

高雄榮民總醫院

鼻咽癌診療原則

2018年05月23日 第二版

鼻咽癌醫療團隊擬訂

注意事項：這個診療原則主要作為醫師和其他保健專家診療癌症病人參考之用。假如你是一個癌症病人，直接引用這個診療原則並不恰當，只有你的醫師才能決定給你最恰當的治療。

會議討論

上次會議：2017/12/27

本共識與上一版的差異

上一版	新版
1. 未標示與期別相關之主要檢查	1. 新增*標示，註明與期別相關之主要檢查(MRI* or CT of H&N*、Chest X-ray*、Bone scan*、Abd. Sono*) (p1)。

Carcinoma of Nasopharynx

高雄榮民總醫院 臨床診療指引 Ver.2 修訂於2018.05.23 Page 1 (Ref. 1)

WORK-UP	STAGING & TREATMENT	FOLLOW-UP
<ul style="list-style-type: none">• <u>History & PE</u>• <u>Biopsy & Pathology</u>• <u>Image</u><ul style="list-style-type: none">→ MRI* or CT of H&N* or PET→ Chest X-ray *→ Bone scan *→ Abd. Sono *→ ± PET scan• <u>EBV status</u>: viral load, ± EB-EA/NA, ± EB-VCA IgG/IgA• <u>Dental evaluation*</u><ul style="list-style-type: none">→ Panorex ± teeth extraction• <u>Hearing evaluation</u><ul style="list-style-type: none">→ PTA, tympanogram• <u>Multidisciplinary consultation</u> <p>(* 期別相關之主要檢查)</p>	<ul style="list-style-type: none">• <u>[T1, N0, M0]</u> Definitive RT • <u>[T1, N1-3, M0] or [T2-4, any N, M0]</u> 詳見 Page 2 • <u>[Any T, any N, M1]</u> 詳見 Page 3 • <u>[M1]</u> 詳見 Page 4	<ul style="list-style-type: none">• <u>[Post-Tx within 6 months]</u><ul style="list-style-type: none">→ Baseline MRI and/or CT→ every 1-2 month: PE • <u>[0.5-3 years after Tx]</u><ul style="list-style-type: none">→ Every 2-3 months: PE, nasopharyngoscopy→ Every 1 year: viral load, ± EB-EA/NA, ± EB-VCA IgG/IgA; MRI ± CT, CxR, bone scan & Abd. Sono as indicated • <u>[3-5 years after Tx]</u><ul style="list-style-type: none">→ Every 4-6 months: PE, nasopharyngoscopy • <u>[5 years later after Tx]</u><ul style="list-style-type: none">→ Every 6-12 months: PE, nasopharyngoscopy

Carcinoma of Nasopharynx

高雄榮民總醫院 臨床診療指引 Ver.2 修訂於2018.05.23 Page 2 (Ref. 1)

**Clinical T1, N1-3
or T2-4, any N, M0**

Primary treatment

CCRT ± Adjuvant CT 註1-3

High risk for distant failure (clinical cT4 or cN3) 建議加打 2-3 courses of adjuvant CT。

Induction CT + CCRT or RT 註1-3

2-3 courses for locally advanced cT4 or cN3；若只打1 cycle 且與後續CCRT間隔小於 2 weeks，視為CCRT only。

Definitive RT 註1

Poor medical condition or patient's preference。

Response and salvage treatment

Complete clinical response

Follow-up

Residual disease or clinically suspicious residue

Surgery if operable* #

Adjuvant CT註3

Salvage neck dissection is indicated if residual neck disease.

* Salvage nasopharyngectomy is indicated for operable residual primary tumor.

Carcinoma of Nasopharynx

高雄榮民總醫院 臨床診療指引 Ver.2 修訂於2018.05.23 Page 3 (Ref. 1)

