Improving effectiveness using nimotuzumab (NTZ) in patients with nasopharyngeal carcinoma based on the 18F-FDG PET/CT maximum standardized uptake value

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Research Article

Keywords: nasopharyngeal carcinoma, nimotuzumab, maximum standardized uptake value, cost-effectiveness

Posted Date: March 15th, 2023

DOI: https://doi.org/10.21203/rs.3.rs-2673519/v1

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Additional Declarations:  
Table 1 to 3 are available in the Supplementary Files section.
Improving effectiveness using nimotuzumab (NTZ) in patients with nasopharyngeal carcinoma based on the 18F-FDG PET/CT maximum standardized uptake value

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Abstract

**Background:** This study was aimed towards improving the efficacy of nimotuzumab (NTZ) in locoregionally advanced nasopharyngeal carcinoma (LA-NPC) using the maximum standardized uptake value (SUVmax) of 18F-fluorodeoxyglucose positron emission tomography (18-FDG PET) as a predictive and prognostic indicator.

**Method:** 248 patients with locoregionally advanced nasopharyngeal carcinoma (LA-NPC) who met the inclusion criteria of our study were subjected to PET/CT scan in our hospital prior to chemoradiotherapy from January 2012 to June 2019. Survival differences and independent factors between groups were assessed by the Kaplan–
Meier method, log-rank test, and Cox proportional hazards regression analysis. Outcome measures included analysis of the cost-effectiveness ratio (ICER).

**Result:** The optimal cutoff value for the maximum standardized uptake value (SUVmax) was 12.92 while the area under concentration-time curve (AUC) for the SUVmax was 0.596. The prognostic significance for overall survival (OS) with NTZ treatment (P=0.023) and SUVmax (P=0.014) was indicated by multivariate analysis. Exploratory subgroup survival analysis revealed that NPC patients with SUVmax >12.92 treated with concurrent chemoradiotherapy (CCRT) plus NTZ had a significantly improved 3-year OS than those treated with CCRT alone (96.2% vs. 73.2%, P=0.047). However, in those with SUVmax ≤12.92 treated with CCRT plus NTZ there was no statistically significant difference from those treated with only CCRT (97.6% vs.94.3%, P=0.129). The treatment cost with nimotuzumab was $6317.61, this additional cost being only $274.68 extra for every 1% increase in the OS rate, as indicated by the cost-effectiveness analysis.

**Conclusion:** In LA-NPC patients with SUVmax >12.92, adding NTZ to CCRT improves overall survival and is cost-effective. However, the addition of NTZ was not
Introduction

Nasopharyngeal carcinoma (NPC) and the morbidity and mortality arising from it in Southern China, Southeastern Asia, and North Africa are the highest in the world, with poorly differentiated or undifferentiated squamous cell carcinoma being the main pathologic types [1, 2]. NPC is a highly invasive tumor, with the majority (up to 70%) being locally advanced at the time of detection [3, 4]. The standard of care for locoregionally advanced nasopharyngeal carcinoma (LA-NPC) is induction chemotherapy (IC) followed by concurrent chemoradiotherapy (CCRT), or CCRT followed by adjuvant chemotherapy (AC), or only CCRT is [5, 6]. Despite overall...
survival in locoregionally advanced cases being significantly improved with intensity modulated radiotherapy (IMRT), an unfavorable prognosis remains in about 20-30% cases because of distant metastasis with or without recurrent disease [7]. Survival in LA-NPC patients can only be improved with new treatment alternatives.

Overexpression of the epidermal growth factor receptor (EGFR)- an Erb-B receptor tyrosine kinase- in nearly 70% NPC cases[8] may lead to a poor prognosis in NPC patients[9, 10] and a high treatment resistance rate due to tumor cell proliferation. Nimotuzumab (NTZ)- an improved version of anti-EGFR monoclonal antibodies- shows promise in LA-NPC patients treated with CCRT, as proved by a large cohort study of CCRT combined with NTZ for a better 5-year overall survival with tolerable side effects, compared with CCRT alone (76.1% against 72.3%, p=0.004) in NPC patients with EGFR, and thus approved for treatment in III-IVa stage NPC in combination with radiotherapy (RT) and CCRT [11]. As observed clinically, TNM staging alone in LA-NPC patients receiving CCRT in combination with NTZ is not adequate for determining clinical outcomes, and other surrogate indicators are needed to guide practice. The cost of NTZ is an enormous financial burden for patients[12], it
is imperative to identify factors leading to a clear survival benefit from NTZ.

