

Research Paper

A Phase II Clinical Trial of Concurrent Helical Tomotherapy plus Cetuximab Followed by Adjuvant Chemotherapy with Cisplatin and Docetaxel for Locally Advanced Nasopharyngeal Carcinoma

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Abstract

Purpose: The present clinical trial was designed to evaluate the efficacy and safety of concurrent helical tomotherapy (HT) with cetuximab followed by adjuvant chemotherapy with docetaxel and cisplatin (TP) in the treatment of patients with locoregionally advanced nasopharyngeal carcinoma.

Materials and Methods: This phase II clinical trial included 43 patients with Stage III/IV LANC (33 Stage III and 10 Stage IV). The treatment consisted of concurrent HT with cetuximab (400 mg/m² loading dose and weekly 250mg/m²), followed by four cycles of chemotherapy [docetaxel (70 mg/m² on Day 1) and cisplatin (40 mg/m² on Days 1 and 2 every 3 weeks). Side effects were evaluated with CTCAE criteria (Common Terminology Criteria for Adverse Events 3.0).

Results: The median follow-up duration was 48.0 months [95% confidence interval (CI) 41.7-58.0 months], the 2-year locoregional failure-free rate (LFFR), progression-free survival (PFS), distant failure-free rate (DFFR) and overall survival (OS) were 95.2%, 79.1%, 88.1% and 93.0% respectively; the 3-year LFFR, DFFR, PFS and OS were 92.7%, 85.6%, 72.0% and 85.7% respectively. The most common grade 3 toxicities were oropharyngeal mucositis (81.4%) and RT-related dermatitis (7.0%). No patients had more than grade 3 radiation related toxicities and no patients required nasogastric feeding. One patient experienced grade 3 osteonecrosis at 18 months after treatment.

Conclusions: Concurrent HT with cetuximab followed by adjuvant chemotherapy with TP is an effective strategy for the treatment of LANC with encouraging survival rates and minimal side effects.

Key words: Locally advanced nasopharyngeal carcinoma; Helical tomotherapy; Cetuximab; Adjuvant chemotherapy; adverse event.

Introduction

Although the worldwide incidence of nasopharyngeal carcinoma (NPC) is relatively low, it is a common head and neck cancer in southern China. Its etiology remains unclear and the prognosis of patients

with NPC is still poor since more than 50% of patients present with locally advanced disease (LANC) at time of diagnosis [1]. Among patients with LANC, the non-keratinizing type is common and different from

other head and neck cancers in terms of its aggressive behavior and high risk of distant metastasis [2]. The current standard care for LANC patients recommended by the National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology (NCCN) is concurrent chemoradiotherapy (CCRT) with cisplatin (P) followed by adjuvant chemotherapy (ACT) with cisplatin and 5-Fluorouracil (F) based on the results of the randomized inter-group study 0099 [3]. Newly developed radiation technology, effective and less toxic chemotherapy regimens and epidermal growth factor receptor (EGFR) targeted therapy have brought new hope for reducing the rate of distant metastasis and improving overall survival (OS) among these patients.

There is increasing evidence from clinical trials supporting that, compared to cisplatin (P)-5-fluorouracil (5FU) regimen, the taxane-containing chemotherapy improves the response rate and OS in patients with squamous cell carcinoma of the head and neck (SCCHN) and that the EGFR inhibitor cetuximab with concurrent radiotherapy improves the local control and OS when compared to radiotherapy alone [4, 5]. In vitro study has demonstrated that cetuximab is effective in radio-resistant CD133+ cancer stem cells isolated from glioma U87MG cells [6]. Ma *et al.* have shown that CCRT with cisplatin and cetuximab and IMRT results in a 2-year progression-free survival (PFS) of 86.5% in LANC patients [7]. Helical tomotherapy (HT) can maximize the protection of normal structures and improve locoregional control [8]. Several clinical trials have demonstrated that HT leads to encouraging local control rate for patients with NPC and have minimal acute and late toxicities [9-11]. Leung *et al.* have reported that patients with NPC treated with HT showed no local recurrence with low late toxicities and a 5-year locoregional control rate of 97% [9]. In our previous study, patients receiving HT had a 1-year relapse-free survival of 95.6% and no grade 2 xerostomia was noted in all patients one year after radiation [11]. In order to minimize treatment related side-effects and to improve efficacy in patients with LANC, in the present study, we designed a treatment strategy that includes concurrent HT plus cetuximab followed by ACT with docetaxel (T) and cisplatin. We evaluated safety and efficacy as measured by locoregional failure-free rate (LFFR), PFS, distant failure-free rate (DFFR), and OS at 2- and 3-year in patients with LANC.

