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ORIGINAL RESEARCH

Efficacy and Safety of Combined PD-1 Inhibitor With Induction Chemotherapy Followed by IMRT Plus Nimotuzumab in Locally Advanced Nasopharyngeal Carcinoma: A Retrospective Analysis

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Background: Induction chemotherapy (IC) is the standard treatment protocol for locally advanced nasopharyngeal carcinoma (LANPC), though concerns persist regarding high rates of recurrence and metastasis. This retrospective study aims to evaluate the efficacy, potential benefits, and safety of combining PD-1 inhibitors with IC, followed by nimotuzumab and intensity-modulated radiation therapy (IMRT).

Methodology: We analyzed data from 103 patients diagnosed with non-keratinizing LANPC (according to WHO criteria) at clinical stages III-IVA. These patients, treated from May 2020 to November 2023, received four cycles of IC combined with PD-1 inhibitors, followed by nimotuzumab and IMRT. Efficacy assessments were conducted according to RECIST v1.1 guidelines, with the primary endpoint being a clinical complete response (CCR), defined as the absence of detectable tumors or mucosal bulges upon nasoendoscopy.

Results: Among the evaluable patients, the CCR rate reached 66% (95% CI, 56–75%), while the objective response rate (ORR) was 97% (95% CI, 92–99%) and the disease control rate (DCR) reached 99% (95% CI, 95–100%). During the median follow-up of 16.1 months, neither the median progression-free survival (PFS) nor median overall survival (OS) was reached. Notably, patients with T4-stage disease exhibited lower CCR rates, highlighting stage-specific variations in treatment responses. The treatment regimen was well-tolerated, with no significant adverse safety events reported.

Conclusion: The combination of PD-1 inhibitors with IC, followed by nimotuzumab and IMRT, shows promising efficacy and safety in the treatment of LANPC.

Keywords: nasopharyngeal carcinoma, PD-1 inhibitors, induction chemoth4erapy, IMRT, efficacy

Introduction

Nasopharyngeal carcinoma (NPC) is a malignant neoplasm arising from the epithelial cells of the nasopharynx. It is particularly prevalent in southern China, Southeast Asia, and North Africa, representing a significant oncological challenge in these regions.[1] According to the 2022 global cancer statistics, NPC accounted for 120,416 new cases and 73,476 deaths worldwide, ranking 21st in cancer mortality, underscoring its substantial public health impact.[2] The anatomically concealed location of the nasopharynx, along with vague early symptoms and a general lack of awareness,

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often results in over 70% of NPC cases being diagnosed at advanced stages. These factors contribute to a relatively poor prognosis, with 5-year overall survival (OS) rates of 89.2% in stage III and 73.7% in stage IV patients, respectively.[3,4] The cornerstone of NPC management is chemoradiotherapy, with intensity-modulated radiation therapy (IMRT) now being the preferred modality. IMRT offers superior dose distribution and target conformity compared to conventional radiation techniques, enhancing treatment precision.[5] Despite these advancements, the recurrence and metastasis rates in patients with locally advanced nasopharyngeal carcinoma (LANPC) post-IMRT remain high, indicating the need for novel therapeutic strategies.[6] To improve therapeutic outcomes, researchers have explored additional strategies, such as the integration of nimotuzumab, a humanized anti-epidermal growth factor receptor (EGFR) monoclonal antibody.[1,7] Clinical studies suggest that combining nimotuzumab with IMRT significantly enhances both progression-free survival (PFS) and OS compared to IMRT alone, offering new hope for patients with LANPC.[8] Data indicate that the addition of nimotuzumab provides superior survival benefits for LANPC patients compared to concurrent chemoradiotherapy (CCRT) alone.[9,10] However, no statistically significant difference in survival rates was observed between the IMRT-alone group and the IMRT + CCRT group.[11] Moreover, while no studies have been identified comparing the combination of nimotuzumab and IMRT with CCRT, existing research suggests that combining nimotuzumab with IMRT can improve survival outcomes.[12,13] Recent studies have demonstrated that replacing CCRT with nimotuzumab combined with IMRT not only improves therapeutic efficacy but also significantly reduces treatment-related side effects, such as oral mucositis. This approach has been associated with less weight loss during the radiotherapy phase, enhancing patient tolerability and overall quality of life.[14,15]

For patients presenting with high-risk features, such as N1 or greater nodal involvement or a tumor stage of T3 or higher, the National Comprehensive Cancer Network guidelines advocate for either induction chemotherapy (IC) or adjuvant chemotherapy, alongside standard chemoradiotherapy.[16] IC is particularly valuable as it controls micrometastases, assesses chemotherapy sensitivity, and enhances the effectiveness of subsequent chemoradiotherapy. Notably, it is linked to significant improvements in OS, PFS, distant metastasis-free survival (DMFS), and locoregional recurrence-free survival in LANPC patients.[17,18] However, the efficacy and risks of different IC regimens, such as paclitaxel + cisplatin (TP) and docetaxel + platinum (DP), differ; while they have demonstrated effectiveness in managing LANPC, some patients continue to respond poorly to chemotherapy or remain at high risk for recurrence and metastasis.[19,20] This highlights the need to optimize new IC strategies to further improve outcomes.

In contrast to traditional modalities such as chemotherapy, radiotherapy, and targeted therapy, immunotherapy has emerged as a promising approach by harnessing the body's immune system to target cancer cells rather than directly the tumor attacking.[21] Among these treatments, immune checkpoint inhibitors that block the PD-1 pathway, have become an integral part of clinical oncology. These inhibitors rejuvenate the body's anti-tumor immune response, often achieving sustained tumor control. Moreover, when combined with chemotherapeutic agents, PD-1 inhibitors can amplify therapeutic efficacy through synergistic effects.[22,23] While these inhibitors have consistently demonstrated improved clinical survival outcomes across various cancers, including LANPC, the selection of specific PD-1 inhibitors and their combination with different chemotherapy regimens remains an area of ongoing research.[24–28] Therefore, this retrospective study evaluates the efficacy and safety of various IC regimens incorporating anti-PD-1 antibodies, including serplulimab, sintilimab, and toripalimab, followed by nimotuzumab and IMRT in treating LANPC. The study aims to inform clinical decision-making to enhance treatment strategies for LANPC by offering tailored therapeutic approaches based on detailed subgroup analyses.

