Original Article

A real-world evaluation of tislelizumab in patients with head and neck cancer

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Background: Various studies support the use of programmed cell death protein 1 (PD-1) blockades, also known as immune checkpoint inhibitors (ICIs), to treat head and neck cancer (HNC). Tislelizumab is a humanised immunoglobulin G4 (IgG4) monoclonal antibody with a high affinity and specificity for PD-1. However, the "real-world" clinical evidence of tislelizumab for HNC is limited.

Methods: In this study, the medical records of 39 patients with head and neck squamous cell carcinoma (HNSCC) or nasopharyngeal carcinoma (NPC) who received tislelizumab between January 2021 and March 2022 were reviewed retrospectively. Tislelizumab was administered to 15 patients during neoadjuvant therapy (Group 1), five patients during adjuvant therapy (Group 2), 14 patients during consolidation therapy (Group 3), and five patients during salvage therapy (Group 4). The Kaplan-Meier method was used to calculate progression-free survival (PFS) and overall survival (OS).

Results: The median age of enrolled patients was 55 (range, 28–83) years. The median follow-up time was 27.1, 26.1, 28.6, and 20.9 months for Groups 1, 2, 3, and 4, respectively. The mean PFS and OS of Groups 1, 2, 3, and 4 were 21.5 and 22.8; 24.1 and 24.2; 26.9 and 28.1; and 13.9 and 17.1 months, respectively. In Groups 1 and 4, the objective response rate (ORR) was 86.7% and 60%, respectively. Meanwhile, except for one (2.6%) patient with grade 4 enteritis, the other observed non-haematological adverse events (AEs) were ≤ grade 2.

Conclusions: Tislelizumab demonstrated promising efficacy and tolerability in patients with HNSCC or NPC in a real-world setting, consistent with previous reports.

Keywords: Head and neck squamous cell carcinoma (HNSCC); nasopharyngeal carcinoma (NPC); anti-PD-1 monoclonal antibodies; tislelizumab

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Introduction

According to global cancer statistics in 2018, head and neck cancer (HNC) was the seventh most common cancer worldwide, with about 890,000 new cases and 450,000 deaths (1). Head and neck squamous cell carcinoma (HNSCC) accounts for 90% of HNC, which is a diverse group of cancers with several histotypes (2). They can develop in the oral cavity, oropharynx, hypopharynx, larynx, or nasopharynx. Because of the etiological differences and unique biological characteristics, nasopharyngeal carcinoma (NPC) is distinguished from other HNC and is frequently diagnosed as a loco-regionally advanced disease (3). Surgical treatment, radiotherapy, systemic therapy, or a combination of these modalities constitute the current standard of care for HNC management (4). The optimal treatment is determined by the primary site and disease stage at the diagnosis, and the prognosis remains dismal, particularly for locally advanced (LA) disease and recurrent/metastatic (R/M) cases (1,4).

Immune checkpoints are activated when proteins on the surface of T cells recognise and bind to partner proteins on tumour cells, causing the T cells to send an "off" signal. The most well-known immune checkpoint pathway is the programmed cell death protein 1 (PD-1)/programmed cell death ligand-1 (PD-L1) axis, which promotes self-tolerance by suppressing T cell activity and preventing the immune system from killing cancer cells (5). PD-1/PD-L1 is thus the target of immunotherapy drugs, which are currently used to treat a variety of cancers, including HNC. Positive expression of PD-L1 was found to be 65% and 57.3% in HNSCC in the Ib phase clinical trial of KEYNOTE-012 and the III phase clinical trial CheckMate-141, respectively (5,6). Chen *et al.* discovered that PD-L1 is expressed in nearly 90% of Epstein-Barr virus (EBV) associated NPCs (7). These findings support the use of anti-PD-1/PD-L1 blockades, also known as immune checkpoint inhibitors (ICIs), to improve the prognosis of patients with HNC.