Materials and Methods

Patients

This prospective phase II study (ChiCTR-OCC-

15005888) enrolled patients with untreated, histologically proven non-keratinizing type of NPC at stage III-IV (American Joint Committee disease stages: any T N2~N3, or T3~T4N0~3 stage). The sample size (patient number) needed for the present study was calculated with the software NCSS&PASS (optimal two-stage design: $\alpha=0.05$, $\beta=0.2$, $P_1-P_0=0.15$). The sample size was determined to be 43 patients.

Their baseline characteristics are listed in **Table 1**. The inclusion criteria were as follows: age between 18 and 70 years; ECOG (Eastern Cooperative Oncology Group) performance status of 0 or 1; life expectancy $\geq +6$ months; no prior chemotherapy, radiotherapy, or surgery; adequate bone marrow (*e.g.*, white blood cell count ≥ 4000 cells/ μ L, platelet counts $\geq 100\ 000$ cells/mL, hemoglobin >8.0 g/dL), normal renal function (creatinine clearance >50 ml) and hepatic function (bilirubin $\leq 1.5 \times$ the upper limit of normal (ULN), alanine aminotransferase $\leq 3 \times$ ULN). To rule out synchronous primary cancers and metastasis disease, all patients were fully evaluated with positron emission computed tomography (PET) or magnetic resonance imaging (MRI) of the head and neck, fabric nasopharyngoscopy, chest CT, abdominal ultrasound, as well as bone scans. Patients with synchronous primary cancers or/and metastasis disease were excluded. The present study was approved by the Ethics Review Committee of the Chinese People Liberation Army General Hospital. Informed consent was obtained from all patients prior to participation in the present study.

Table 1. Characteristics of patients.

Feature	n (%)
Age (years)	
Range	19~67
Median	44(95%CI 41~47)
Sex	
Male	30(70.0)
Female	13(30.0)
WHO performance status, n (%)	
0	33 (76.7)
1	10 (23.3)
T classification, n (%)	
T1	5 (11.6)
T2	17(39.5)
T3	14 (32.6)
T4	7 (16.3)
N classification, n (%)	
N0	2 (4.7)
N1	6 (14.0)
N2	32 (74.4)
N3	3 (7.0)
2002AJCC stage, n (%)	
III	33 (76.7)
IV	10 (23.3)

AJCC: American Joint Committee on Cancer

Treatments

Chemotherapy and EGFR inhibitor therapy

The therapy regimen was determined by our previous study [12]. Briefly, the patients were treated with concurrent HT with weekly cetuximab, followed by four cycles of ACT with TP one month after radiotherapy. Cetuximab was used at a 250 mg/m² on a weekly basis (400 mg/m² initial dose) for 7 times, starting the first day of radiotherapy. The TP regimen consisted of docetaxel (70 mg/m², Day 1) and cisplatin (40 mg/m², Days 1 and 2) every 3 weeks.

Radiotherapy

HT was delivered once daily, 5 days per week. The detail treatment plans was the same as previously reported [11]. In brief, the planning dose at D95 (dose received by 95% of the target volume) was prescribed to pGTVnx (the planning gross target volume of primary tumor, pGTVnx) and pGTVnd (the planning gross target volume of metastatic lymph node, pGTVnd) at 70–74Gy, PTV1 (planning target volume, PTV) at 60–62.7 Gy and PTV2 at 52–56 Gy in 33 fractions. No more than 5% of PTV volume received more than 110% of the prescribed dose. Dose-volume constraints for organs at risk (OARs) were utilized: 1) parotid gland V30 < 50% or Dmean < 28Gy; 2) brain-stem Dmax < 54 Gy; 3) spinal cord Dmax < 45 Gy; 4) optic nerve Dmax < 54 Gy; 5) temporo-mandibular joint Dmax < 60 Gy; and 6) lens Dmax < 5 Gy. Helical tomotherapy plans were developed with a field width of 2.5 cm, a pitch of 0.30–0.38, and a modulation factor equal to 2.0–3.0. During the radiation therapy, the patients underwent megavoltage computed tomography (MVCT) imaging at least once every week to verify patient setup. The imaging frequency was determined by the magnitude of setup errors from initial daily scans.