Materials and Methods

Patients and Information Collection

This retrospective study analyzed data from the electronic medical records at Hainan General Hospital and Hainan Affiliated Hospital of Hainan Medical University. A total of 108 patients diagnosed with LANPC were initially prescreened, and 103 patients treated from May 2020 to November 2023 with PD-1 inhibitors in combination with IC, followed by nimotuzumab and IMRT, were ultimately included. Three patients were excluded due to incomplete treatment data, two were excluded due to loss of follow-up. Ethical approval was granted by the Institutional Review

Board of Hainan General Hospital and Hainan Affiliated Hospital of Hainan Medical University (ethical approval number: 2024–719). Each patient provided informed consent. We declare that all patient data were kept strictly confidential, and our study complies with the Declaration of Helsinki.

Eligibility Criteria

The inclusion criteria were as follows: patients aged 18 years or older; histologically confirmed non-keratinizing nasopharyngeal carcinoma; stage III-IVA according to the 8th edition of the American Joint Committee on Cancer (AJCC 8th) staging system;[29] availability of pre-and post-treatment computed tomography (CT) or magnetic resonance imaging (MRI) imaging data suitable for evaluating tumor response based on the Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1; and accessible, complete medical records. Exclusion criteria included pregnant or lactating women and patients deemed unsuitable for the study participation by their treating physicians.

Treatment

All patients received four cycles of IC at three-week intervals, which included the administration of PD-1 inhibitors: serplulimab (a fixed dose of 300 mg on day 1), sintilimab (a fixed dose of 200 mg on day 1), or toripalimab (240 mg on day 1). The IC regimens included TP (nab-paclitaxel 260 mg/m^2 on day 1), DP (docetaxel 75 mg/m^2 on day 1), or GP (cisplatin + gemcitabine). For TP and DP regimens, nedaplatin (85 mg/m^2 on day 1) was administered. Following IC, IMRT was conducted based on the RTOG 0615 protocol and the ESTRO ACROP guidelines.[30] The dosing was as follows: 68–70 Gy to the planning target volume (PTV) of the primary tumor, 66–70 Gy to the PTV of the cervical lymph nodes, at least 60 Gy to the PTV of the high-risk clinical target volume (CTV)-1, and 54–56 Gy to the PTV of CTV-2, which includes the lower-risk neck nodal regions. Treatment was delivered over 32–33 daily fractions. Concurrently, nimotuzumab (200 mg weekly) was administered with IMRT for six cycles.

Outcome Assessment

The primary endpoint of the study was clinical complete response (CCR), which was defined as the absence of any detectable nasopharyngeal tumor or mucosal bulge upon endoscopy. Partial responses (PR) were required as a reduction of at least 30% in the sum of the diameters of target lesions, consistent with RECIST version 1.1. The objective response rate (ORR) was defined as the sum of the rates of CCR and PR. Assessments were conducted using imaging studies and nasopharyngeal endoscopy after completing four rounds of IC and immunotherapy, prior to the initiation of radiotherapy. Secondary endpoints included the disease control rate (DCR), PFS, OS, and evaluation of safety profiles. DCR was defined as the sum of patients achieving CCR, PR, and stable disease (SD). Progressive disease (PD) was defined as at least a 20% increase in the sum of the diameters of target lesions, referencing the smallest sum during the study. This included the appearance of one or more new lesions and/or unequivocal progression of existing non-target lesions.[31] PFS and OS were measured from treatment initiation to the first occurrence of disease progression, death, or the last follow-up. Survival rates were calculated using Kaplan-Meier estimates, and medians for PFS and OS were not reached within the follow-up period. Safety profiles were systematically recorded, focusing on treatment-related adverse events.

Statistical Analysis

Data were analyzed was conducted using SPSS software (version 25.0, IBM Corp). The median follow-up time, survival curves, and specific time-point rates for PFS and OS were estimated using the Kaplan-Meier method, with 95% confidence intervals (CIs) determined via Greenwood's formula. CR, PR, ORR, and DCR were calculated with their respective 95% CIs based on the Clopper-Pearson method. Variability in CCR and ORR across different patient subgroups was analyzed using the Chi-square test or Fisher's exact test where appropriate. Furthermore, treatment effect heterogeneity was visually depicted through forest plots generated by R software (version 2.1.0). Two-sided p-values < 0.05 were considered statistically significant.

Results

Patient Characteristics

In this study, 108 patients were screened, of whom 106 met the eligibility criteria and were enrolled; two were excluded due to having stage II disease. Additionally, 3 patients were excluded due to incomplete treatment and lack of post-baseline tumor assessments, resulting in 103 patients included in the full analysis set (FAS), as shown in Figure 1. Baseline characteristics are detailed in Table 1. The median age of participants was 51 years (range 28–79), with 75 males (72.82%) and 28 females (27.18%). The cohort predominantly consisted of patients in advanced stages, with 42 (40.8%) classified at clinical stage III and 61 (59.2%) at stage IVA according to AJCC 8th criteria. The median baseline EBV DNA level was 400 copies/mL, ranging up to 146,000 copies/mL.

