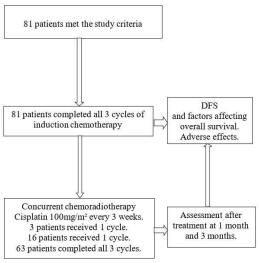
Oct 30, 2024

Treatment outcome of gemcitabine and cisplatin induction followed by concurrent chemoradiotherapy for stage III-IVA nasopharyngeal carcinoma: A retrospective study



DOI
https://dx.doi.org/10.17504/protocols.io.eq2ly6z9qgx9/v1

Son Nguyen Viet[1]

[1]NgheAn Oncology Hospital

Son Nguyen Viet
NgheAn Oncology Hospital

OPEN ACCESS

DOI: https://dx.doi.org/10.17504/protocols.io.eq2ly6z9qgx9/v1

Protocol Citation: Son Nguyen Viet 2024. Treatment outcome of gemcitabine and cisplatin induction followed by concurrent chemoradiotherapy for stage III-IVA nasopharyngeal carcinoma: A retrospective study. **protocols.io** https://dx.doi.org/10.17504/protocols.io.eq2ly6z9qgx9/v1

Protocol status: In development
We are still developing and optimizing this protocol

Created: October 24, 2024

Last Modified: October 30, 2024

Protocol Integer ID: 110895

Keywords: Nasopharyngeal carcinoma, chemoradiotherapy, Vietnam National Cancer Hospital, induction chemotherapy, disease-free survival, gemcitabine and cisplatin, nasopharyngeal cancer, nasopharyngeal carcinoma, iva nasopharyngeal cancer, iva nasopharyngeal carcinoma, cisplatin induction chemotherapy, concurrent chemoradiotherapy for stage iii, chemotherapy with concurrent chemoradiotherapy, treatment outcome of gemcitabine, concurrent chemoradiotherapy, efficacy of this therapy regimen, chemotherapy, patients with stage iii, therapy regimen, chemoradiotherapy, cisplatin induction, vietnam national cancer hospital, treating stage iii, treatment outcome, barr virus, cisplatin, initial treatment, treatment interruption

Disclaimer

Abstract

BackgroundCombining induction chemotherapy with concurrent chemoradiotherapy is becoming increasingly popular for treating stage III-IVA nasopharyngeal cancer (NPC), especially in patients with Epstein-Barr virus (EBV)-associated disorders. The objective of this study is to assess the efficacy of this therapy regimen in terms of treatment response and disease control.

Method

This retrospective descriptive study analyzed 81 patients with stage III-IVA nasopharyngeal cancer (excluding T3N0M0) who underwent gemcitabine and cisplatin induction chemotherapy, followed by concurrent chemoradiotherapy at the Vietnam National Cancer Hospital. Data for the study were collected between 03/06/2021 and 03/06/2024. The study also involved a longitudinal follow-up of the patients. The primary endpoint was disease-free survival (DFS), with secondary outcomes assessing factors influencing DFS and treatment-related toxicity.

Results

During the initial 3-month period, 76 out of 81 patients achieved a complete response (CR), whereas 5 out of 81 patients achieved a partial response. The duration of the follow-up period was 18.7 ± 5.3 months, and the rate of 2-year disease-free survival (DFS) was 77.6%. The disease-free survival (DFS) was influenced by patient-related variables including age group, N stage, disease stage, and treatment interruptions. The toxicity observed in grade 3 were neutropenia (17.3%) and mucositis (32.1%), whereas grade 4 toxic effect was characterized by nausea (2.4%). 2.6% of patients experienced Grade I and II delayed toxic effects, as well as Grade III anorexia.

Conclusion

The combination of Gemcitabine and Cisplatin as an initial treatment, followed by chemoradiotherapy, demonstrated a significant rate of positive response, effectively controlling the disease with tolerable consequences. Additional investigation is required to ascertain the long-term effectiveness and delayed adverse effects.