Any T, any N, M1

Primary treatment

Platinum-based combination CT
± RT or CCRT 註1-3

CCRT 註1-2

Definitive RT 註1
Poor medical condition or patient's preference

Palliative care

Adjuvant treatment

Complete clinical response

Residual disease

Follow-up

Palliative CT 註3

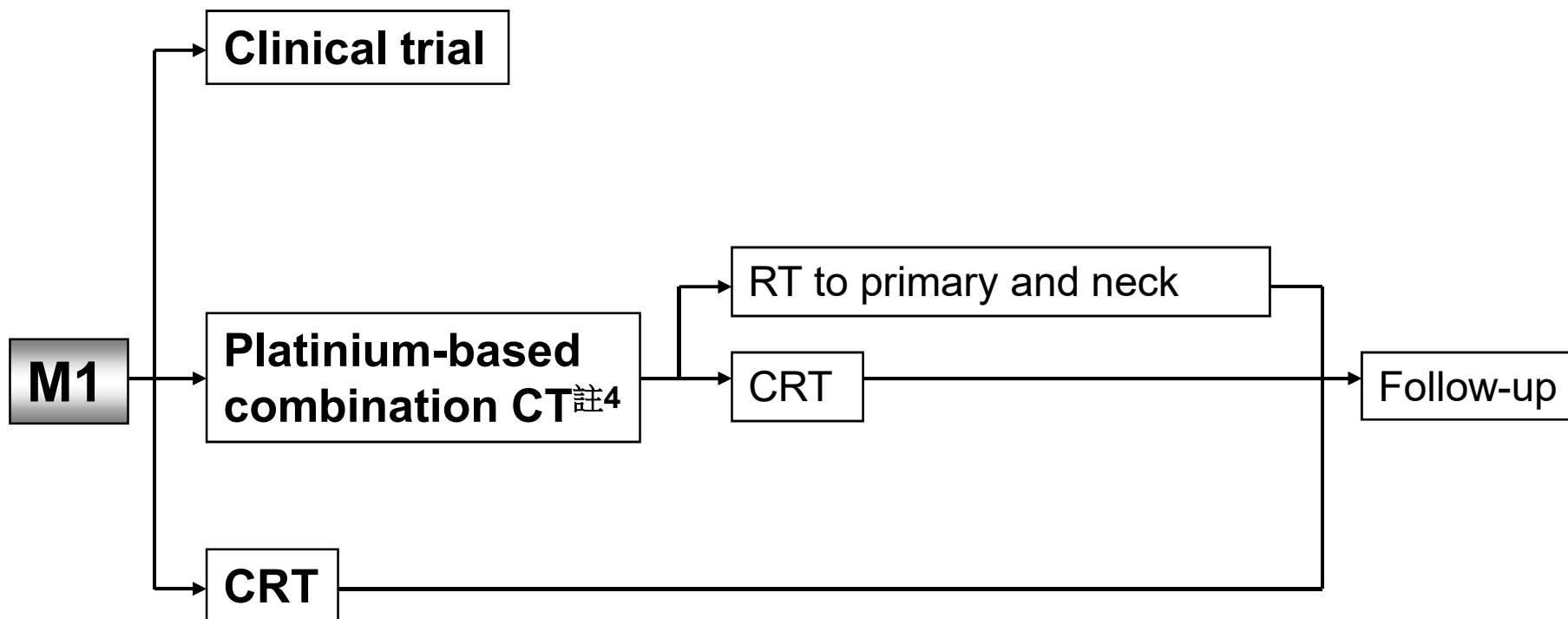
Palliative RT 註1

Supportive care

Surgery if applicable

Carcinoma of Nasopharynx

高雄榮民總醫院 臨床診療指引 Ver.2 修訂於2018.05.23 Page 4 (Ref. 1,13-14)



Carcinoma of Nasopharynx

高雄榮民總醫院 臨床診療指引 Ver.2 修訂於2018.05.23 Page 5 (Ref. 1,5,6)

註1

Principles of Radiotherapy

Definitive Radiotherapy

- Primary and gross adenopathy : 66 - 74 Gy (2.0 Gy/fraction)
- Neck uninvolved nodal stations : 44 - 64 Gy (1.6-2.0 Gy/fractions)

CCRT or RT

- RT alone if : Old age, Impaired renal function, Poor condition

Palliative RT

- Indicated in : Relieve local symptoms, Prevent debilitation such as spinal cord compression and pathological fracture, Achieve durable locoregional control.