Positron emission tomography/computed with 18F-fluorodeoxyglucose (18F-FDG PET/CT) is used to stage, assess curative effect, and predict prognosis in patients with solid tumors [13-16]. Modern imaging techniques, apart from the obvious information about the dimensions of a tumor, provide useful metrics for biomarkers, especially when using PET/CT and among these are metabolic tumor volume (MTV), total lesion glycolysis (TLG), and the maximum standardized uptake value (SUVmax). Our previous study demonstrated that SUVmax plays a crucial role in reflecting invasive and metastatic potential in NPC [17]. Some studies have also revealed that SUVmax is useful in the prognosis of NPC[18, 19]. There is however no known study that indicates if the SUVmax could predict treatment response in NPC patients treated with NTZ. Therefore, this study, even though retrospective, was an attempt to find if a pattern or association exists between LA-NPC patients with EGFR expression who underwent CCRT in combination with NTZ, with a possible predictive value of SUVmax in PET/CT, to justify the efficacy of NTZ in LA-NPC.
Materials and methods

Patient selection

We reviewed the medical records of newly diagnosed NPC patients in our center from January 2012 to June 2019 in this retrospective study. 248 NPC patients satisfying the inclusion criteria were recruited in our study: (1) Karnofsky performance score (KPS) ≥ 90; (2) histologically confirmed NPC; (3) immunohistochemical confirmed EGFR expression; (4) classified as stage III-IVa NPC as described in the American Joint Committee on Cancer (AJCC) 7\textsuperscript{th} TNM staging system; (5) induction chemotherapy (IC) followed by concurrent chemoradiotherapy (CCRT) with or without NTZ; (6) data available from 18F-FDG PET/CT prior to IC; (7) no history of malignant disease; (8) no targeted therapy with any other anti-EGFR antibody.

Radiotherapy and chemotherapy

All patients received IMRT. The target volume, at risk organ(s), and dose for radiotherapy were delineated using a treatment protocol previously described [20]. A total radiation dose of 69.7–70.0 Gy given over 33–35 fractions was prescribed for the primary gross tumor planning target volume, or the gross
tumor volume if lymph nodes were involved. The high-risk region (CTV1) had a recommended dose of 62–62.7 Gy, while the low-risk region (CTV2) could only be given 54.4–56.2 Gy, in corresponding fractions. A margin of 3 mm was added to determine the planning target volume (PTV). 2-3 cycles of IC were administered to all the patients prior to CCRT. The IC regimen used was TP (paclitaxel + cisplatin) and GP (gemcitabine + cisplatin). Cisplatin was used for the CCRT regimen. The IC and CCRT were administered by the intravenous route, repeating every 3 weeks, with radiotherapy simultaneously administered in the first cycle of CCRT.

Nimotuzumab

The full dose of nimotuzumab was administered to 110 patients, according to the decision of the patient to receive the medication, 200mg intravenously and repeated once a week for 7 weeks prior to IMRT.

18-FDG PET/CT imaging

All the 248 NPC patients in the study were subjected to 18-FDG PET/CT scan on the Gemini TF 64 PET/CT device (Philips, Holland) in supine position, and with at least 6 hours of fasting prior to PET/CT scanning in order to
maintain a blood glucose level between 3.9 and 6.5 mmol/L. A dose of 148 to 296 MBq of 18-FDG was administered intravenously, with the patients given a resting period of 40 to 60 minutes in a comfortable room with subdued lighting prior to the PET/CT scan. Scanning was performed from the head to the proximal thigh using a slice width of 4 mm, 140 kVp, 2.5 mA, and a matrix of 512×512. An iterative reconstruction of the PET images was done with a CT-based attenuation correction. The region of interest (ROI) of the tumor lesion was used to define the 18-FDG maximum standardized uptake value (SUVmax), which was calculated as the ratio of the decay corrected tissue activity (nCi/mL) to the sum of the injected dose of FDG (nCi) and body weight (g) of the patient. The highest SUV of the primary tumor was calculated as the SUVmax.