Attachments

DOCX

Manuscript.docx

86KB

Image Attribution

All images were created by the authors and are used with permission

Guidelines

- **Patient Selection Criteria**: Ensure that only patients meeting the inclusion criteria are enrolled. Obtain informed consent after explaining all risks, benefits, and potential outcomes of the treatment.
- **Chemotherapy Administration**: Adhere to the prescribed dosages for gemcitabine and cisplatin. Monitor patients closely for toxicity or adverse reactions during each cycle.
- **Radiation Safety**: During concurrent chemoradiotherapy, ensure all radiation safety protocols are followed to prevent unnec

Materials

Method

This study is a retrospective descriptive investigation that involves longitudinal follow-up from 03/06/2021 to 03/06/2024. It includes a total of 81 patients who were treated at the Vietnam National Cancer Hospital. The eligibility requirements are as follows: a) confirmation of NPC through pathological diagnosis, b) classification as stage III or IVA according to the AJCC 8th edition, c) undergoing treatment with Gemcitabine and Cisplatin induction chemotherapy followed by concurrent chemoradiotherapy, d) having an ECOG performance status score of 0-1, and e) possessing accessible patient data. The exclusion criteria include a) T3N0M0 stage, b) secondary cancers, c) chronic disorders such as heart failure or renal failure, d) prior treatment of the nasopharynx and/or neck region with radiotherapy, chemotherapy, or surgery, and e) pregnancy.
All patients at Vietnam National Cancer Hospital received the same treatment protocol. We documented the patient's attributes and their responses to therapy, and we monitored the occurrence of relapse, advancement, metastasis, the period without disease (disease-free survival), and harmful effects through follow-up phone calls and subsequent examinations. The data were accessed and analyzed by the authors for research purposes from July 1, 2024, to September 1, 2024.

Endpoints

The primary endpoint is disease-free survival (DFS) that refers to the period following the completion of initial cancer therapy, during which the patient is alive and free from any indications or symptoms of the cancer. Secondary endpoints encompass variables influencing DFS and adverse consequences.

Statistical analysis

Data were analyzed using SPSS version 20.0, employing the following methods:

- Descriptive statistics: Mean, standard deviation, maximum, and minimum values.
- Chi-square (χ^2) test: 95% confidence interval, $p < 0.05$.
- Kaplan-Meier method: Evaluating disease-free survival (DFS) duration, with group comparisons using the Log-rank test ($p < 0.05$).

Safety warnings

- **Toxicity Risk**: The combination of gemcitabine and cisplatin carries a risk of severe toxicity. Immediate medical attention is required if patients exhibit signs of serious toxicity, such as renal impairment or severe myelosuppression.
- **Radiation Exposure**: Ensure strict adherence to radiation protocols to prevent overexposure, which can lead to long-term health risks for b
- **Adverse Effects**: Closely monitor patients for severe side effects, including nausea, vomiting, neutropenia, or neuropathy. If side effects become intolerable, treatment may need to be paused or adjusted.
- **Early Termination**: If a patient develops severe contraindications or life-threatening side effects, early termination of the treatment protocol is advised to prevent further harm.

Ethics statement

Ethics Statement

This study was approved by the Ethics Committee in Biomedical Research of Hanoi Medical University (IRB – VN01001; IRB00003121). Oral informed consent was obtained from all patients for data collection and usage. Written consent could not be obtained due to the retrospective nature of the study, where patients had already completed their treatment. The Ethics Committee approved the use of oral consent in this context. Oral consent was documented by recording each patient's agreement in their medical records at the Vietnam National Cancer Hospital, following the ethical guidelines established by the Institutional Review Board.

Before start

- **Medical History**: Review the patient’s medical history to assess suitability for chemotherapy and radiation.
- **Physical Examination**: Perform a thorough examination to evaluate overall health status.
- **Laboratory Tests**: Conduct necessary tests (e.g., blood work, organ function tests) to ensure the patient is fit for treatment.

Treatment outcome of gemcitabine and cisplatin induction followed by concurrent chemoradiotherapy for stage III-IVA nasopharyngeal carcinoma: A retrospective study