Dose modifications

The cetuximab dose was reduced if a patient experienced uncontrollable and persistent grade 2 acne-like rash. The chemotherapy doses were adjusted, based on the severity of myelosuppression using the methods reported previously [12]. All patients were given 3-day hydration, and carboplatin was given instead of cisplatin if grade 1 renal toxicity was caused by cisplatin.

Assessment of Outcomes

The toxicities were assessed using the Radiation Therapy Oncology Group (RTOG) toxicity criteria. The assessment of the tumor response was carried out by MRI and flexible fabric nasopharyngoscopy after concurrent HT with cetuximab and 4 weeks after the last cycle of ACT according to the Response Evalua-

tion Criteria in Solid Tumor criteria and reviewed by the committee working in our hospital (otolaryngologist, radiation oncologist, and medical oncologist). Patients were followed up every 3 months in the first year, every 4 months in the second and third year, every 6 months in the fourth and fifth years and then 12 months until progression or death.

Endpoints

The endpoints of the present clinical trial were similar to that of our previous study [12]. The safety of the treatment, including the concurrent HT with cetuximab followed by ACT with TP, was the primary endpoint. The secondary endpoints were the following: the response rate, LFFR, PFS, DFFR, and OS at 2 and 3 years after the treatment. In the present study, LFFR was defined as free from local failure. Locoregional failure was defined as the presence of biopsy-proven residual disease at the nasopharynx and/or regional lymph nodes at the scheduled visit at 3 months after RT or the subsequent development of recurrent disease, while distant failure (DF) was defined as the presence of distant metastases. Progression-free survival (PFS) was defined as the duration from the date of enrollment to the date of first occurrence of distant or locoregional recurrence or to the date of last follow-up. Overall survival (OS) was defined as the duration between the date of enrollment and the date of death, due to any cause, or the date of last follow-up. The acute and late toxicities of patients after treatment were graded according to the National Cancer Institute—Common Toxicity Criteria for Adverse Events, version 3.0, and the Radiation Therapy Oncology Group (RTOG) Late Radiation Morbidity Scoring Criteria, respectively.

Statistical Analysis

All the patients have been followed up until recurrence or death and one patient was lost to follow-up. 95% confidence intervals (CIs) have been calculated for means and percentages and the survival curves of LFFR, PFS, DFFR and OS were estimated with the Kaplan–Meier method (R software package *Epicalc.StatView* 3.0).

Results

Patient characteristics, treatment compliance, and toxicity

In the present study, 46 consecutive patients were screened for the clinical trial from May 2008 to June 2012 and 43 were enrolled. Three patients were excluded because of ineligibility (T2N1 stage). All the patients completed planned HT with 7 cycles of cetuximab, and only one patient received reduced dose because of grade 2 acne-like rash; all patients received

ACT with TP. Of these 43 patients, 40 (93.0%) underwent four cycles of treatment at the planned doses. The remaining 2 patients (4.7%) received 3 cycles and 1 patient (2.3%) received reduced doses due to toxicity.

Acute toxicity was observed during concurrent HT with cetuximab and ACT with TP (**Table 2**). During concurrent HT with cetuximab, the most common grade 2-3 toxicities were oropharyngeal mucositis, radiotherapy (RT)-related dermatitis, cetuximab-related acne-like rash, and weight loss. Three patients needed intravenous (IV) infusion for nutrition due to dysphagia and oropharyngeal pain caused by oropharyngeal mucositis. Grade 3 Oropharyngeal mucositis occurred in 81.4% (35/43) of the patients, but was managed effectively with our previously reported method without radiation break [13]. Briefly, our supportive care regimen for grade 3 oropharyngeal mucositis included Moxifloxacin Hydrochloride and Sodium Chloride Injection 0.4 g IV infusion qd and 15 mL of *Sophora flavescens* in 250 mL of 0.9% saline IV infusion qd. No patients required nasogastric feeding (NF) and percutaneous endoscopic gastrostomy during and after treatment.