**Clinical endpoints and Follow-up**

Regular reviews were carried out at intervals of 3 months in the first 2 years, followed by intervals of 6 months into the first 5 years, followed by once a year. Routine surveillance included physical examination, hematological and
biochemical tests, nasopharyngoscopy, enhanced magnetic resonance imaging (MRI) of the head and neck, computed tomography (CT) of the thorax, and ultrasound (USG) of the abdomen. Clinical endpoints were documented up to January 2022.

The survival time (OS) and progression-free survival (PFS) were the primary clinical endpoints, the others being the local recurrence-free survival (LRFS), regional recurrence-free survival (RRFS), locoregional relapse-free survival (LRRFS), and distant metastasis-free survival (DMFS). The periods between the date of diagnosis and each event or the last review were defined as the clinical endpoints.

**Statistical analysis**

SPSS 23.0 (Chicago, IL, USA) and R (version 4.0.5) were used to analyze all the recorded data. The optimal cutoff value of SUVmax for prognosis in LA-NPC patients was determined with the receiver operating characteristic (ROC) curve. Kaplan-Meier method was used to determine the survival rate, and the OS, PFS, LRFS, RRFS, LRRFS, and DMFS differences between the groups, were calculated using the log-rank
test. Multivariable analysis was used to study correlation of age and gender, TNM stage, and SUVmax with nimotuzumab (NTZ). Independent variables associated with the 3-year OS and 3-year PFS of the patients in the study were determined using Cox proportional hazards regression analysis.

Using the exchange rate as of January 2022 (1 USD = 6.36 China Yuan (CNY)), all cost calculations were done in US dollars (USD). The cost-effectiveness analysis and the cost-effectiveness ratio (ICER) were used to determine the outcome measures for the 3-year OS. The Diagnosis Related Groups (DRG) issued by the National Healthcare Security Bureau were used to determine the total cost of CCRT. The price of nimotuzumab was $902.52 per week.

**Results**

**Patient demographics**

In all, 248 LA-NPC patients (177 males; 71 females) satisfying all inclusion criteria were recruited in the study (Table 1). The median age of the patients was 47, and the range from 19 to 83 years. The absolute numbers and proportions of patients according
to the extent of the primary tumor- T1, T2, T3, or T4- were 35 (14.1%), 36 (14.5%), 124 (50.0%), and 53 (21.4%), respectively. The regional lymph node distributions for N0, N1, N2, and N3 were 14 (5.6%), 71 (28.6%), 93 (37.5%), and 70 (28.3%), respectively. Patients with age <65 years and ≥65 years were 228 (91.9%) and 20 (8.1%), respectively. Deaths, local-regional relapse, local recurrence, and distant metastasis were 19 (7.6%), 13 (5.2%), 27 (10.9%), and 30 (12.1%), respectively.

**Clinical outcomes of the whole cohort**

42 months was the median follow-up time (range, 6-96 months). The 3-year OS, PFS, LRFS, RRFS, LRRFS, and DMFS were 93.8%, 87.8%, 93.4%, 91.4%, 96.3%, and 90.9%, respectively among the 248 cases of III-IVa NPC. There was no loss to follow-up; all causes of death were cancer-related among all the patients who died.

**Impact of NTZ on overall survival**

The clinical characteristics of the patients treated with CCRT alone and those treated with CCRT plus NTZ did not differ significantly (Table 2). For the patients with CCRT alone, the 3-year rates for the OS, PFS, LRFS, RRFS, LRRFS and DMFS were 91.0%, 80.1%, 89.2%, 86.4%, 93.0% and 90.1%, respectively. For the patients with CCRT plus
NTZ, the 3-year OS, PFS, LRFS, RRFS, LRRFS and DMFS were 97.2%, 83.3%, 96.3%, 95.4%, 98.2%, and 87.0%, respectively. The CCRT plus NTZ had a better OS in comparison to the group receiving only CCRT (P=0.018) (Fig. 1a), as determined by Kaplan-Meier analysis. No statistically significant difference was found for the PFS, LRFS, RRFS, LRRFS and DMFS for patients receiving NTZ (P=0.407, 0.193, 0.086, 0.121, and 0.515).