Efficacy

Efficacy outcomes were impressive, with the ORR reaching 97% (95% CI, 92–99%) among the 103 evaluable patients in the FAS (Table 2 and Supplement Table 1). Specifically, 66% achieved a CCR (95% CI, 56–75%) and 31% achieved a PR, as detailed in Table 2. The DCR was equally robust at 99% (95% CI, 95–100%). During a median follow-up period of 16.1 months (ranged 11.4–18.6 months), the median PFS, OS, and duration of response (DOR) were not reached. This suggests that the treatment regimens analyzed in the present study illustrated promising long-term efficacy, highlighting the potential durability and effectiveness. The estimated two-year rates for PFS and OS were exceptionally high at 91.9% (95% CI, 79.5–97.0%) and 93.2% (95% CI, 79.6–97.9%), respectively. These results demonstrate the potential of this treatment protocol in effectively managing advanced-stage patients, showing both high efficacy and substantial disease control.

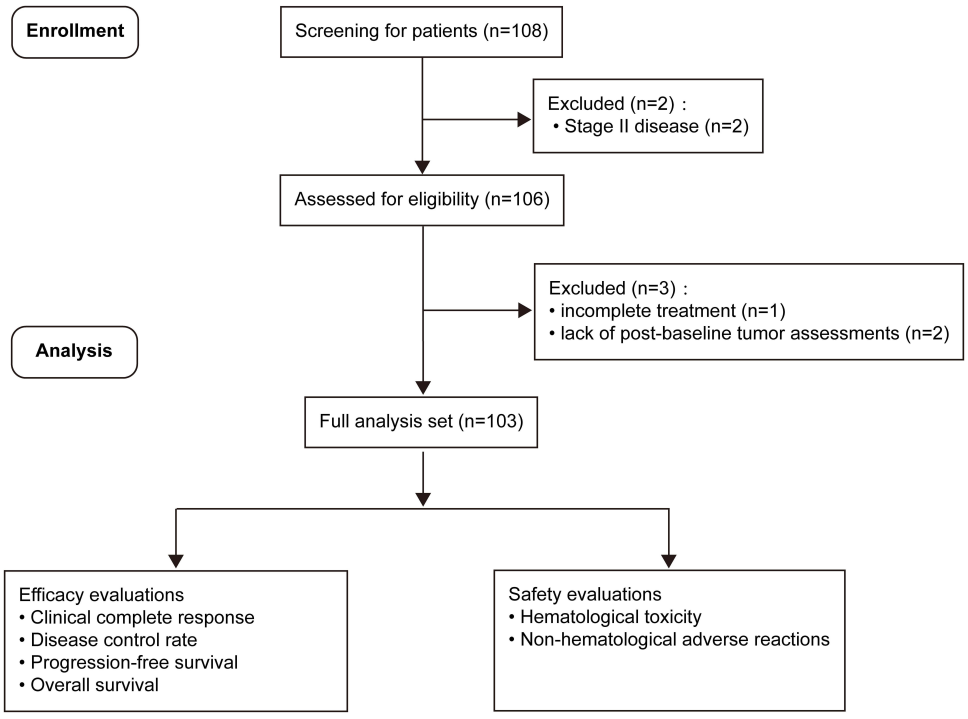

Figure 1 Flow chart of this study.

Table 1 Baseline Characteristics of Patients

Characteristics	n (%) (N=103)
Age (year), mean (SD)	51.00 (41.00, 58.00)
Gender	
Male	75 (72.82)
Female	28 (27.18)
Ethnic	
Han Chinese	98 (95.1)
Other	5 (4.9)
Clinical stage (cases)	
III	42 (40.78)
IVA	61 (59.22)
TNM stage - T stage (cases)	
1	2 (1.94)
2	14 (13.59)
3	54 (52.43)
4	33 (32.04)
TNM stage - N stage (cases)	
0	7 (6.80)
1	15 (14.56)
2	46 (44.66)
3	35 (33.98)
History of smoking	
Nonsmoker	56 (54.4)
Former smoker	6 (5.8)
Current smoker	41 (39.9)
Alcohol consumption	
Nondrinker	72 (69.9)
Former drinker	6 (5.8)
Current drinker	25 (24.2)
EBV DNA (IU/mL), median (IQR)	400.00 (400.00, 2140.00)
Neutrophil-to-lymphocyte ratio	
≤3.5	100 (97.1)
>3.5	3 (2.9)
Therapy received	
TP (nab-paclitaxel)	61 (59.22%)
DP (docetaxel)	38 (36.89%)
GP (cisplatin + gemcitabine)	4 (3.88%)
PD-1 inhibitors	
Serplulimab	39 (37.86%)
Sintilimab	37 (35.92%)
Toripalimab	27 (26.21%)

Abbreviations: n, number of cases; SD, standard deviation; TNM stage, Tumor-Node-Metastasis stage; EBV DNA, Epstein-Barr Virus Deoxyribonucleic Acid; IU/mL, International Units per milliliter; IQR, Interquartile Range; PD-1 inhibitors, Programmed Cell Death Protein 1 Inhibitors.

Subgroup Analyses

To evaluate the variability in patient responses to different treatment regimens, detailed subgroup analyses were conducted (Figure 2). Patients younger than 65 years and those aged 65 years and older showed no significant difference in CCR ($p = 1.000$). Similarly, no significant differences were observed between patients with baseline EBV DNA levels ≤500 copies/mL compared to those with >500 copies/mL ($p = 0.859$). Although patients with stage III disease demonstrated a CCR rate of 71% (95% CI, 55–84%), compared to 62% for those with stage IVA (95% CI, 49–74%),

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Table 2 Efficacy of the Treatments

Index	n (%) Total (N=103)
Objective response rate (ORR)	100 (97)
Clinical complete response (CCR)	68 (66)
Partial response (PR)	32 (31)
Include also Stable Disease (SD)	5 cases
Progressive disease (PD)	1 case

Abbreviation: n, number of cases.

this difference was not statistically significant (p = 0.721). In the PD-1 inhibitors subgroup analysis, the ORR for serplulimab, toripalimab, and sintilimab was 100%, 100%, and 89%, respectively, with CCR rates of 69% (95% CI, 52–83%), 59% (95% CI, 41–75%), and 70% (95% CI, 50–86%). No statistically significant differences in efficacy were observed in serplulimab-based protocol and counterparts integrating the other two PD-1 inhibitors (Figure 3). Of the 103 patients included in the FAS, three patients who received single-agent IC were subsequently removed from the analysis.