Anti-PD-1 agents nivolumab and pembrolizumab were initially investigated in HNSCC, and the landmark phase III CheckMate 141 trial resulted in nivolumab approval in the R/M second-line HNSCC setting (6). Similarly, pembrolizumab was compared to standard of care regiment (methotrexate, docetaxel, or cetuximab) for R/M HNSCC patients who had received platinum-containing therapy in phase III Keynote-040 trial, which led to the US Food and Drug Administration (FDA) approval of pembrolizumab (8). After this, the phase III KEYNOTE-048 trial established a new paradigm. The FDA approved pembrolizumab monotherapy in the first-line for R/M HNSCC with a combined positive score (CPS) of PD-L1 expression ≥1 and pembrolizumab plus platinum-based chemotherapy for those with CPS <1 (8,9). For R/M NPC, Captain 1st (10) and Jupiter-2 (11) have shown that ICIs, as a first-line treatment, have significantly improved progression-free survival (PFS) and overall survival (OS) than the chemotherapy control group and have a good safety profile.

Tislelizumab, a humanised immunoglobulin G4 (IgG4) monoclonal antibody, has a higher affinity for PD-1 than pembrolizumab and nivolumab, which can be partially attributed to the different binding mechanisms to PD-1 (12,13). The safety and efficiency of tislelizumab have already been evaluated in some solid tumours (14-16). However, the "real-world" clinical outcomes of tislelizumab specific to HNC are very limited. To further validate the efficacy and safety of tislelizumab in the real world, this study evaluated tislelizumab alone or in combination with chemotherapy as neoadjuvant, adjuvant, consolidation, and salvage therapy in patients with HNSCC and NPC. We present this article in accordance with the STROBE reporting checklist (available at https://tcr.amegroups.com/article/view/10.21037/tcr-23-1502/rc).

Highlight box

Key findings

- Tislelizumab demonstrated promising efficacy and tolerability in patients with head and neck squamous cell carcinoma (HNSCC) or nasopharyngeal carcinoma (NPC) in a real-world setting.

What is known and what is new?

- The efficacy and safety of tislelizumab have been proved in recurrent/metastatic (R/M) NPC patients, but unclear in R/M HNSCC patients.
- It is also unknown the efficacy and safety of tislelizumab in induction, adjuvant, and consolidation therapy for HSCC and NPC patients.
- The initial results showed tislelizumab was a promising effective and safe drug for HNSCC and NPC.

What is the implication, and what should change now?

- Future phase III clinical trials are needed to confirm our findings.

Methods

Patient selection

This retrospective study was conducted using data from patients with HNSCC and NPC who had received

tislelizumab treatment at the Peking University Cancer Hospital and Institute from January 2021 to March 2022. Inclusion criteria: (I) age 18 years or above; (II) patients with pathologically confirmed oral cavity, oropharynx, hypopharynx, larynx and nasopharynx cancer; (III) patients with PD-L1 expression ≥1% (IV) received at least one cycle of tislelizumab (BeiGene Co., Ltd., Beijing, China). The exclusion criteria included: (I) patients with two different tumour subtypes; and (II) patients who lack clinicopathological information. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The Institutional Review Board of Peking University Cancer Hospital and Institute approved the study (approval number: 2020YJZ72), and informed consent was waived due to the retrospective nature of the present study.

Study design

A total of 41 patients were treated with tislelizumab. One patient was excluded due to the pathology being mucinous carcinoma, and another due to concurrent esophageal cancer, leaving 39 patients in the final analysis. According to the stage of using tislelizumab, 39 patients were divided into four groups, 15 in the neoadjuvant immunotherapy group (Group 1), 5 in the adjuvant immunotherapy group following definitive surgery (Group 2), 14 in the consolidation immunotherapy group following definitive concurrent chemoradiotherapy/radiotherapy (CCRT/RT) (Group 3), and 5 in the salvage immunotherapy group (Group 4).

