequent-line therapy for patients who progressed with previous ICI-based treatments in R/M-HNSCC.[43] A French multi-center retrospective study compared the treatment effect of taxanes as third-line therapy between two groups of patients who had and had not previously received nivolumab. The results showed better ORR and DCR, with statistical significance in the postnivolumab group.[44] In contrast, an exploratory analysis of the TPExtreme trial showed a survival benefit when using IO as next-line strategy following the cetuximab and taxane-containing treatment (TPExtreme) compared to those without previous taxane exposure (EXTREME), with a significant prolongation of 7 months OS2 noted.[45]

The synergic effect of ICIs and standard chemotherapies has also been widely discussed and studied. A preclinical study of taxane-IO assessed the effect of the above regimen on immune cells, and the results supported the immune-adjuvant effect of taxanes, as they not only reduced tumor burden but may also have reversed the immunosuppressive pathways by inhibiting immunoregulatory T cells.[46] The recently published single-arm phase IV KEYNOTE-B10 study with pembrolizumab, carboplatin AUC 5, and paclitaxel revealed a promising ORR (ORR = 49% [95% CI: 38.4–58.7]) and manageable toxicity profile.[47] Encouragingly, results of the multicenter, single-arm, phase II FRAIL-IMMUNE trial that combined durvalumab with weekly paclitaxel (80 mg/m^2) and carboplatin AUC 2 in a first-line setting for cisplatin-ineligible R/M-HNSCC reported an ORR of up to 71% (11.3% CR rate and 59.7% PR rate).[48]

However, in real-world practice, a considerable proportion of R/M-HNSCC patients are cisplatin-ineligible due to either resistance, adverse effects or comorbidities, thereby limiting their treatment options. Clinical trials of cisplatin-sparing regimens have been designed in recent years,[12] including some studies using ICI-based, non-platinum chemotherapy combinations. An Austrian single-center, single-arm, prospective phase I/II trial evaluated 22 R/M-HNSCC patients receiving pembrolizumab plus docetaxel as first-or second-line therapy and reported an ORR of 22.7% (95% CI: 10.1%–43.4%), with one patient (1/22, 4.5%) reaching a complete response, and a 54.6% (95% CI: 34.7%–73.1%) DCR.[49] Results of the nivolumab-paclitaxel arm in the randomized, phase II Spanish NIVOTAX study reported an 11.4% increase in 2-year OS rate compared to the cetuximab-paclitaxel arm for platinum-refractory previously untreated R/M-HNSCC patients.[50]

Unlike ICIs, which have shown mostly favorable toxicity and tolerability in real-world practice, taxanes are known to cause serious adverse effects such as neutropenia, painful peripheral neuropathy which can sometimes become irreversible, infusion reactions, and edema and gastrointestinal disorders, leading to decreased quality of life and treatment adherence. In our study, the doses of taxanes were modified to approximately 70%–80% accumulative dose or lower (paclitaxel 80 or 90 mg/m^2 biweekly, or docetaxel 75 mg/m^2 every 3 weeks until disease progression or intolerance) compared to the KEYNOTE-B10 trial (paclitaxel 175 mg/m^2 every 3 weeks or 100 mg/m^2 on day 1, day 8).[47]

While similar to NCT02718820 (docetaxel 75 mg/m^2 every 3 weeks plus pembrolizumab up to six cycles then pembrolizumab maintenance)[12] and NIVOTAX (paclitaxel 80 mg/m^2 weekly up to 12 weeks),[50] the average number of treatment cycle in the present study was 8, and the treatment-related grade 3–4 side effect rate (5/24, 20.8%) was compatible with the known immune-related adverse event profile of ICIs [Table 3]. Our real-world retrospective analysis demonstrated a satisfactory ORR (50%), mPFS, mOS, and a manageable toxicity profile of ICI/modified-dose taxane combination therapy in ≥1-line, ICI-naïve, R/M-HNSCC patients. Palliative local therapies including surgery, RT and the additional short-term low-dose usage of platinum can also be considered in patients who require a reduction of tumor burden.

Conclusion

There are limitations to the current study. First, this is a single-center, retrospective study with a small sample size

($n = 24$), which limits the statistical power and generalizability of the conclusions. Therefore, subgroup analyses by primary site, line of treatment, and type of paclitaxel are clearly underpowered. Larger-scale, multicenter, prospective clinical trials should be conducted in the future to further confirm the results of this study. Second, because this was a single-center, retrospective study with a small sample size, only 15 patients had evaluable results for PD-L1 expression. Specifically, CPS data were available for only two patients, while the tumor proportion score (TPS) was available for all 15 patients. TPS results showed that four patients had a high expression (≥50%), while seven patients had a low to intermediate expression (1%–49%); the other patient had a negative expression (<1%). Eight of the 24 patients had a neutrophil/lymphocyte ratio (NLR) >3, while the others had an NLR <3, and all five patients with OPC had negative p16 status. Due to limited statistical power, subgroup analyses stratified by PD-L1 expression (TPS or CPS), NLR, and p16 status in OPC or other relevant predictive biomarkers could not be performed. This information is of great significance in IO research. Future larger-scale, multicenter, prospective clinical trials are warranted to further examine the clinical significance of these predictive biomarkers and other relevant information in this treatment strategy. Furthermore, interpretation of the results is complicated by the heterogeneity of the included patient population with respect to primary tumor site (2 patients with sinus, 5 with pharynx, 9 with oral cavity, 2 with larynx, and 7 with hypopharynx), histopathological type (21 with squamous cell carcinoma, 1 with adenocarcinoma, and 2 with sarcomatoid squamous cell carcinoma), and treatment regimen (nivolumab or pembrolizumab, paclitaxel or docetaxel, additional platinum therapy). Future studies should conduct larger, multicenter, prospective, and homogenous clinical trials tailored to primary tumor site, histopathological type, and treatment regimen to provide more precise clinical interpretation.

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Author contributions

Conception and design of study: Y.F. Chang. Acquisition of data and drafting the manuscript: T.W. Liu. Analysis and interpretation of data: T.W. Liu, N.W. Su. Revising the manuscript: N.W. Su, Y.F. Chang. All authors have read and approved to the final version of the manuscript.

Data availability statement

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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