**Impact of SUVmax on the overall survival (OS)**

The SUVmax for the entire cohort was on an average 10.33±5.69 (range, 1.7–48.88). The area under concentration-time curve (AUC) for the SUVmax was 0.596, and the sensitivity and specificity were 0.438 and 0.92, respectively, as calculated by the ROC curve analysis. The optimal cutoff value was 12.92, using the Jorden index (sensitivity+specificity-1). When the SUVmax was >12.92, the 3-year OS, PFS, LRFS, RRFS, LRRFS and DMFS were 87.2%, 59.7%, 85.3%, 75.4%, 87.5% and 79.3%, respectively. When the SUVmax was ≤12.92, the 3-year OS, PFS, LRFS, RRFS, LRRFS and DMFS were 95.7%, 84.7%, 95.2%, 93.1%, 97.3%, and 90.9% respectively. Kaplan-Meier analysis showed that SUVmax ≤12.92 had superior OS, PFS, and
LRRFS compared with SUVmax >12.92 (P=0.029, 0.034, and 0.039) (Fig. 1b, 1c, 1d).

There was no statistically significant difference in the LRFS, RRFS, and DMFS according to SUVmax (P=0.127, 0.062, and 0.121).

**Multivariate analysis**

Cox regression models were used to analyze the OS and PFS for 248 patients in the study. Using univariate analysis and the results of previous studies, the patients’ age, gender, TNM stage, SUVmax, and use of NTZ were further studied with multivariate analysis. The prognosis for OS was significant for SUVmax (P=0.014) and treatment with NTZ (P=0.023). SUVmax was an independent prognostic factor for PFS (P=0.045) (Fig. 2a, b).

**Survival analysis between NTZ and SUVmax in subgroups**

According to the multivariate analysis, NTZ and SUVmax were independent prognostic factors for the OS. To identify III-IVa stage NPC patients who may benefit from NTZ, an exploratory subgroup survival analysis was conducted after stratification by SUVmax (≤12.92 and >12.92) to evaluate whether NTZ treatment was optimal for NPC patients treated with SUVmax >12.92. For patients with SUVmax >12.92, the 3-year
OS and PFS for the group receiving only CCRT were 73.2% and 57.1% (P=0.047) (Figure 3a) as compared to the group receiving CCRT plus NTZ, which was 96.2% and 60.0% (P=0.433), respectively. For patients with SUVmax ≤12.92, the 3-year OS and PFS for the group receiving only CCRT was 94.3% and 80.0% (P=0.563), as compared to the group receiving CCRT plus NTZ, which was 97.6% and 84.1%, P=0.129) (Figure 3b), respectively. The 3-year OS increased 23% in the CCRT plus NTZ group compared with CCRT alone group in the III-IVa stage NPC patients with SUVmax ≥12.92. The result demonstrated that compared with corresponding subgroups, NTZ treatment benefited patients with SUVmax >12.92. In those with SUVmax ≤12.92, there was no statistically significant difference in the OS according to treatment with NTZ (Table 3).

Cost-effectiveness and sensitivity analysis

For stage III-IVa NPC patients with SUVmax >12.92, the total treatment cost for the group receiving CCRT plus NTZ (n=26) was $17166.67, and for the group receiving only CCRT (n=29) it was $10849.06. The extra treatment cost for nimotuzumab was $6317.61. The cost effectiveness differences (C/E %) for the 3-year OS in the CCRT plus NTZ group compared to the CCRT alone group were $178.45 and $148.21,
respectively. The difference in effectiveness for the 3-year OS was 23%. Therefore, the ICER was $274.68, which translated to an increase of 1% in the OS rate in the NPC patients with SUVmax >12.92 after adding nimotuzumab. In the sensitivity analysis, the OS was varied by±10%, yielding a C/E% in the 3-year OS for the CCRT plus NTZ group against the CCRT alone group, of $199.15 versus $130.40, respectively.