Safety

To prevent rashes associated with the combination of immunotherapy and chemotherapy, prophylactically cetirizine tablets, fexofenadine hydrochloride tablets, vitamin C, and compound glycyrrhizin tablets were administered after chemotherapy. Despite this, 48 patients developed rashes of varying severity, but the overall extent was minor, and topical ointment AONe improved the condition. Neutropenia was the most common hematological toxicity, occurring in 100% of patients. Grade 3 or higher neutropenia occurred in 35% of patients. Grades 3 or higher anemia and thrombocytopenia were not observed (Table 3). As no concurrent chemotherapy was used, the overall response to radiation-induced oral mucositis was mild, with good patient tolerance and no significant weight loss.

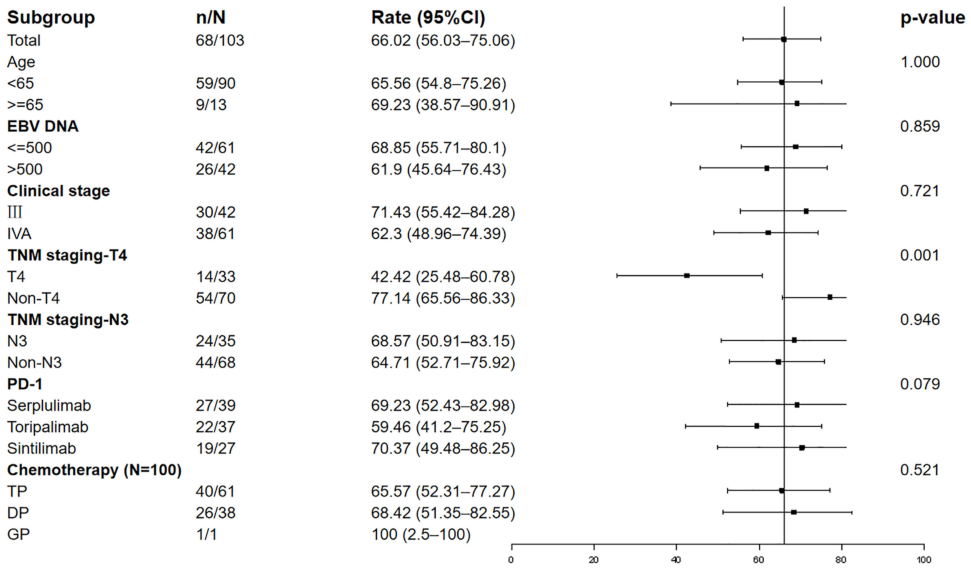

Figure 2 Forest plot of complete response rate in subgroup analyses.
Abbreviations: EBV DNA, Epstein-Barr Virus Deoxyribonucleic Acid; TNM staging, Tumor-Node-Metastasis staging; PD-1, Programmed Cell Death Protein 1 Inhibitors. TP, nab-paclitaxel; DP, docetaxel; GP, cisplatin + gemcitabine.

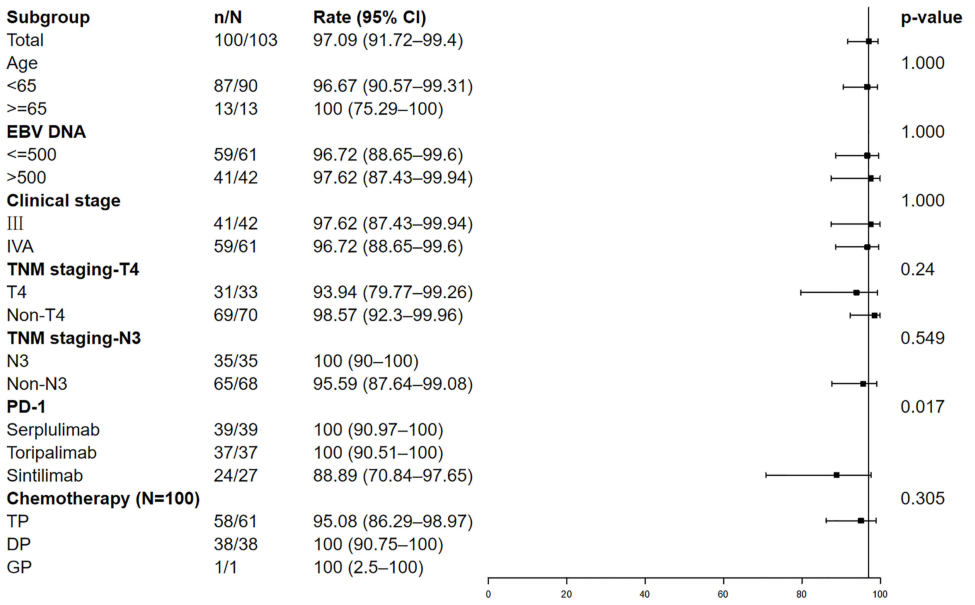

Figure 3 Forest plot of objective response rate in subgroup analyses.
Abbreviations: EBV DNA, Epstein-Barr Virus Deoxyribonucleic Acid; TNM staging, Tumor-Node-Metastasis staging; PD-1, Programmed Cell Death Protein 1 Inhibitors; TP, nab-paclitaxel; DP, docetaxel; GP, cisplatin + gemcitabine.

Survival Rates and Analysis

During the median follow-up period of 16.1 months (range 11.4–18.6 months), neither the median PFS nor OS was reached, indicating sustained treatment efficacy. The estimated two-year PFS and OS rates (Table 4) were exceptionally high at 91.9% (95% CI, 79.5–97.0%) and 93.2% (95% CI, 79.6–97.9%), respectively. These rates underscore the treatment's effectiveness.