Radiotherapy

Intensity-modulated radiotherapy (IMRT) was used in patients who received definitive or postoperative radiotherapy. The prescribed doses for definitive radiotherapy were 70, 70, 60, and 54 Gy in 33 fractions to the primary planning gross tumour volume (PGTVp), planning gross tumour volume of lymph nodes (PGTVnd), and high- and low-risk planning target volumes (PTV), respectively. The prescribed doses for postoperative radiotherapy were 63 and 60 Gy in 30 fractions to the planning gross tumour bed volume (PGTVtb) and PTV, respectively.

Chemotherapy

In Group 1, all 15 patients received paclitaxel- and platinum-based neoadjuvant chemotherapy with a median cycle number of 2 (range, 2–4). The regimen included paclitaxel liposome administrated 175 mg/m^2 intravenously on day 1 in combination with carboplatin with the area under the concentration curve (AUC) 5 intravenously on day 1, and was repeated every 21 days. Additionally, some patients were treated with nab-paclitaxel (220–260 mg/m^2 intravenously on day 1) in combination with carboplatin (AUC 5 intravenously on day 1), also on a 21-day cycle. Chemotherapy dose adjustments were made based on the lowest blood counts and acute toxic effects of the preceding cycle.

In Group 2, all five patients received postoperative CCRT with nedaplatin 100 mg/m^2 d1 q3w, and the median cycle number was 2 (range, 1–2).

In Group 3, 4 of the 14 patients received paclitaxel- and platinum-based consolidation chemotherapy with a median cycle number of 3 (range, 1–3). The treatment included paclitaxel liposome (175 mg/m^2 intravenously on day 1) and carboplatin (AUC 5 intravenously on day 1), which was repeated every 21 days. A second regimen used nab-paclitaxel (220–260 mg/m^2 intravenously on day 1) in combination with carboplatin (AUC 5 intravenously on day 1), also on a 21-day cycle.

In Group 4, all five patients received paclitaxel- and platinum-based salvage chemotherapy with a median cycle number of 6 (range, 5–9). The regimen was similar to that of Group 1, with paclitaxel liposome and carboplatin administered intravenously on day 1, every 21 days. An additional regimen using nab-paclitaxel with carboplatin was also employed, following the same schedule.

Immunotherapy

Tislelizumab was administered at a dose of 200 mg intravenously every three weeks. In Group 1, tislelizumab was administered with neoadjuvant chemotherapy for 2–3 cycles. In Group 2, tislelizumab was administered every 3 weeks for 6 months after definitive surgery. In Group 3, tislelizumab was administered for 6 months or 1 year after definitive CCRT/RT depending on patient's disease features. In Group 4, tislelizumab was used until disease progression or unacceptable toxicity.

Data collection

Clinicopathologic features such as age, gender, Eastern Cooperative Oncology Group (ECOG) performance status,

tumour site, PD-L1 expression, T stage, N stage, clinical disease stage, follow-up time, and recurrence status were investigated. Tumour responses were evaluated according to the modified Response Evaluation Criteria in Solid Tumours (RECIST) 1.1 for immune-based therapeutics (iRECIST). The response to treatment was evaluated using imaging records of the head, neck, chest, abdomen, and pelvis. The objective response rate (ORR) is defined as the proportion of patients who achieved complete remission (CR) and partial remission (PR). OS for patients in Groups 1, 2, 3, and 4 was calculated from the date of diagnosis, radical surgery, end of radiation therapy, or disease recurrence to the date of death from any cause or the date of final follow-up. PFS in Groups 1, 2, 3, and 4 was measured from the date of diagnosis, radical surgery, end of radiation therapy, or disease recurrence, respectively, to the date of relapse or distant metastases; to the date of death from any cause; or to the date of final follow-up. At baseline and throughout the treatment period, adverse events (AEs) were documented based on chief patient complaints and abnormal laboratory measures such as blood chemistry, haematology, coagulation, and urinalysis and were assessed using the Common Terminology Criteria for Adverse Events (CTCAE) version 5.0.