**Discussion**

NPC arises from the epithelial cells in the nasopharynx and is one of the most aggressive malignancies known. In 2020 there were 133,354 newly reported cases and 80,008 new cancer-related deaths of NPC worldwide, as reported by the International Agency for Research on Cancer. Current guidelines from the National Comprehensive Cancer Network (NCCN) recommend IC with CCRT, CCRT, or CCRT plus adjuvant chemotherapy as the standard treatment for stage III-IVa (locoregionally advanced) NPC. Even with precision radiation therapy and standard cisplatin-based chemotherapy, the prognosis for LA-NPC remains unsatisfactory, with 20-30% recurrent disease and/or distant
metastasis. With the significant development of biotechnology, a number of tumor gene targets drew the attention of researchers. Targeted therapy with epidermal growth factor receptor (EGFR) antibody has shown promise for improving prognosis in NPC patients. EGFR, an Erb-B receptor tyrosine kinase, is widely overexpressed in head and neck cancer. Its intracellular signal transduction leads to enhanced cell proliferation, inhibition of apoptosis, increased angiogenesis, and promotion of metastasis. In a recent study reporting high EGFR expression leading to early recurrence, a low overall survival (OS) ratio along with a low disease free survival (DFS) ratio in stage II-IV head and neck tumors[21] were observed. Anti-EGFR monoclonal antibodies including cetuximab (CTX) and nimotuzumab (NTZ) can specifically inhibit EGFR and enhance radio sensitivity, increasing the effect of synchronous chemoradiotherapy in NPC patients [22, 23]. A large retrospective cohort study with a long follow-up revealed that treatment with CTX/NTZ alongside concurrent chemoradiotherapy (CCRT) in patients with II-IVb NPC significantly prolonged OS as compared to CCRT alone (3-year OS being 96.6% compared to 92.9%; P=0.015) and DFS (3-year DFS being 93.5% compared to 89.3%; P=0.03). However, significant differences of acute toxicities such
as skin reaction and mucositis were observed in patients receiving CTX and CCRT as compared to NTZ and CCRT or CCRT alone [24]. NTZ, an improved and humanized anti-EGFR monoclonal antibody with preferential tumor cell uptake compared to normal tissue, has significantly fewer adverse effects on normal mucosa and skin. In the last 5 years, many clinical studies have shown better clinical outcomes and less radiation-related toxicity for CCRT in combination with NTZ for locoregionally advanced nasopharyngeal carcinoma (LA-NPC) patients [25-27], similar to our study, where CCRT plus NTZ had superior OS compared to the CCRT alone group (3-year OS, 97.2% against 91.0%), and this difference was statistically significant. However, the TNM stage in LA-NPC patients remaining the same, among those who received CCRT in combination with NTZ, the clinical outcomes varied greatly. This revealed that the TNM stage by itself is not adequate for the application of NTZ without considering other clinical factors. Thus, it is necessary to explore other important prognostic indicators in order to identify which III-IVa stage NPC patients could achieve a survival benefit from NTZ.