The Kaplan-Meier curves for OS, PFS, and DOR visually depict these outcomes (Figures 4–6, Supplemental Figures 1–3). These curves provide insights into survival probabilities over time, illustrating the prolonged impact of the treatment regimen across different disease stages.

Additionally, the DOR, which reflects the period during which patients continue to benefit from therapy without disease progression, has not reached a median. This observation aligns with the sustained responses observed, further emphasizing the treatment's long-term efficacy. Detailed DOR data are represented in Figure 6, alongside other survival metrics.

Table 3 Common Treatment-Related Toxicities

Adverse Reaction	Grade I + II	Grade III + IV	n (%) Total (N=103)
Neutropenia	67	36	103 (100%)
Anemia	81	0	81 (78.6%)
Thrombocytopenia	9	0	9 (8.7%)
Liver toxicity	34	1	35 (34.0%)
Rashes	47	1	48 (46.6%)
Hypothyroidism	1	0	1 (0.97%)
Musculoskeletal pain	52	0	52 (50.5%)
Fatigue	37	0	37 (35.9%)
Nausea, vomiting	21	0	21 (20.4%)
Radiation-induced oral mucositis	93	10	103 (100%)
Limb numbness	23	0	23 (22.3%)

Abbreviation: n, number of cases.

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Table 4 Two-year Progression-Free Survival Rate (PFS) and Overall Survival Rates (OS)

Item	Total (N=103)
2-year PFS rate (95% CI)[a]	91.9 (79.5, 97.0)
2-year OS rate (95% CI)[a]	93.2 (79.6, 97.9)

Note: PFS (months) = (Date of first tumor progression/ censoring - First administration date + 1) / 30.4375. [a]95% confidence interval calculated using the Kaplan-Meier method. OS (months) = (Date of death/censoring - First administration date + 1) / 30.4375. [a]95% confidence interval calculated using the Kaplan-Meier method.
Abbreviations: n, number of cases; CI, Confidence Interval.

Further survival analysis across subgroups shows the 1-year and 2-year survival rates for serplulimab, sintilimab, and toripalimab. The absence of 2-year data for serplulimab, due to shorter follow-up periods, underscores the need for extended observation in future studies. Survival rates for sintilimab and toripalimab were plotted into survival curves to facilitate direct comparison across treatments. Additionally, statistical comparison of 1-year and 2-year survival rates provided significant insights into their relative efficacy.

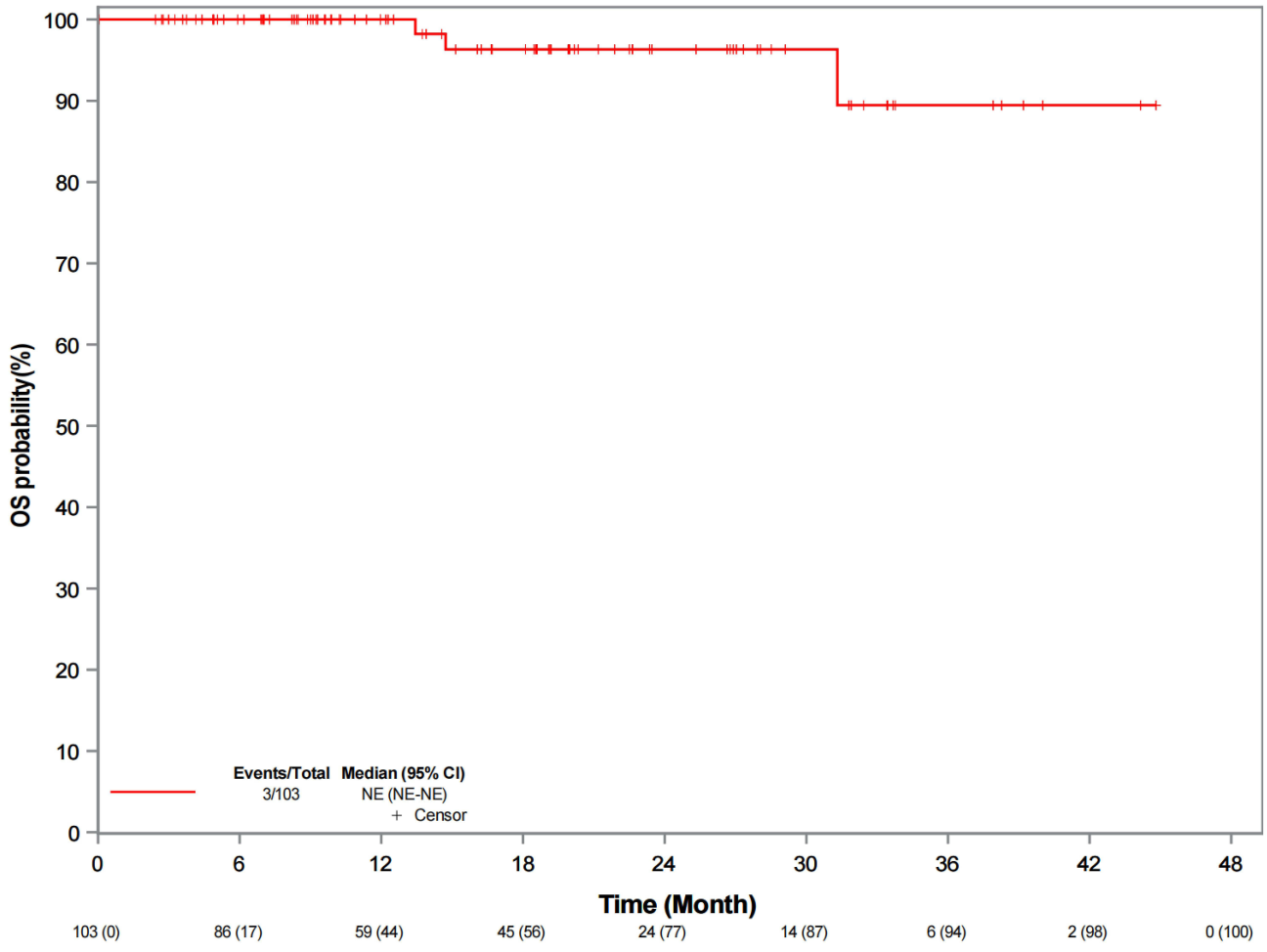

Figure 4 Overall survival (OS) (months) Kaplan-Meier curve.
Abbreviation: NE, Not Estimable.