Statistical analysis

Statistical analyses were performed using the SPSS version 25.0 (SPSS Inc., Chicago, IL, USA). The general characteristics of the study subjects were expressed as frequencies and percentages. PFS and OS were estimated using the Kaplan-Meier method.

Results

Basic characterisation

The median age of all 39 patients was 55 years (range, 28–83 years), with 31 (79.5%) being male, 18 (46.2%) having NPC and the rest having HNSCC. The median PD-L1 expression positive rate was 20% (1–100%), and 26 (66.7%) of them were ≥20%. The included patients are mainly in clinical stages III and IV, with 8 (20.5%) and 26 (66.7%), respectively; 21 (53.8%) are in T3–4, and 35 (89.7%) are in N2–3. Baseline demographics and disease characteristics are shown in *Table 1*. The PFS time for all patients is shown in *Figure 1*.

Efficacy

Among the 15 patients in Group 1 (*Table 1*), 8 (53.3%) have NPC, 5 (33.3%) have hypopharyngeal HNSCC, and the remaining 2 (13.3%) have oral and oropharyngeal HNSCC, respectively. All patients received neoadjuvant chemotherapy, with a median of two cycles of neoadjuvant immunotherapy (range, 1–4 cycles). After neoadjuvant therapy, 12 patients received definitive radiotherapy, while three patients declined further treatment for personal reasons. Of the 12 patients who received definitive radiotherapy, 10 received concurrent chemotherapy, and 2 received radiotherapy alone because of their advanced age. Thirteen patients (86.7%) achieved PR, while two (13.3%) achieved stable disease (SD). At a median follow-up duration of 27.1 months, the ORR was 86.7% (13/15) (*Table 2*), and the median PFS and OS were not reached. The mean PFS and OS were 21.5 and 22.8 months, respectively (*Table 2*, *Figure 1*). The 1-year PFS and OS rates were 66.7% and 80.0%, and the 2-year PFS and OS rates were both 66.0%.

All five (100.0%) patients in Group 2 had oral HNSCC and received adjuvant immunotherapy for a median of 5 cycles (range, 3–6 cycles). These patients received radical surgery and postoperative CCRT, with a median radiotherapy dose of 63 Gy/30 fractions (F). After a median follow-up time of 26.1 months, the mean PFS and OS were 24.1 and 24.2 months, respectively (*Table 2*, *Figure 1*). The 1-year rates for both PFS and OS were 80.0%, and the 2-year rates for both PFS and OS were also 80.0%. The median PFS and OS were not reached.

Group 3 included 8 (57.1%) patients with NPC, 2 (14.3%) with oral HNSCC, 2 (14.3%) with oropharyngeal HNSCC (*Table 1*), 1 (7.1%) with hypopharyngeal HNSCC, and 1 (7.1%) with laryngeal HNSCC. Among 14 patients in this group, 4 patients received consolidation chemotherapy combined with immunotherapy, while 10 patients were treated with immunotherapy alone for a median of 6 cycles (range, 2–20 cycles). All 14 patients received definitive radiotherapy at a median dose of 70 Gy/33 F, with 13 receiving concurrent chemotherapy and 1 receiving concurrent targeted therapy due to advanced age. After a median follow-up time of 28.6 months, the median PFS and OS were still not reached, and the mean PFS and OS were 26.9 and 28.1 months, respectively (*Table 2*, *Figure 1*). The 1-year PFS and OS rates were both 100.0%, while the 2-year rates for both PFS and OS were 92.9%.