Table 2. Incidence of acute major toxicities

Toxicity	No. of patients (%)		
	Grade 1	Grade 2	Grade 3
Hematologic toxicity			
Leukopenia	2(4.7)	13(30.2)	1(2.3)
Neutropenia	0	2(4.7)	0
Thrombocytopenia	7(16.2)	1(2.3)	0
Anemia	6(14.0)	3(7.0)	1(2.3)
Non-hematologic toxicity			
Nausea	26(60.5)	3(7.0)	0
Vomiting	18(41.9)	2(4.7)	0
Oropharyngeal Mucositis	3(7.0)	5(11.6)	35(81.4)
Weight loss	20(46.5)	10(23.3)	0
RT-related dermatitis	28(65.1)	10(23.3)	3(7.0)
Hypokalaemia	12(27.9)	2(4.7)	1(2.3)
Hyponatremia	1(2.3)	0	0
Creatinine elevation	1(2.3)	1(2.3)	0
Cetuximab-related rash	16(37.2)	5(11.6)	0
Hypomagnesemia	0	3(7.0)	0
Alanine transferase	4(9.3)	0	3(7.0)

During ACT with TP, acute toxic effects were very mild without grade 4 toxicity except for one patient experiencing febrile neutropenia. The rate of grade 3 Leukopenia and anemia were 2.3% (1/43) and 2.3% (1/43), respectively. Grade 3 non-hematologic toxic effects occurring in 7.0% (3/43) patients was abnormal level of Alanine transferase; one (2.3%) patient had a grade 2 increase in creatinine level. His

creatinine level returned to normal at 8 months after the treatment. One (2.3%) patient had a grade 3 hypokalaemia.

Regarding late toxic effects (**Table 3**), grade 2 xerostomia was the most common late toxicity. Hearing impairment was observed in 20 patients (46.5%); 5 (11.6%) experienced sensorineural hearing loss (SNHL); and 15 (34.9%) developed conduction hearing loss, and 10 of the 15 patients needed trans-tympanic ventilation. Two patients (4.7%) had endocrine dysfunction (Thyroid dysfunction) 6 months after HT; one patient (2.3%) experienced osteonecrosis 18 months after treatment. No patients had dysphagia. There were no treatment-related deaths.

Table 3 Incidence of Major Late Toxicities

Toxicity	No. of patients (%)		
	Grade 1	Grade 2	Grade 3
Xerostomia	21(48.8)	2(4.7)	0
Subcutaneous tissue	2(4.7)	2(4.7)	0
Endocrine	2(4.7)	0	0
Neuropathy	4(9.3)	1(2.3)	0
Osteonecrosis	0	0	1(2.3)
Sensorineural hearing loss	3(7.0)	2(4.7)	0

Efficacy

Treatment response

All the 43 patients underwent MRI assessment one month after concurrent HT with cetuximab, the primary site showed a 95.3% (41/43) complete response (CR) and a 4.7% (2/43) partial response (PR). The neck node sites showed a 97.6% (40/41) CR and a 2.4% (1/41) PR. After 4 cycles of ACT with TP, 4.7% PR at the primary site shifted from PR to CR; only one patient with PR at the neck node sites had biopsy-confirmed residual disease and received salvage neck dissection. No patients progressed during treatment.

Survivals

Figure 1 shows the LFFR, DFFR, PFS and OS survival curves. At a median follow-up of 48.0 months [95% CI 41.7-58.0 months], the 2 -year LFFR, DFFR, PFS and OS were 95.2% (95% CI 82.1-98.8), 88.1% (95% CI 78.3-97.9%), 79.1% (95% CI 63.6-88.5%) and 93.0% (95% CI 79.9-95.0%), respectively; the 3-year LFFR, DFFR, PFS and OS were 92.7% (95% CI 78.8-97.6%), 85.6% (75.5-96.3%) , 72.0% (56.0-83.0%) and 85.7% (71.0-93.3%), respectively.