Carcinoma of Nasopharynx

註2

高雄榮民總醫院 臨床診療指引 Ver.2 修訂於2018.05.23 Page 6 (Ref. 1,5-9)

Principles of Chemotherapy

Concurrent with RT

Regimen 1: q3w CDDP ± Cetuximab + RT 註5

- Cisplatin (80-100mg/ m²) q3w during R/T
- Cetuximab(400mg/ m²) loading dose first week, then Cetuximab(250mg/ m²) maintain dose D1 + Cisplatin (80-100mg/ m²) q3w D2 during R/T

Regimen 2: Weekly CDDP ± Cetuximab + RT 註5

- Cisplatin (30-40mg/ m²) weekly during R/T
- Cetuximab(400mg/ m²) loading dose first week, and then Cisplatin (30-40mg/ m²) weekly D1 + Cetuximab(250mg/ m²) maintain dose D2 during R/T

Regimen 3: q3w Carboplatin ± Cetuximab + RT 註5

- Carboplatin (AUC x 5mg) q3w during R/T
- Cetuximab(400mg/ m²) loading dose first week, then Cetuximab(250mg/ m²) maintain dose D1 + Carboplatin (AUC x 5mg) q3w D2 during R/T

Regimen 4: Weekly Cetuximab + RT 註5

- Cetuximab(400mg/ m²) loading dose first week, then Cetuximab(250mg/ m²) maintain dose during RT

Carcinoma of Nasopharynx

註3

高雄榮民總醫院 臨床診療指引 Ver.2 修訂於2018.05.23 Page 7 (Ref. 5-8)

Regimens of Chemotherapy

Induction or adjuvant, 建議2-3cycles

Regimen 1: q3-4 weeks CDDP ± F ± weekly Cetuximab 註5

- Cisplatin (20mg/ m²) D1-D5
- Fluorouracil (5-FU) (1000mg/ m²) D1-D5
- Cetuximab(400mg/ m²) loading dose first week, then weekly Cetuximab (250mg/ m²)

Regimen 2: q3-4 weeks CDDP ± F ± weekly Cetuximab 註5

- Cisplatin(80-100mg/ m²) D1
- Fluorouracil (5-FU) (1000mg/ m²) D2-D5
- Cetuximab(400mg/ m²) loading dose first week, then weekly Cetuximab (250mg/ m²)

Regimen 3: q3-4 weeks Carboplatin ± F ± weekly Cetuximab 註5

- Carboplatin (AUC x 5mg) D1
- Fluorouracil (5-FU) (1000mg/ m²) D2-D5
- Cetuximab(400mg/ m²) loading dose first week, then weekly Cetuximab (250mg/ m²)

Carcinoma of Nasopharynx

註3

高雄榮民總醫院 臨床診療指引 Ver.2 修訂於2018.05.23 Page 8 (Ref. 5-12)

Regimens of Chemotherapy

Induction or adjuvant, 建議2-3cycles

Regimen 4: q3-4 weeks T + P ± F ± weekly Cetuximab

- Taxotere(60 mg/ m²) D1 註5
- Cisplatin(60-75 mg/ m²) D1
- Fluorouracil (5-FU)(600-750mg/ m²) D2-D5
- Cetuximab (400mg/ m²) loading dose first week, then Cetuximab (250mg/ m²) maintain dose

Regimen 5: weekly Cetuximab 註5

- Cetuximab (400mg/ m²) loading dose first week, then Cetuximab (250mg/ m²) maintain dose

Regimen 6: oral Fluorouracil

- Ufur cap (tegafur 100mg+uracil 224mg) 2# TID
(Salvage or palliative CT中作為取代iv-formed 5-FU之替代藥物)

Carcinoma of Nasopharynx

註3

高雄榮民總醫院 臨床診療指引 Ver.2 修訂於2018.05.23 Page 9 (Ref. 5-12)

Regimens of Chemotherapy

Induction or adjuvant, 建議2-3cycles

Regimen 7: q4w GGGP (6 courses)

- Gemcitabine (1000mg/ m²) D1, 8, 15
- Cisplatin (50-60mg/ m²) D22

Regimen 8: P-FL

- Cisplatin (60mg/ m²) week 1, 3, 5, 7
- Fluorouracil (5-FU)(2500mg/ m²) + Leucovorin (250mg/ m²) mixed week 2, 4, 6, 8

Regimen 9: weekly Methotrexate

- Methotrexate (40-60mg/ m²)

Carcinoma of Nasopharynx

註4

高雄榮民總醫院 臨床診療指引 Ver.2 修訂於2018.05.23 Page 10 (Ref. 13-22)

Regimens of Chemotherapy

Recurrent or metastatic

Regimen 1: q3-4 weeks CDDP ± F

- Cisplatin(80-100mg/ m²) D1 or Cisplatin (20mg/ m²) D1-D5
- Fluorouracil (5-FU) (600-1000 mg/m²) D2-D5