Table 1 Clinicopathological characteristics

Characteristics	Total (N=39)	NAC group (N=15)	Adjuvant group (N=5)	Consolidation group (N=14)	Salvage group (N=5)
Median age, years [range]	55 [28–83]	59 [34–83]	55 [42–67]	53 [31–73]	52 [28–70]
Sex, N (%)					
Male	31 (79.5)	11 (73.3)	1 (20.0)	14 (100.0)	5 (100.0)
Female	8 (20.5)	4 (26.7)	4 (80.0)	0	0
ECOG status, N (%)					
0	22 (56.4)	9 (60.0)	4 (80.0)	6 (42.9)	3 (60.0)
1	17 (43.6)	6 (40.0)	1 (20.0)	8 (57.1)	2 (40.0)
Tumour site, N (%)					
Nasopharyngeal	18 (46.2)	8 (53.3)	0	8 (57.1)	2 (40.0)
Oral cavity	11 (28.2)	1 (6.7)	5 (100.0)	2 (14.3)	3 (60.0)
Oropharynx	3 (7.7)	1 (6.7)	0	2 (14.3)	0
Hypopharynx	6 (15.4)	5 (33.3)	0	1 (7.1)	0
Larynx	1 (2.6)	0	0	1 (7.1)	0
PD-L1, N (%)					
<20%	13 (33.3)	6 (40.0)	3 (60.0)	3 (21.4)	1 (20.0)
≥20%	26 (66.7)	9 (60.0)	2 (40.0)	11 (78.6)	4 (80.0)
T stage, N (%)					
T0–2	18 (46.2)	9 (60.0)	2 (40.0)	5 (35.7)	2 (40.0)
T3–4	21 (53.8)	6 (40.0)	3 (60.0)	9 (64.3)	3 (60.0)
N stage, N (%)					
N0–1	4 (10.3)	1 (6.7)	0	1 (7.1)	2 (40.0)
N2–3	35 (89.7)	14 (93.3)	5 (100.0)	13 (92.9)	3 (60.0)
Clinical disease stage, N (%)					
II	1 (2.6)	0	0	1 (7.1)	0
III	8 (20.5)	3 (20.0)	0	5 (35.7)	0
IV	26 (66.7)	12 (80.0)	5 (100.0)	8 (57.1)	1 (20.0)
Recurrent, N (%)	4 (10.3)	0	0	0	4 (80.0)
Response to treatment, N (%)					
CR	–	0	–	–	0
PR	–	13 (86.7)	–	–	3 (60.0)
SD	–	2 (13.3)	–	–	2 (40.0)
PD	–	0	–	–	0

NAC, neoadjuvant chemotherapy; ECOG, Eastern Cooperative Oncology Group; PD-L1, programmed cell death ligand-1; CR, complete remission; PR, partial remission; SD, stable disease; PD, progressive disease.