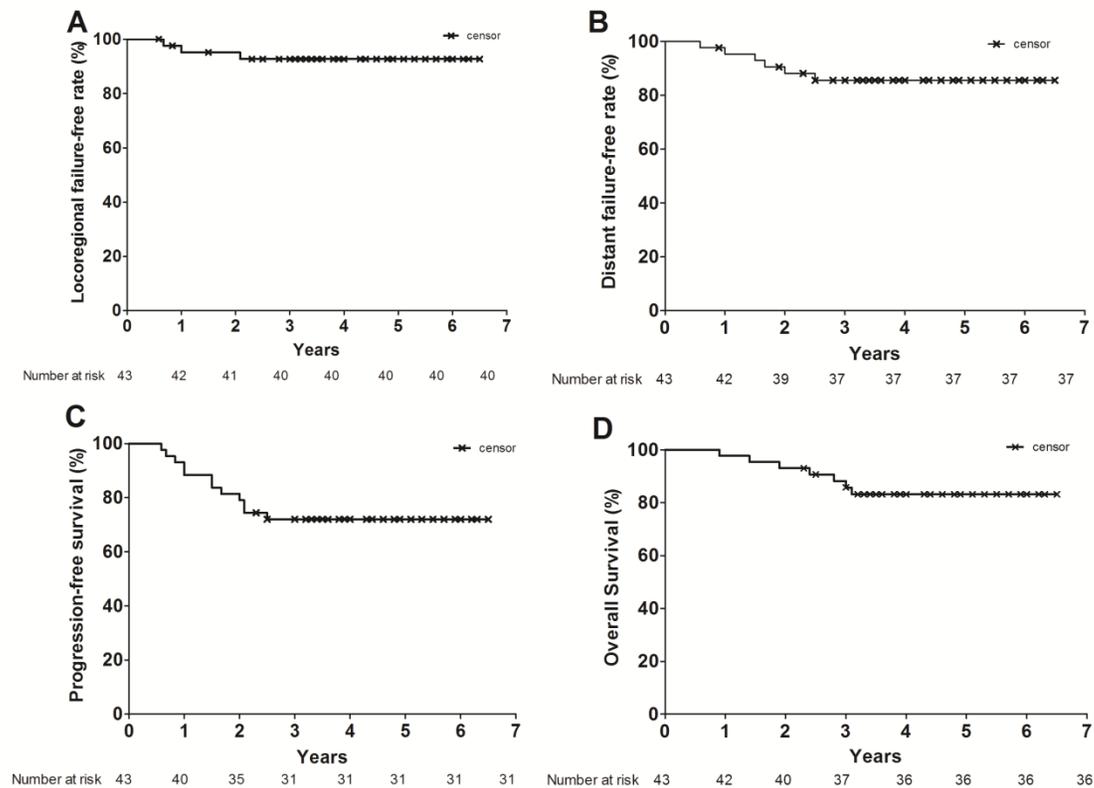


Figure 1. Kaplan-Meier estimates of OS (A), PFS (B), LFFR (C), and DFFR (D) among the patients with locally advanced nasopharyngeal carcinoma. Crosses indicate censored patients.

By the end of the study, seven out of the 43 patients had died. One (T4N1 stage) died of cranial recurrent NPC, 2 (1 patient with T3N0 stage and 1 patient with T3N2 stage) died of live metastases, 1 with T3N0 died of lung metastases, 1 with T2N2 died of bone metastases, 1 with T3N1 died of torrential bleeding caused by osteonecrosis, and 1 with T4N0 died of RT-related brain injury. Two patients had second primary cancers, including one meningeal cancer and one kidney cancer found at 18th and 20th months after treatment, respectively; both of them were still alive after surgery.

Discussion

The present study demonstrated that concurrent HT with cetuximab followed by ACT with TP was a feasible strategy in the treatment of patients with LANC. No patients had greater than grade 3 radiation related side-effects. No patient required nasogastric feeding. During concurrent HT with cetuximab, the most common grade 3 toxicities were oropharyngeal mucositis (81.4%) and RT-related dermatitis (7.0%). No hematological toxicity was observed. Previous studies in the literature have reported that the incidence of grade 3~4 oropharyngeal mucositis and rad-

iation dermatitis caused by CCRT with cisplatin in the treatment of NPC ranged from 23.9% to 48% and from 2% to 13.2% respectively [14-17]; the incidences are increased up to 38~87% and 6~24% when cetuximab or bevacizumab is added to the CCRT with cisplatin [7, 18, 19]. The present study found no grade 4 oropharyngeal mucositis or RT dermatitis. The possible reason may be that the patients did not receive the treatment with cytotoxic chemotherapeutic agents during their radiotherapy and therefore, the side effects of cytotoxic reagents such as mucositis did not occur in these patients. In addition, HT appears to have the advantage of reducing the incidence of radiation related toxicity. Leung *et al.* [9] have shown that acute and late complications after HT for NPC patients are fewer and milder than that of conventional IMRT technique. In their study, 62.5% patients received concurrent HT with chemotherapy: acute grade 3 mucositis occurred in 4% patients (3/72), grade 4 mucositis in 1% patient (1/72) and grade 4 dermatitis in 1% patient (1/72). Shueng *et al.* [10] have also demonstrated that NPC patients treated with neoadjuvant chemotherapy followed by concurrent HT with chemotherapy show Grade 3 mucositis and dermatitis in 7% (2/28) and 46.4% (13/28) patients respectively. In our previous retrospective NPC

study, the incidence of grade 3 mucositis and dermatitis were 5.5% and 6.8 % respectively [11].