Regimen 2: q3-4 weeks Carboplatin ± F

- Carboplatin (AUC x 5mg) D1
- Fluorouracil (5-FU) (1000mg/ m²) D2-D5

Regimen 3: q4w GGGP (6 courses)

- Gemcitabine (1000mg/ m²) D1, 8, 15
- Cisplatin (50-60mg/ m²) D22

Regimen 4: weekly Gemcitabine

- Gemcitabine (1000mg/ m²) D1

Carcinoma of Nasopharynx

註4

高雄榮民總醫院 臨床診療指引 Ver.2 修訂於2018.05.23 Page 11 (Ref. 13-22)

Regimens of Chemotherapy

Recurrent or metastatic

Regimen 5: q3-4 weeks T ± CDDP

- Taxotere(60 mg/ m²) D1 註5
- Cisplatin(60-75 mg/ m²) D1

Regimen 6: q3-4 weeks T ± Carboplatin

- Taxotere(60 mg/ m²) D1 註5
- Carboplatin (AUC x 5mg) D1

Regimen 7: q3-4 weeks Carboplatin ± weekly Cetuximab 註5

- Carboplatin (AUC x 5mg) D1
- Cetuximab(400mg/ m²) loading dose first week, then weekly Cetuximab (250mg/ m²)

Regimen 8: weekly Methotrexate

- Methotrexate (40-60mg/ m²)

Carcinoma of Nasopharynx

註5

高雄榮民總醫院 臨床診療指引 Ver.2 修訂於2018.05.23 Page 12

特殊用藥健保給付規定

Taxotere

- 頭頸部癌，限局部晚期且無遠端轉移之頭頸部鱗狀細胞癌且無法手術切除者。
- 與Cisplatin 及5-FU 併用，作為放射治療前的引導治療，限使用四個療程。

Cetuximab

- 限與放射線療法合併使用於局部晚期之口咽癌、下咽癌及喉癌患者，且符合下列條件之一：
 1. 年齡 ≥ 70 歲
 2. $Ccr < 50ml/min$
 3. 聽力障礙者 (聽力障礙定義為500Hz、1000Hz、2000Hz 平均聽力損失大於25 分貝)
 4. 無法耐受platinum-based 化學治療。
- 使用總療程以接受8 次輸注為上限。
- 需經事前審查核准後使用。