The relationship between image-derived biomarkers in PET/CT (SUVmax, TLG, or
MTV) and clinical outcomes in solid tumors has been extensively studied. Wei-Hsiang Feng et. al studied 50 patients suffering from esophageal carcinoma retrospectively, where post neo-adjuvant concurrent chemoradiotherapy SUVmax ≥3 was a poor prognostic factor for DFS (HR:3.417, P=0.011) and OS (HR:3.665, P=0.013)[28]. In another retrospective study G.D Di Stasio et. al revealed that SUVmax ≥10.08, MTV ≥27.89, and TLG ≥134.85 conferred a significantly worse prognosis in 49 patients with pleomorphic lung carcinoma, and that the metabolic biomarkers mentioned above could be used to predict recurrence and death[29]. Ewa Burchardt et. al, in a multivariate COX regression analysis of 93 locally advanced squamous cervical cancer patients who received radical cisplatin-based chemoradiotherapy, found that SUVmax above 12.6 and TLG above 245.7 were independent predictors of OS[30]. Lin Ching Chan et al. studied 108 patients with NPC receiving chemoradiotherapy and found that a pretreatment SUV >8.35 could lead to a significantly worse 3-year OS compared to a lower SUV value. Pretreatment SUV could also independently predict an adverse 3-year DFS and 3-year OS, similar to our previous study, where the best cutoff value for SUVmax was 8.2 as derived from the ROC curve. The NPC patients with SUVmax <
8.2 appeared to show a clinical outcome benefit (3-year PFS, 91.1% against 73.0%, P=0.027). In addition to exploring the relationship between prognosis and solid tumor as mentioned above, other studies have also focused on the relationship between image-derived biomarkers using PET/CT for solid tumors and the response to chemoradiotherapy. Dae Hee Pyo et.al reported that after neoadjuvant chemoradiotherapy (nCRT) the SUVmax, TLG, and MTV may predict a pathological complete response (pCR). Their study assessed the SUVmax, TLG, and MTV before and after nCRT in 137 patients with rectal cancer which was locally advanced, and found that the post-SUVmax, post-TLG, and post-MTV values were smaller in the pCR group as compared to the non-pCR group. Multivariate analysis revealed that post-SUVmax, post-TLG, and post-MTV values were independent factors for pCR[31]. Sayed Assif Lqbal et.al indicated that the percentage fall in SUVmax after nCRT can be used as a predictor for pCR in locally advanced ESCC patients receiving nCRT[32]. There are no reported studies of the predictive value(s) when using image-derived biomarkers in PET/CT for assessing the response to treatment in NPC patients receiving NTZ. Moreover, SUVmax has the advantage of repeatability, objectivity and steady
parameters. Thus, our study has evaluated the predictive value of SUVmax for selecting which stage III-IVa NPC patients might benefit from the addition of NTZ to their treatment protocol, revealing that NPC patients in stage III-IVa with SUVmax >12.92 had a worse 3-year OS than those with SUVmax ≤12.92 (87.2% against 95.7%, P=0.029). Further subgroup analyses found that for NPC patients in stage III-IVa with SUVmax >12.92, CCRT plus NTZ treatment resulted in a higher 3-year OS than CCRT alone. However, for NPC patients in stage III-IVa with SUVmax ≤12.92, no statistically significant difference existed in the 3-year OS between the two groups. NTZ treatment benefited stage III-IVa patients with SUVmax >12.92.

Our previous study revealed that the additional cost for every one percent increase in OS rate was $2,052.09. And it is not cost-effective[12]. In this study, we found high-risk patients to receive targeted therapy of nimotuzumab. Nimotuzumab may further help improve outcomes of high-risk NPC patients. The high-risk factor of NPC in this study was SUVmax >12.92. The difference in the cost effectiveness for the 3-year OS for NPC patients in stage III-IVa with SUVmax >12.92 was 23% higher. The extra treatment cost of nimotuzumab was $6317.61. Therefore, the ICER was calculated as
$274.68, which means that the additional cost of treatment was only $274.68 for every 1% improvement in the OS rate. Nimotuzumab was thus found to be cost effective and may thus be recommended for LA-NPC patients with SUVmax >12.9.

This is the first study of its kind to assess the predictive value of SUVmax to justify the addition of NTZ to CCRT in patients with LA-NPC, and to identify high-risk patients who would benefit from nimotuzumab, to the best of our knowledge. The cost-effectiveness of adding nimotuzumab in high risk III-IVa EGFR positive NPC patients was also proved beyond doubt. The limitations of our single institution study would be resolved by a larger multicenter longitudinal randomized control design.

**Conclusion**

In summary, the overall survival in NPC patients with SUVmax >12.92 improved significantly and was also cost-effective when nimotuzumab was added to concurrent chemoradiotherapy. However, the addition of nimotuzumab to concurrent chemoradiotherapy was not cost-effective for NPC patients with SUVmax ≤12.92.

**Declarations**
Ethics approval and consent to participate

This retrospective study was approved by Fujian Province Cancer Hospital Institutional Review Board (NO. YKT2020-011-01). All patients provided written informed consent prior to treatment, and all information was anonymized prior to analysis.