1

Protocol references

1. Global Cancer Statistics 2022.pdf. Accessed July 23, 2024. [Online]. Available: https://doi.org/10.3322/caac.21262.
2. Global Cancer Statistics in Vietnam 2022.pdf. Accessed July 23, 2024. [Online]. Available: **http://doi: 10.1002/ijc.33588**.
3. Alsafadi N, Alqarni MS, Attar M, Mgarry R, Bokhari A. Nasopharyngeal Cancer: Prevalence, Outcome, and Impact on Health-Related Quality of Life at Princess Norah Oncology Center, Jeddah, Saudi Arabia. *Cureus*. 2020;12(5):e8199. https://doi:10.7759/cureus.8199.
4. Al-Sarraf M, LeBlanc M, Giri PG, et al. Chemoradiotherapy versus radiotherapy in patients with advanced nasopharyngeal cancer: phase III randomized Intergroup study 0099. *J Clin Oncol Off J Am Soc Clin Oncol*. 1998;16(4):1310-1317. https://doi:10.1200/JCO.1998.16.4.1310.
5. Sun Y, Li WF, Chen NY, et al. Induction chemotherapy plus concurrent chemoradiotherapy versus concurrent chemoradiotherapy alone in locoregionally advanced nasopharyngeal carcinoma: a phase 3, multicentre, randomised controlled trial. *Lancet Oncol*. 2016;17(11):1509-1520. https://doi:10.1016/S1470-2045(16)30410-7.
6. Zhang Y, Chen L, Hu GQ, et al. Gemcitabine and Cisplatin Induction Chemotherapy in Nasopharyngeal Carcinoma. *N Engl J Med*. 2019;381(12):1124-1135. https://doi:10.1056/NEJMoa1905287.
7. Zhang Y, Chen L, Hu GQ, et al. Final Overall Survival Analysis of Gemcitabine and Cisplatin Induction Chemotherapy in Nasopharyngeal Carcinoma: A Multicenter, Randomized Phase III Trial. *J Clin Oncol Off J Am Soc Clin Oncol*. 2022;40(22):2420-2425. https://doi:10.1200/JCO.22.00327.
8. Hong RL, Hsiao CF, Ting LL, et al. Final results of a randomized phase III trial of induction chemotherapy followed by concurrent chemoradiotherapy versus concurrent chemoradiotherapy alone in patients with stage IVA and IVB nasopharyngeal carcinoma-Taiwan Cooperative Oncology Group (TCOG) 1303 Study. *Ann Oncol Off J Eur Soc Med Oncol*. 2018;29(9):1972-1979. https://doi:10.1093/annonc/mdy249.
9. Li WF, Chen NY, Zhang N, et al. Concurrent chemoradiotherapy with/without induction chemotherapy in locoregionally advanced nasopharyngeal carcinoma: Long-term results of phase 3 randomized controlled trial. *Int J Cancer*. 2019;145(1):295-305. https://doi:10.1002/ijc.32099.
10. Wang Y, Wang C, He S, et al. Induction chemotherapy regimen of docetaxel plus cisplatin versus docetaxel, cisplatin plus fluorouracil followed by concurrent chemoradiotherapy in locoregionally advanced nasopharyngeal carcinoma: Preliminary results of an open-label, noninferiority, multicentre, randomised, controlled phase 3 trial. *eClinicalMedicine*. 2022;53. https://doi:10.1016/j.eclinm.2022.101625.

11. Zhao LN, Zhou B, Shi M, et al. Clinical outcome for nasopharyngeal carcinoma with predominantly WHO II histology treated with intensity-modulated radiation therapy in non-endemic region of China. *Oral Oncol*. 2012;48(9):864-869. https://doi:10.1016/j.oraloncology.2012.03.001.
12. Ou X, Zhou X, Shi Q, et al. Treatment outcomes and late toxicities of 869 patients with nasopharyngeal carcinoma treated with definitive intensity modulated radiation therapy: new insight into the value of total dose of cisplatin and radiation boost. *Oncotarget*. 2015;6(35):38381-38397. https://doi:10.18632/oncotarget.5420.
13. Lee AW, Foo W, Law SC, et al. Recurrent nasopharyngeal carcinoma: the puzzles of long latency. *Int J Radiat Oncol Biol Phys*. 1999;44(1):149-156. https://doi:10.1016/s0360-3016(98)00524-0.
14. Li JX, Lu TX, Huang Y, Han F, Chen CY, Xiao WW. [Clinical features of 337 patients with recurrent nasopharyngeal carcinoma]. *Chin J Cancer*. 2010;29(1):82-86. https://doi:10.5732/cjc.009.10412.
15. Yang Q, Cao SM, Guo L, et al. Induction chemotherapy followed by concurrent chemoradiotherapy versus concurrent chemoradiotherapy alone in locoregionally advanced nasopharyngeal carcinoma: long-term results of a phase III multicentre randomised controlled trial. *Eur J Cancer Oxf Engl 1990*. 2019;119:87-96. https://doi:10.1016/j.ejca.2019.07.007.
16. Peng H, Chen L, Zhang J, et al. Induction Chemotherapy Improved Long-term Outcomes of Patients with Locoregionally Advanced Nasopharyngeal Carcinoma: A Propensity Matched Analysis of 5-year Survival Outcomes in the Era of Intensity-modulated Radiotherapy. *J Cancer*. 2017;8:371-377. https://doi:10.7150/jca.16732.
17. Moon SH, Cho KH, Lee CG, et al. IMRT vs. 2D-radiotherapy or 3D-conformal radiotherapy of nasopharyngeal carcinoma : Survival outcome in a Korean multi-institutional retrospective study (KROG 11-06). *Strahlenther Onkol Organ Dtsch Rontgengesellschaft Al*. 2016;192(6):377-385. https://doi:10.1007/s00066-016-0959-y.
18. Kristensen CA, Kjaer-Kristoffersen F, Sapru W, Berthelsen AK, Loft A, Specht L. Nasopharyngeal carcinoma. Treatment planning with IMRT and 3D conformal radiotherapy. *Acta Oncol Stockh Swed*. 2007;46(2):214-220. https://doi:10.1080/02841860600635862.
19. Fountzilas G, Ciuleanu E, Bobos M, et al. Induction chemotherapy followed by concomitant radiotherapy and weekly cisplatin versus the same concomitant chemoradiotherapy in patients with nasopharyngeal carcinoma: a randomized phase II study conducted by the Hellenic Cooperative Oncology Group (HeCOG) with biomarker evaluation. *Ann Oncol Off J Eur Soc Med Oncol*. 2012;23(2):427-435. https://doi:10.1093/annonc/mdr116.
20. Yi J lin, Gao L, Huang X dong, et al. Nasopharyngeal carcinoma treated by radical radiotherapy alone: Ten-year