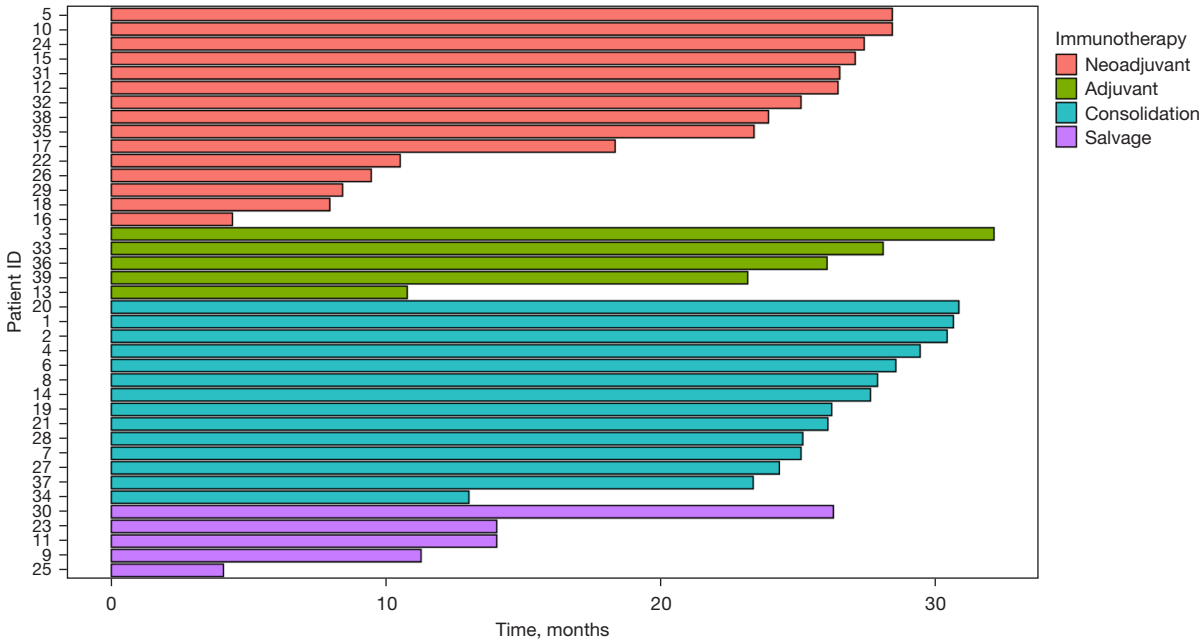

Figure 1 PFS time of patients in four different therapy groups. PFS, progression-free survival.

Table 2 Results for each group

Efficacy	NAC group (N=15)	Adjuvant group (N=5)	Consolidation group (N=14)	Salvage group (N=5)
ORR (%)	86.7	–	–	60.0
Mean PFS (months)	21.5	24.1	26.9	13.9
Mean OS (months)	22.8	24.2	28.1	17.1
2-year OS rates (%)	66.0	80.0	92.9	0.0

NAC, neoadjuvant chemotherapy; ORR, objective response rate; PFS, progression-free survival; OS, overall survival.

In Group 4, two (40.0%) patients had nasopharyngeal HNSCC, and 3 (60.0%) had oral HNSCC. The 5 patients who received salvage immunotherapy were all treated with chemotherapy combined with a median of 9 cycles of immunotherapy (range, 5–16 cycles). Three (60.0%) patients achieved PR, while two (40.0%) achieved SD. After a median follow-up duration of 20.9 months, the ORR was 60.0% (3/5), and the mean PFS and OS were 13.9 and 17.1 months, respectively (*Table 2*, *Figure 1*). The median PFS and OS were 14.4 and 16.0 months, respectively. The 1-year PFS and OS rates were both 60.0%; the 2-year PFS and OS rates were 20.0% and 0.0%, respectively.

Safety

Among the 39 patients, 31 (79.5%) experienced AEs of varying severity (*Table 3*). The most frequent non-haematological AE was hypothyroidism, which was observed in five individuals (12.8%), where three had grade 1 and two had grade 2 hypothyroidism. Dermatitis occurred in four patients (10.3%), three of whom had grade 1 and one with grade 2 dermatitis. Anemia was present in three patients (7.7%), with two experiencing grade 2 and one having grade 1. Leukopenia was seen in 17 patients (43.6%), distributed as four with grade 1, seven with moderate grade 2, and three patients each of grade 3 and 4. Additionally, one patient (2.6%) suffered from grade 4 colitis.

Discussion

Tislelizumab has demonstrated activity across multiple disease types, including non-small cell lung cancer, liver

Table 3 Adverse effects

Adverse events (N)	Total patients	Grade 1	Grade 2	Grade 3	Grade 4
Dermatitis	4	3	1	–	–
Hypothyroidism	5	3	2	–	–
Colitis/diarrhoea	1	–	–	–	1
Liver dysfunction	1	1	–	–	–
Leukopenia	17	4	7	3	3
Anaemia	3	1	2	–	–

cancer, and NPC patients with advanced disease (16-19). In this retrospective investigation, we studied the efficacy and safety of tislelizumab for patients with HNSCC and NPC in the real world. We discovered that the responding rate and survival outcomes observed in neoadjuvant, adjuvant, consolidation, and salvage therapy settings were comparable to those in clinical trials.