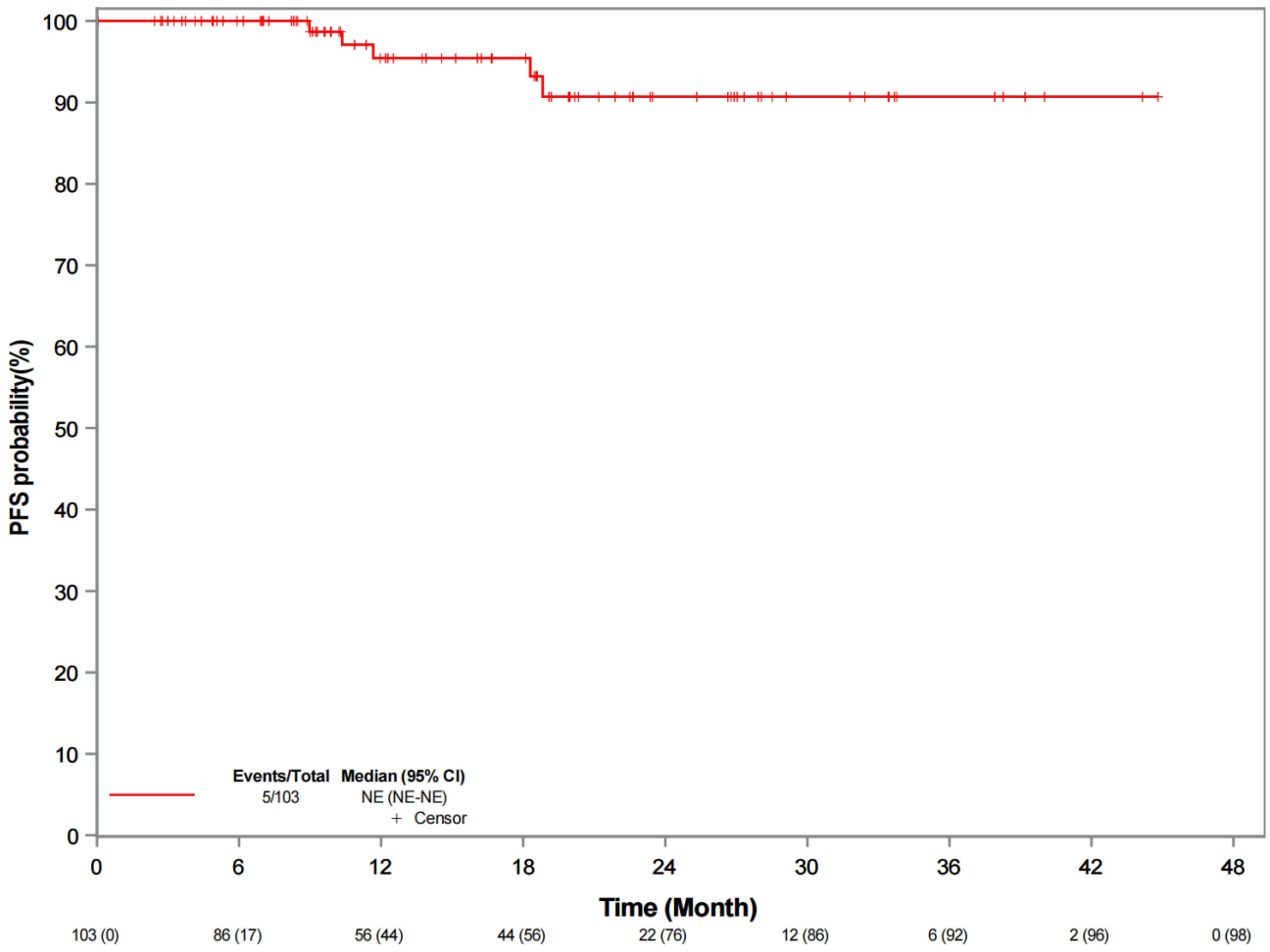

Figure 5 Progression-free survival (PFS) (months) Kaplan-Meier curve.
Abbreviation: NE, Not Estimable.

Discussion

In this retrospective study, we explored the efficacy and safety of a treatment protocol combining immune checkpoint inhibitors with IC, followed by nimotuzumab and IMRT, in patients with LANPC. The observed ORR of 97% and DCR of 99% highlight the considerable potential of this multifaceted approach to elicit favorable clinical responses in LANPC patients. During the median follow-up period of 16.1 months, neither median PFS nor OS was reached, indicating the sustained treatment efficacy. The estimated 2-year PFS and OS rates of 91.9% (95% CI, 79.5–97.0%) and 93.2% (95% CI, 79.6–97.9%), respectively, demonstrate prolonged treatment effectiveness. The anatomically concealed location of LANPC and its high sensitivity to radiotherapy make IMRT a preferred technique, as it delivers precise radiation doses to the tumor while sparing surrounding normal tissues. The efficacy of IMRT is well-supported by numerous studies and clinical trials, which have demonstrated its superior capability to reduce the risk of locoregional relapse and improve patients' quality of life during and after treatment compared to conventional techniques.[32,33]

Moreover, in a study involving 6908 patients treated with IMRT, OS, and PFS rates were notably enhanced by the inclusion of nimotuzumab, supporting the use of IMRT combined with targeted therapy in our current protocol.[34] While EGFR inhibitors combined with radiotherapy have shown significant benefits in LANPC treatment, the role of IC in treatment protocols continues to be an area of active research. Both the Chinese Society of Clinical Oncology (CSCO) and the American Society of Clinical Oncology (ASCO) endorse IC for managing LANPC.[35] Administering IC prior to definitive treatment reduces tumor size, improves local control, and decreases the risk of recurrence.[36] Importantly, IC also reduces the likelihood of distant metastasis, which is crucial for improving long-term survival outcomes.