Although Bonner *et al.* have reported that the incidence of acute RT-related toxicity is not significantly increased when HNSCC is treated with RT plus cetuximab [20], our results showed that the incidence of grade 3 oropharyngeal mucositis and RT-related dermatitis were still as high as 81.4 % and 7.0% respectively when cetuximab was added to RT in the treatment of LANC. Giro *et al.* have also found up to 50% of grade 3–4 of radiation dermatitis during radiotherapy with concurrent cetuximab in head and neck cancer [21]. However, in the present study, grade 3 oropharyngeal mucositis was controlled effectively by using our previously reported method [13]. This result may also be associated with the low toxicity of cetuximab that did not show any significant side effects that are often seen with chemotherapeutic agents, including nausea, vomiting, and mucositis. Only three patients need 7 ~ 12 days IV infusion for nutritional supports due to dysphagia and oropharyngeal pain caused by oropharyngeal mucositis; the remaining patients had a good eating condition; and 23.3 % of patients had only grade 2 weight loss. No patients experienced radiation break and no patients needed NF. Two important phase II clinical trials with novel molecular targeted agents have been reported by Ma *et al.* and Lee *et al.* [7, 18]. Ma *et al.* [7] treated 30 LANC patients with concurrent IMRT and cisplatin plus cetuximab, and reported that 26% patients showed grade 3 weight loss, 33% patients needed NF for a median duration of 41 days (range, 3–200 days), and IMRT was interrupted for 2 days in one patients who experienced a grade 3 oropharyngeal mucositis. Lee *et al.* [18] treated 44 LANC patients with CCRT with cisplatin-ACT with PF plus six cycles of bevacizumab (anti-vascular endothelial growth factor), and reported that 9% of patients (4/44) needed a feeding tube before therapy and 12% (5/41) of patients and 6% (2/36) of patients needed a NF at 1 year and 2 years after the start of treatment, respectively. Therefore, the incidence of acute grade 3 toxicities observed in this study was significantly less than the aforementioned trials [7, 18].

In the present study, during ACT with TP, no patients had greater than grade 3 hematologic toxicity, except for 1 patient having grade 4 leukopenia with fever; 4.7% patients (2/43) had mildly elevated creatinine. As the patients received ACT one month after concurrent HT with cetuximab, 93.0% (42/43) patients completed 4 cycles of chemotherapy. During HT with cetuximab, 100% of patients received 7 cycles of cetuximab; only one patient received reduced dose of cetuximab.

The compliance of treatment in our study was

also better than in previous reports [7, 18]. In Lee *et al.*'s study [18]; the concurrent and adjuvant phases were both tolerable in 68% (30/44) of patients. In Ma *et al.*'s study [7], 86% and 50% of patients received +5 and +6 cycles of cisplatin, respectively; and 93% and 73% of patients received +5 and +6 cycles of cetuximab, respectively. However, cisplatin and cetuximab were interrupted in 60% and 33% patients, respectively.

Considering that HT can protect the contralateral parotid gland for preventing late xerostomia and less damage to the cochlea, xerostomia and SNHL caused by HT seemed less common in comparison to IMRT [22, 23]. HT-related grade 2 xerostomia (no Grade 3+ xerostomia) and SNHL are reported to range from 3~14% and 3~3.6% in the treatment of NPC reported by few studies [9, 10, 23]. Our previous report showed that no patient with nasopharyngeal carcinoma treated with HT reported grade 2+ xerostomia one year after radiotherapy [11]. In the present study, with a median follow-up of 48.0 years, only 4.7% patients (2/43) had Grade 2+ xerostomia one year after radiotherapy and recovered at 18 months after treatment. 11.6% patients (5/43) experienced SNHL and 34.9% patients (15/43) developed conduction hearing loss. Other severe late toxicities, including 4.7% (2/43) grade 1 endocrine dysfunction, 4.7% (2/43) grade 2 subcutaneous fibrosis and 2.3% (1/43) osteonecrosis, were found in our study after HT. Dysphagia was not observed in any of the patients.