experience of a single institution. *Int J Radiat Oncol Biol Phys*. 2006;65(1):161-168. https://doi:10.1016/j.ijrobp.2005.12.003.
21. Liu X, Luo W, Liu M, Ye L, Sun Y, Xia Y. Treatment results and prognostic analysis of 1093 primary nasopharyngeal carcinoma: the experience of a single institution of Guangzhou in the beginning of the 21st century. *Chin-Ger J Clin Oncol*. 2008;7(4):187-195. https://doi:10.1007/s10330-007-0177-2.
22. Mao YP, Tang LL, Chen L, et al. Prognostic factors and failure patterns in non-metastatic nasopharyngeal carcinoma after intensity-modulated radiotherapy. *Chin J Cancer*. 2016;35:103. https://doi:10.1186/s40880-016-0167-2.
23. Au KH, Ngan RKC, Ng AWY, et al. Treatment outcomes of nasopharyngeal carcinoma in modern era after intensity modulated radiotherapy (IMRT) in Hong Kong: A report of 3328 patients (HKNPCSG 1301 study). *Oral Oncol*. 2018;77:16-21. https://doi:10.1016/j.oraloncology.2017.12.004.
24. Xu GZ, Li L, Zhu XD. Effect of interrupted time during intensity modulated radiation therapy on survival outcomes in patients with nasopharyngeal cancer. *Oncotarget*. 2017;8(23):37817-37825. https://doi:10.18632/oncotarget.13713.
25. Wang W, Feng M, Fan Z, Li J, Lang J. Clinical outcomes and prognostic factors of 695 nasopharyngeal carcinoma patients treated with intensity-modulated radiotherapy. *BioMed Res Int*. 2014;2014:814948. https://doi:10.1155/2014/814948.
26. Yao JJ, Zhang F, Gao TS, et al. Survival impact of radiotherapy interruption in nasopharyngeal carcinoma in the intensity-modulated radiotherapy era: A big-data intelligence platform-based analysis. *Radiother Oncol J Eur Soc Ther Radiol Oncol*. 2019;132:178-187. https://doi:10.1016/j.radonc.2018.10.018.
27. Jensen AR, Nellemann HM, Overgaard J. Tumor progression in waiting time for radiotherapy in head and neck cancer. *Radiother Oncol J Eur Soc Ther Radiol Oncol*. 2007;84(1):5-10. https://doi:10.1016/j.radonc.2007.04.001.
28. Guo R, Tang LL, Mao YP, et al. Proposed modifications and incorporation of plasma Epstein-Barr virus DNA improve the TNM staging system for Epstein-Barr virus-related nasopharyngeal carcinoma. *Cancer*. 2019;125(1):79-89. https://doi:10.1002/cncr.31741.
29. Li WZ, Wu HJ, Lv SH, et al. Assessment of Survival Model Performance Following Inclusion of Epstein-Barr Virus DNA Status in Conventional TNM Staging Groups in Epstein-Barr Virus-Related Nasopharyngeal Carcinoma. *JAMA Netw Open*. 2021;4(9):e2124721. https://doi:10.1001/jamanetworkopen.2021.24721.