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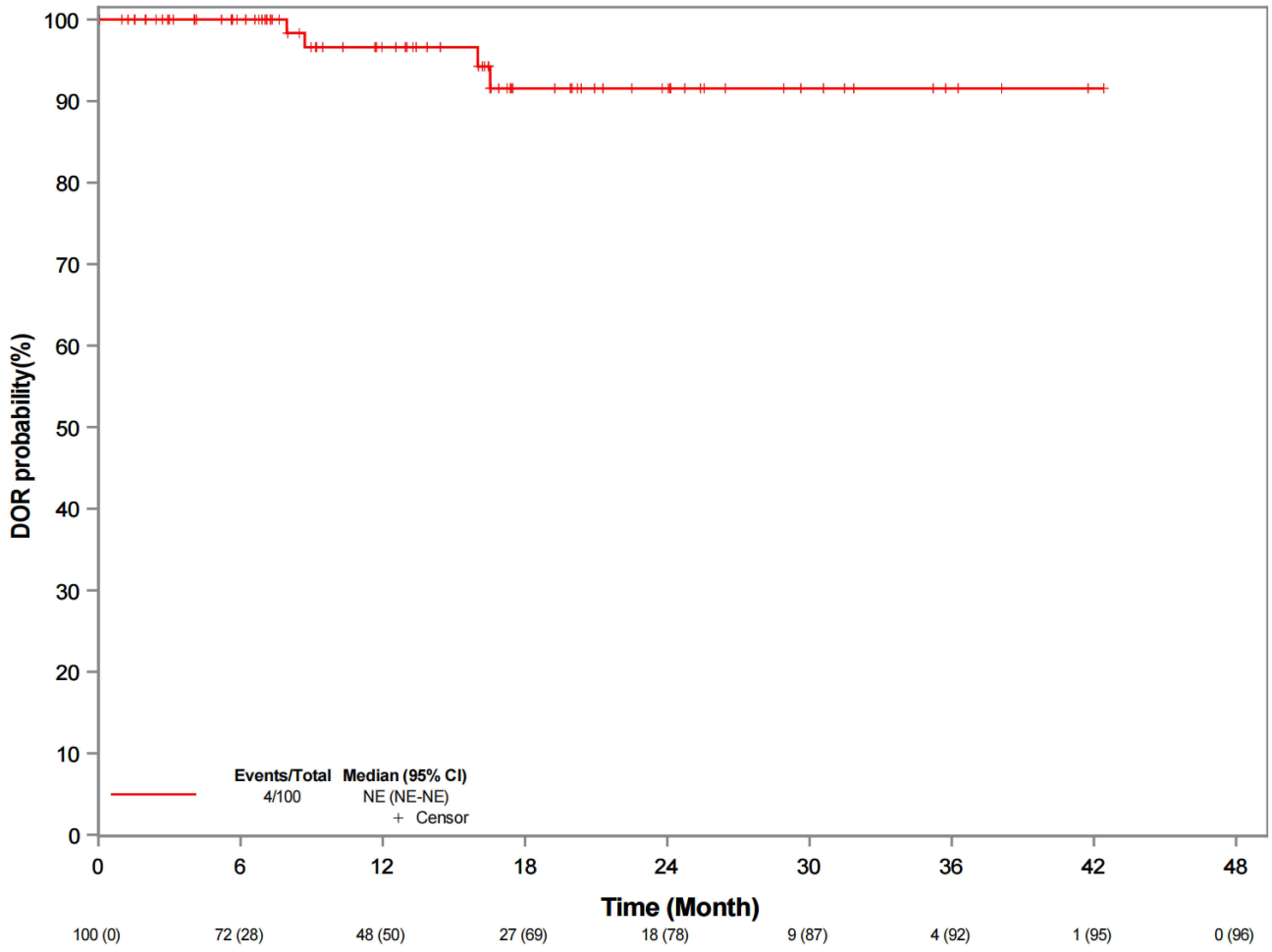

Figure 6 Duration of response (DOR) (months) Kaplan-Meier curve.
Abbreviation: NE, Not Estimable.

A propensity-matched analysis demonstrated a significant decrease in 5-year OS and DMFS when IC is combined with concurrent chemoradiotherapy (CCRT).[37]

In a retrospective study involving 213 LANPC patients, those classified as stage IV-A and N2-3 illustrated higher 5-year DMFS with the TPF regimen compared to the TP regimen, underscoring the importance of personalized IC regimen selection to optimize patient outcomes.[38] Multiple meta-analyses have compared different IC regimens for LANPC and prioritized paclitaxel-based IC regimens over others, including those with docetaxel, for their optimal efficacy in improving survival outcomes.[39,40] However, in our subgroup analysis, we revealed no differences in CCR and ORR between the DP and TP regimens. This discrepancy could be attributed to inherent efficacy differences among PD-1 inhibitors combined with IC regimens. The integration of serplulimab with docetaxel in the DP regimen may compensate for docetaxel's comparative disadvantages relative to paclitaxel, leading to comparable outcomes. However, the synergistic effect of serplulimab requires further prospective validation.[41,42]