Regarding the efficacy of our new treatment options, we obtained 79.1% PFS, 93.0% OS, 95.2% LFFR and 88.1% DFFR at 2- year, and 72.0% PFS, 85.7% OS, 92.7% LFFR and 85.6% DFFR at 3-year. Similar survival data are reported from two aforementioned phase II clinical trials. Ma *et al.* have reported that the 2-year PFS, OS, LFFR, and DFFR are 86.5%, 89.9%, 93%, and 92.8% respectively [7], and Lee *et al.* have reported 74.7% PFS, 90.9% OS, 83.7% locoregional progression-free interval, and 90.8% distant metastasis-free interval at 2-year [18].

The present study and Ma *et al.*'s study [7] were both single-center studies with Chinese patients with non-keratinizing type LANC. We employed the treatment strategy of concurrent radiotherapy and targeted agent-ACT, while Ma *et al.* only treated LANC patients with concurrent phase. The similar survival data might imply that addition of cetuximab to CCRT without ACT might be an adequate treatment for LANC patients. Chen *et al.* reported on a phase III clinical study, demonstrating that there is no significant difference between CCRT and CCRT-ACT at 2-year DFFR [24]. However, NPC-9901 and NPC-9902 trials indicate that CCRT could result in significant benefit in both event-free survival and OS

[25, 26], but NPC-9902 trial [26] has demonstrated that DFFR is significantly better in patients receiving 3 or more cycles ACT than that in those receiving 0-1 ACT. More recently, Hui *et al.* [27] showed induction chemotherapy (ICT) is beneficial in LANC patients as measured by 3-year OS. ICT is generally better tolerated than ACT; early use of cytotoxic drugs at full dose would theoretically be more effective in eradicating distant micro-metastasis [2]. Therefore, further studies are needed to validate the optimal timing of chemotherapy for the treatment of LANC.

In addition, 93.0% OS and 95.2% LFFR at 2 year, and 85.7% OS and 92.7% LFFR at 3 year might benefit from HT in the present study. Several retrospective studies have reported the clinical outcomes of HT treatment in NPC patients. Leung *et al.* [9] have shown that HT has advantages over IMRT for their NPC patients, as shown by better local control and survival, with 5-year locoregional control rate (LCR) and OS being 97% and 90%, respectively. Shueng *et al.* [10] reported 88.4% LCR and 83.5% OS at 3year, respectively. In our previous retrospective NPC study [11], the 1-year relapse-free survival and OS were 97.2% and 94.8%, respectively.

Summary

The present study demonstrated that the treatment with concurrent HT plus cetuximab followed by ACT with TP LANC patients yielded an acceptable safety profile with minimal side effects and an encouraging survival data. Future randomized phase 3 study is needed to confirm our results.

Abbreviations

LANC: Locoregionally advanced nasopharyngeal carcinoma;
 HT: Helical tomotherapy;
 EGFR: Epidermal growth factor receptor;
 LFFR: Locoregional failure-free rate;
 PFS: Progression-free survival;
 DFFR: Distant failure-free rate;
 OS: overall survival;
 LCR: Locoregional control rate;
 T: Docetaxel;
 P: Cisplatin;
 F: 5-FU;
 NPC: Nasopharyngeal carcinoma;
 NCCN: National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology;
 SCCHN: Squamous cell carcinoma of the head and neck;
 ACT: Adjuvant chemotherapy;
 ECOG: Eastern Cooperative Oncology Group;
 RTOG: Radiation Therapy Oncology Group;
 AJCC: American Joint Committee on Cancer;

Cis: Confidence intervals;
 SNHL: Sensorineural hearing loss;
 CR: Complete response;
 PR: Partial response;
 NF: Nasogastric feeding;
 CCRT: Concurrent chemoradiotherapy;
 IMRT: Intensity-modulated radiotherapy;
 RT: Radiotherapy;
 IV: Intravenous;
 MRI: Magnetic resonance imaging;
 PET: Positron emission computed tomography;
 CT: Computed tomography;
 ICT: Induction chemotherapy.

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Authors' contributions

ZX and ML designed the study; DL, ZF, and YS collected and assembled the data; ZX and ML wrote the manuscript. All authors read and approved the final manuscript.

Competing Interests

The authors have declared that no competing interest exists.

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