The rationale for neoadjuvant immunotherapy stems from the fact that early systemic therapy can potentially reduce the risk of distant metastases and convert unresectable disease to resectable disease, potentially changing the extent of surgery and reducing surgical morbidity (20). Tumour downstaging can also result in less aggressive adjuvant therapy. Furthermore, compared to chemotherapy cytotoxic agents, neoadjuvant immunotherapy has a lower toxicity profile.

Emerging evidence has demonstrated that incorporating ICIs may be a potential neoadjuvant regimen in HNC with encouraging efficacy results (21,22). In a study of 36 cases with human papillomavirus (HPV) negative oropharynx HNSCC that received neoadjuvant pembrolizumab before surgery, tumour response >10% was observed in 44% of patients; two of them even decreased more than 90%. In addition, the 1-year recurrence rate of high-risk patients with extracapsular lymph node invasion or positive surgical margin was 18%, which is lower than the historical data of 35% (23). Schoenfeld *et al.* (24) randomised 29 patients with oral squamous cell carcinoma to the nivolumab group or nivolumab + ipilimumab group in a phase 2 clinical study. All patients received two cycles of neoadjuvant immunotherapy followed by surgery. The results showed that in the nivolumab and nivolumab + ipilimumab groups, the pathological response was as high as 54% and 73%, the pathological downstaging was 53% and 69%, the RECIST response was 13% and 38%, and the 1-year PFS was 85% and 89%, respectively. Four patients had major or complete pathologic responses greater than 90%. Our study suggested that in Group 1, the ORR was 86.7% (13/15), and the 1-year PFS rate was 66.7%. The high ORR might be attributed to the combined use of chemotherapy and immunotherapy rather than immunotherapy alone compared with the above two studies. However, both NPC and HSNCC were included in this study, and the majority of the 15 patients were treated with definitive radiotherapy rather than surgery after neoadjuvant therapy, which could explain why the 1-year PFS rate in this study was lower than in previous studies.

One rationale for using immunotherapy in the adjuvant/consolidation setting is based on the biological mechanism that supports the use of ICIs in combination with standard regimens, such as RT and chemotherapy or surgery. For example, RT can determine immunogenic forms of cell death and can lead to the abscopal effect, which means that local irradiation results in regression of non-irradiated metastases through anti-tumour immune reactions (25).

Clinical phase III study and network meta-analysis demonstrated that adding consolidation chemotherapy to CCRT did not improve survival (3,26,27). However, consolidation chemotherapy benefits patients with certain adverse clinical features (28-30). In our institution, consolidation therapy is considered when an NPC patient has one of the following characteristics after definitive CCRT/RT: clinical T4 or N3 stage, significant residual of primary lesion, residual neck lymph node size >2 cm, and EBV DNA titer higher than 1,000 copies/mL.

The promising efficiency and safety of ICIs in combination with chemotherapy in locally advanced NPC (LANPC) have been reported (3,31). CCRT is the standard treatment for LANPC. The phase III trial of NCT04907370 will help us to clarify the role of ICIs

in the treatment of LANPC, which adds toripalimab to induction chemotherapy followed by CCRT combined with toripalimab, and then adjuvant toripalimab will be given every three weeks for 11 cycles (31). Furthermore, another phase III clinical trial (NCT04453826) focused on high-risk LANPC will explore the value of camrelizumab combined with chemoradiotherapy followed by adjuvant camrelizumab. The results of these trials are worth looking forward to (3). For the HNSCC setting, the published JAVELIN study (32) in high-risk LA HNSCC showed no improvement with adding avelumab, an anti-PD-1 antibody, to the current standard chemoradiotherapy. Another randomised phase III study, KEYNOTE-412 (NCT03040999), compares the efficacy and safety of CCRT +/– pembrolizumab in LA HNSCC (one priming dose of pembrolizumab followed by two doses of pembrolizumab during CCRT and pembrolizumab maintenance up to an additional 14 cycles after that), with the primary endpoint being event-free survival (EFS) (33). The final analysis found that patients who received the KEYTRUDA regimen had better EFS than those who received placebo plus CCRT, though the difference was not statistically significant (34). In our study, 14 patients received tislelizumab as consolidation therapy after definitive radiotherapy. The mean PFS and OS were 26.9 and 28.1 months, which is a relatively longer PFS. Further studies are still needed to clarify the role of ICIs in treating locally advanced HNC.