Consent for publication

Not applicable

Funding

This study was supported in part by grants from the Natural Science Foundation of Fujian Province (Grant/ Award Number: 2020J011124). Bethune-Translational Medicine Research Fund for Oncology Radiotherapy (Grant/ Award Number: flzh202126)

Conflict of interest statement

The authors declare that the submitted work was not carried out in the presence of any
personal, professional, or financial relationships that could potentially be construed as a conflict of interest.

Authors’ contributions statement

All authors listed have made a substantial, direct, and intellectual contribution to the work, and approved it for publication.

Acknowledgments

The authors thank all patients who participated in the study.

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Figure legends

Figure 1 The survival curves of 248 patients with LA-NPC, according to the (a) OS for CCRT group versus CCRT + NTZ group, (b) OS for SUVmax >12.92 versus SUVmax ≤12.92, (c) PFS for SUVmax >12.92 versus SUVmax ≤12.92, (d) LRRFS for SUVmax >12.92 versus SUVmax ≤12.92.

Figure 2 The survival curves of (a) 193 patients LA-NPC of SUVmax ≤12.92 in CCRT group versus CCRT + NTZ group, (b) 55 patients LA-NPC of SUVmax >12.92 in CCRT group versus CCRT + NTZ group.

Figure 3 Forrest plots of multivariate analysis of (a) OS, and (b) PFS for 248 patients with LA=NPC. HR= hazard ratio.

Table legends

Table 1 Characteristics of 248 patients with LA-NPC.

Table 2 Characteristics of 248 LA-NPC patients treated with CCRT alone and those treated with CCRT plus NTZ.
Table 3 Subgroup survival analysis of OS and PFS for LA-NPC stratified by (SUV\text{max} \leq 12.92 \text{ and } SUV\text{max} > 12.92) in CCRT group versus CCRT + NTZ group.
Fig 3

**Subgroup**

**Gender**

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**Age**

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**T stage**

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**N stage**

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**Nimotuzumab**

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**SUVmax**

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<td>&lt;12.62</td>
<td>Ref,</td>
<td></td>
</tr>
<tr>
<td>≥12.62</td>
<td>3.736(1.300-10.734)</td>
<td>0.014</td>
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</tbody>
</table>

---

**Subgroup**

**Gender**

<table>
<thead>
<tr>
<th>Gender</th>
<th>HR(95%CI)</th>
<th>pvalue</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>Ref,</td>
<td>0.435</td>
</tr>
<tr>
<td>Female</td>
<td>0.794(0.444-1.418)</td>
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**Age**

<table>
<thead>
<tr>
<th>Age</th>
<th>HR(95%CI)</th>
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<tbody>
<tr>
<td>&lt;65</td>
<td>Ref,</td>
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<tr>
<td>≥65</td>
<td>0.365(0.087-1.491)</td>
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**T stage**

<table>
<thead>
<tr>
<th>T stage</th>
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</thead>
<tbody>
<tr>
<td>T1</td>
<td>Ref,</td>
<td>0.512</td>
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<tr>
<td>T2</td>
<td>0.563(0.204-1.558)</td>
<td>0.288</td>
</tr>
<tr>
<td>T3</td>
<td>0.758(0.346-1.688)</td>
<td>0.493</td>
</tr>
<tr>
<td>T4</td>
<td>1.043(0.443-2.443)</td>
<td>0.927</td>
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</table>

**N stage**

<table>
<thead>
<tr>
<th>N stage</th>
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<tbody>
<tr>
<td>N0</td>
<td>Ref,</td>
<td>0.117</td>
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<tr>
<td>N1</td>
<td>2.630(0.619-11.331)</td>
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<tr>
<td>N2</td>
<td>1.603(0.407-7.993)</td>
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<tr>
<td>N3</td>
<td>3.469(0.793-15.385)</td>
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</table>

**Nimotuzumab**

<table>
<thead>
<tr>
<th>Without</th>
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**SUVmax**

<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>&lt;12.62</td>
<td>Ref,</td>
<td></td>
</tr>
<tr>
<td>≥12.62</td>
<td>1.787(1.014-3.150)</td>
<td>0.045</td>
</tr>
</tbody>
</table>

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Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- nitotable.docx