Carboplatin

- 限腎功能不佳 ($CCr < 60$) 或曾作單側或以上腎切除之惡性腫瘤患者使用。

Carcinoma of Nasopharynx

高雄榮民總醫院 臨床診療指引 Ver.2 修訂於2018.05.23 Page 13

References

1. NCCN Clinical Practice Guidelines in Oncology – Head and Neck Cancers Version 2. 2017
2. AJCC (American Joint Committee on Cancer) Manual for Staging of Cancer, 8th ed, Amin M, Edge S, Greene F, et al. (Eds), Springer-Verlag, New York 2017.
3. Lee SW, Nam SY, Im KC, et al. Prediction of prognosis using standardized uptake value of 2-[(18)F] fluoro-2-deoxy- d-glucose positron emission tomography for nasopharyngeal carcinomas. *Radiother Oncol* 2008;87:211–216.
4. Chan SC, Chang JT, Wang HM, et al. Prediction for distant failure in patients with stage M0 nasopharyngeal carcinoma: The role of standardized uptake value. *Oral Oncol* 2009;45: 52–58.
5. Wen-Shan Liu, Ming-Fang Wu, Hsien-Chun Tseng, Jung-Tung Liu, Jui-Hung Weng, Yueh-Chun Lee, Jong-Kang Lee. The role of pre-treatment FDG PET in nasopharyngeal carcinoma treated with intensity-modulated radiotherapy. *Int. J. Radiat. Oncol. Biol. Phys.* 2012 82(2): 561-566.
6. Chua DT, Ma J, Sham JS et al (2005): Long-term survival after cisplatin-based chemotherapy and radiotherapy for nasopharyngeal carcinoma: a pooled data analysis of two phase III trials *J Clin Oncol* 23: 1118-1124.
7. Al-Amro A, Al-Rajhi N, Khafaga Y et al. (2005): Neoadjuvant chemotherapy followed by concurrent chemo-radiation therapy in locally advanced nasopharyngeal carcinoma. *Int J Radiat Oncol Biol Phys* 62: 508-513
8. Chan AT, Ma BB, Lo YM et al. (2004): Phase II study of neoadjuvant carboplatin and paclitaxel followed by radiotherapy and concurrent cisplatin in patients with locoregionally advanced nasopharyngeal carcinoma: therapeutic monitoring with plasma Epstein-Barr virus DNA. *J Clin Oncol* 22:3053-3060
9. Johnson FM, Garden Asm Oakner HK et al, (2005): A phase I/II study of enoadjuvant chemotherapy followed by radiation with boost chemotherapy for advance T-stage nasopharyngeal carcinoma. *Int J Radiat Oncol Biol Phys* 63: 717-724
10. Chan AT, Leung SF, Ngan RK et al. (2005): Overall survival after concurrent cisplatin-radiotherapy compared with radiotherapy alone in locoregionally advanced nasopharyngeal carcinoma. *J natl Cancer Inst* 97:536-539
11. Hong RL, Ting LL, Ko JY, et al. Induction Chemotherapy With Mitomycin, Epirubicin, Cisplatin, Fluorouracil, and Leucovorin Followed by Radiotherapy in the Treatment of Locoregionally Advanced Nasopharyngeal Carcinoma. *J Clin Oncol* 19:4305-4313, 2001
12. Ma BB, Tannock IF, Pond GR, et al. Chemotherapy with gemcitabine-containing regimens for locally recurrent or metastatic nasopharyngeal carcinoma. *Cancer*. 2002; 95: 2516–2523.
13. Gibson MK, Li Y, Murphy B, et al. Randomized phase III evaluation of cisplatin plus fluorouracil versus cisplatin plus paclitaxel in advanced head and neck cancer (E1395): An Intergroup Trial of the Eastern Cooperative Oncology Group. *J Clin Oncol* 2005;23:3562-3567.
14. Forastiere AA, Metch B, Schuller DE, et al. Randomized comparison of cisplatin plus fluorouracil and carboplatin plus fluorouracil versus methotrexate in advanced squamous cell carcinoma of the head and neck: A Southwest Oncology Group Study. *J Clin Oncol* 1992;10:1245-1251.
15. Jin Y, Cai XY, Shi YX, et al. Comparison of five cisplatin-based regimens frequently used as the first-line protocols in metastatic nasopharyngeal carcinoma. *J Cancer Res Clin Oncol* 2012 Oct;138(10):1717-25.

Carcinoma of Nasopharynx

高雄榮民總醫院 臨床診療指引 Ver.2 修訂於2018.05.23

Page 14

References

16. Chan AT, Hsu MM, Goh BC, et al. Multicenter, phase II study of cetuximab in combination with carboplatin in patients with recurrent or metastatic nasopharyngeal carcinoma. *J Clin Oncol* 2005;23:3568-3576.
17. Burtneess B, Goldwasser MA, Flood W, et al. Phase III randomized trial of cisplatin plus placebo versus cisplatin plus cetuximab in metastatic/recurrent head and neck cancer: An Eastern Cooperative Oncology Group Study. *J Clin Oncol* 2005;23:8646-8654.
18. Jacobs C, Lyman G, Velez-García E, et al. A phase III randomized study comparing cisplatin and fluorouracil as single agents and in combination for advanced squamous cell carcinoma of the head and neck *J Clin Oncol* 1992;10:257-263.
19. Al-Sarraf M, Metch B, Kish J, et al. Platinum analogs in recurrent and advanced head and neck cancer: a Southwest Oncology Group and Wayne State University Study. *Cancer Treat Rep* 1987;71:732-736.
20. Catimel G, Verweij J, Mattijssen V, et al. Docetaxel (Taxotere): an active drug for the treatment of patients with advanced squamous cell carcinoma of the head and neck. EORTC Early Clinical Trials Group. *Ann Oncol* 1994;5:533-537.
21. Guardiola E, Peyrade F, Chaigneau L, et al. Results of a randomised phase II study comparing docetaxel with methotrexate in patients with recurrent head and neck cancer. *Eur J Cancer* 2004;40:2071-2076.
22. Zhang L, Zhang Y, Huang PY, et al. Phase II clinical study of gemcitabine in the treatment of patients with advanced nasopharyngeal carcinoma after the failure of platinum-based chemotherapy. *Cancer Chemother Pharmacol* 2008;61:33-38. Epub 2007 Mar 20.