Salvage immunotherapy is administered after other treatments have failed. Among patients with R/M HNC, ICIs added to first-line standard chemotherapy provide significantly better efficacy outcomes than chemotherapy alone. Keynote 048 study (9) assessed the role of ICIs treatment among R/M HNSCC patients. The results showed that pembrolizumab with cisplatin plus 5-fluorouracil (PF) chemotherapy significantly prolonged OS compared with cetuximab with PF (13.0 *vs.* 10.7 months, P=0.0034). Based on the findings of this study, PF plus pembrolizumab has already been designated as the first-line treatment regimen for R/M HNSCC patients. In CheckMate 141, nivolumab improved both response (ORR 13.3% *vs.* 5.8%) and median OS (7.1 *vs.* 5.5 months, P=0.01) compared to standard treatment (docetaxel, methotrexate, or cetuximab), and was also associated with fewer toxic effects (35). At a longer follow-up, nivolumab nearly tripled the estimated 24-month OS rate (16.9%) *vs.* standard therapy (6.0%), demonstrating an OS benefit irrespective of PD-L1 expression and HPV status (36). Our study included only five patients who received tislelizumab as first-line therapy, with an ORR of 60% and a disease control rate (DCR) of 100%, which is consistent with previously published results. In this study, the median PFS was 14.4 months for R/M-NPC or -HNSCC, which was longer than the 9.6 months in the Rational 309 study (16), 9.7 months in the Captain 1st study (10), and 11.7 months in the Jupiter-2 study (11). Given the small sample size, the median PFS should be interpreted with caution, but the findings suggest that tislelizumab plus chemotherapy as first-line treatment is a promising regimen for R/M-NPC or -HNSCC.

Previous studies have shown that high PD-L1 expression levels are associated with a favourable prognosis for immunotherapy in various solid tumours, including HNC. In the KEYNOTE-048 trial (9), HNSCC patients with a PD-L1 expression positive rate greater than 20% had a longer median OS than those with a rate less than 20% (14.9 *vs.* 10.7 months). However, the predictive value of PD-L1 in NPC is not clear. In the POLARIS-02 study (37), NPC patients with PD-L1-positive or -negative had similar response rates to toripalimab in the second-line-plus setting (27.1% *vs.* 19.4%). In the Jupiter-2 study (11), PD-L1-positive patients had a similar median PFS to PD-L1-negative patients during first-line treatment for R/M NPC (11.4 *vs.* 11.0 months). Due to the small sample size and rare events in each group, the current study could not examine the relationship between PD-L1 expression level and survival time.

ICIs typically have an acceptable toxicity profile, with AEs primarily consistent with their mechanism of action. To date, neoadjuvant ICIs are safe and have not resulted in surgical delays (23,38). In this study, we found that tislelizumab, alone or in combination with chemotherapy, was generally well tolerated, with few severe immune-related side effects. Except for one case of grade 4 enteritis and three of grade 4 leukopenia, most toxicities were grade 1–2.

Conclusions

Because of the relatively short observation period, most patients have not experienced recurrence or metastasis, and it is impossible to analyse the factors that influence PFS or OS. Aside from these limitations, this study found that tislelizumab, alone or in combination with chemotherapy, was effective and safe in patients with locally advanced or

metastatic HSNCC and NPC. It provided initial efficacy and safety data for clinical practice. Future phase III clinical trials are needed to confirm our findings.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://tcr.amegroups.com/article/view/10.21037/tcr-23-1502/rc

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://tcr.amegroups.com/article/view/10.21037/tcr-23-1502/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The Institutional Review Board of Peking University Cancer Hospital and Institute approved the study (approval number: 2020YJZ72). Informed consent was waived due to the retrospective character of the present study.

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