As research in immunotherapy advances, PD-1 inhibitors are recognized for their significant anticancer potential. These immune checkpoint inhibitors enhance the anti-tumor immune response and durable immune memory by promoting tumor antigen release and immune activation, as well as improving the tumor microenvironment by reducing immunosuppressive cells and factors. Consistent with our findings, PD-1 inhibitors combined with chemotherapy have been shown to benefit LANPC patients in previous retrospective studies.[26] However, the selection of PD-1 inhibitors remains diverse, and comparative clinical evidence for choosing them in LANPC patients is still limited. A recent multicenter Phase 3 trial found that adding the PD-1 inhibitor sintilimab to treatment for LANPC patients indicated

superior long-term efficacy compared to the standard therapy group (36-month rates: 86% vs 76%), although it was associated with a higher incidence of adverse events (Grade 3–4, 74% vs 65%).[43] Similarly, a Phase 2 trial evaluating PD-1 inhibitors showed comparable results, with a 2-year PFS of 92.0% vs 74.0%, with a slightly higher rate of Grade 3 or higher adverse events (10% vs 0).[44] Further, an observational study comparing PD-1 blockades plus standard treatment (IC-CCRT) to IC-CCRT alone found improved efficacy after three cycles of induction chemotherapy (CCR rates: 24% vs 9%) without a significant difference in adverse events (47% vs 41%, $p = 0.396$).[45] In our study, the combination with serplulimab also demonstrated significant benefits for LANPC patients, showing comparable short-term efficacy to sintilimab and toripalimab. The outcomes for BOR (CR: 69% vs 70% vs 59%, $p = 0.128$, 0.374) and ORR (CR+PR: 100% vs 89% vs 100%, $p = 0.064$, NA) further suggest that serplulimab is also a viable option for clinical decision-making. However, clinical trials comparing the efficacy of treatment with and without serplulimab are still needed to support this finding. Notably, while combining immunotherapy with EGFR inhibitors can pose challenges due to toxic reactions, our analysis, fortunately, revealed that the integration of serplulimab did not increase the incidence of adverse events. Two patients in the serplulimab group with baseline renal impairment still showed good adherence to the regimen, indicating the overall safety and tolerability of this treatment approach. In this study, only one patient, who was not in the serplulimab group, progressed during the induction phase. This elderly female presented with a nasopharyngeal tumor that partially shrank and partially enlarged, subsequently brainstem compression. Three months after radiotherapy, despite achieving a CCR, the patient rapidly developed widespread liver and bone metastases, This case illustrates who progress during induction often have a very poor prognosis and are prone to metastases, potentially requiring more intensive combined treatment regimens. Additionally, we observed a patient with a history of hyperthyroidism who experienced chest tightness, shortness of breath, and tachycardia following PD-1 inhibitors. These symptoms of thyroid toxicity improved with symptomatic treatment using a β-blocker and methimazole, and no further thyroid toxicity occurred with continued PD-1 inhibitor use.

In our treatment protocol, we considered the economic burden on patients, particularly in resource-constrained settings. To balance clinical efficacy with cost, we limited PD-1 inhibitors to 4 doses during the neoadjuvant phase. Treatment was discontinued after inducing memory T-cell generation. Additionally, comparing our results with studies that have follow-up periods exceeding 40 months, while our follow-up was only 16 months, may not be optimal. Our study has several limitations, including a small patient cohort and a relatively short follow-up period, which limit thecomprehensive evaluation of PFS, OS, and DOR. Future studies should aim to expand the sample size and extend the follow-up period to validate our findings and optimize treatment protocols, thereby improving outcomes. Despite the overall promising results, our study also recorded three fatalities. The first patient, who was treated with sintilimab, experienced resistance to both chemotherapy and radiotherapy, likely due to genetic mutations and the overexpression of drug efflux pumps, which ultimately led to treatment failure and disease progression. The remaining two patients, treated with toripalimab, both diagnosed with stage T4 nasopharyngeal carcinoma, encountered significant due to the highly invasive and widespread nature of their tumors. This finding is consistent with our subgroup analysis that revealed lower CCR rates among those with stage T4 disease. To advance more effective treatment strategies for this subgroup, it is imperative to conduct further genomic and molecular biological studies to unravel the mechanisms driving tumor resistance. Moreover, exploring more precise radiotherapy techniques and targeted therapies could provide crucial insights into enhancing patient outcomes.

Conclusion

In conclusion, this study evaluates the combination of PD-1 inhibitors with IC, followed by nimotuzumab and IMRT in the treatment of LANPC. The combination demonstrated significant efficacy in achieving tumor control, with high response rates and a strong overall disease control profile. Additionally, the treatment protocol was well-tolerated, with manageable adverse events, highlighting its safety and feasibility.

Despite a relatively short follow-up period, the results suggest the potential for sustained long-term efficacy. This study underscores the importance of integrating PD-1 inhibitors with traditional treatment approaches to improve survival outcomes and disease control in LANPC. However, to validate these results and further optimize treatment protocols, larger prospective studies and randomized controlled trials are essential.

Data Sharing Statement

The datasets used and/or analysed during the current study are available from the corresponding author, Jiawei Chen, upon reasonable request.

Ethics Approval and Informed Consent

This study was approved by the ethics committee of Hainan General Hospital, Hainan Affiliated Hospital of Hainan Medical University (NO: 2024-719). Each patient provided informed consent. We declare that all patient data were kept strictly confidential, and our study complies with the Declaration of Helsinki.

Author Contributions

All authors made substantial contributions to the conception and design, acquisition of data, or analysis and interpretation of data; took part in drafting the article or revising it critically for important intellectual content; agreed to submit to the current journal; gave final approval of the version to be published; and agree to be accountable for all aspects of the work.

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Disclosure

Kebin Chen and Xiaopeng Huang are co-first authors for this study. The authors report no conflict of interest in this work.

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