

# 抗癌藥物治療指引

## 頭頸癌

### 討論日期

團隊修訂：2019/12/2

核備日期：2020/3/31

## 《頭頸癌抗癌藥物治療指引》

## Squamous Cell Cancers

Lip, Oral Cavity, Oropharynx, Hypopharynx, Glottic Larynx, Supraglottic Larynx, Ethmoid Sinus, Maxillary Sinus, Occult Primary

## Primary Systemic Therapy + Concurrent Radiotherapy

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Cisplatin	100	1	Q3W	3 with RT	1, 2

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Cetuximab	400* → 250	1	QW	8	3

\*1<sup>st</sup> dose 400 mg/m<sup>2</sup> then followed by 250 mg/m<sup>2</sup>

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Carboplatin	70	1-4	Q3W	3 with RT	4
5-FU	600	1-4	Q3W	3 with RT	

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Carboplatin	70	1-5	Q4W	2 with RT	5
5-FU	600	1-5	Q4W	2 with RT	

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Paclitaxel	30	1	QW	7	6
Cisplatin	20	2	QW	7	

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Paclitaxel	175	1	Q3W	Min 6	18
Cisplatin	75	1	Q3W	Min 6	

藥品名	劑量 mg/m <sup>2</sup>	給藥日*	頻率	週期	參考文獻
Cisplatin	100	1	Q3W	3 with RT	7
5-FU	1000*	1-5	Q3W	3 with RT	

\*Continuous infusion

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Cisplatin	60	1	Q2W	7 with RT	7
5-FU	800*	1-5	Q2W	7 with RT	

\*Continuous infusion

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Cisplatin	20	1-4	Q4W	2 with RT	19
5-FU	1000	1-4	Q4W	2 with RT	

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Cisplatin	100	1	Q3W	Min 6	18
5-FU	1000*	1-4	Q3W	Min 6	

\*Continuous infusion

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Carboplatin	100	1	QW	8	8
Paclitaxel	40	1	QW	8	

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Cisplatin	40	1	QW	4	9, 10

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Carboplatin	25	1-5	QW	5 with RT	16

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Cisplatin	50	1	Q2W	6	30
UFUR	800 mg* PO QD	1-14	Q2W	6	
Leucovorin	60 mg PO QD	1-14	Q2W	6	

\*Or 300 mg/m<sup>2</sup>

## Postoperative Chemoradiation

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Cisplatin	75-100	1	Q3W	3 with RT	11-13, 15, 31

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Cisplatin	30*	1	QW	6	14, 31

\*50 mg for 7-9 cycles with RT

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Cetuximab	400* → 250	1	QW	#	20
Cisplatin	30	1	QW	#	

\*1<sup>st</sup> dose 400 mg/m<sup>2</sup> then followed by 250 mg/m<sup>2</sup>  
#1<sup>st</sup> cycle before RT and continued cycles during RT

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Cetuximab	400* → 250	1	QW	#	20
Docetaxel	15	1	QW	#	

\*1<sup>st</sup> dose 400 mg/m<sup>2</sup> then followed by 250 mg/m<sup>2</sup>  
#1<sup>st</sup> cycle before RT and continued cycles during RT

## Induction/Sequential chemotherapy

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Docetaxel	75	1	Q3W	3-4	22, 24
Cisplatin	75	1	Q3W	3-4	
5-FU	750	1-5	Q3W	3-4	

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Docetaxel	75	1	Q3W	3	23
Cisplatin	100	1	Q3W	3	
5-FU	1000*	1-4 <sup>#</sup>	Q3W	3	

\*Continuous infusion for 24 h

<sup>#</sup> May extend to day 5 if tolerable

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Paclitaxel	175	1	Q3W	3	25
Cisplatin	100	2	Q3W	3	
5-FU	500	2-6	Q3W	3	

**Following induction, agents to be used with concurrent chemoradiation typically include weekly carboplatin or cisplatin or cetuximab**

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Cisplatin	100	1	QW	6 with RT	26

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Carboplatin	AUC 1.5	1	QW	7	27

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Cetuximab	400* → 250	1	QW	7 with RT	28

\*1<sup>st</sup> dose 400 mg/m<sup>2</sup> then followed by 250 mg/m<sup>2</sup>

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Cisplatin	50	1	Q2W	6	29
UFUR	800 mg* PO QD	1-14	Q2W		
Leucovorin	60 mg PO QD	1-14	Q2W		

\*Or 300 mg/m<sup>2</sup>

## 參考文獻

1. Forastiere AA, Zhang Q, Weber RS, et al. Long-term results of radiotherapy OG 91-11: a comparison of three nonsurgical treatment strategies to preserve the larynx in patients with locally advanced larynx cancer. *J Clin Oncol* 2013;31:845-852.
2. Adelstein DJ, Li Y, Adams GL, et al. An intergroup phase III comparison of standard radiation therapy and two schedules of concurrent chemoradiotherapy in patients with unresectable squamous cell head and neck cancer. *J Clin Oncol* 2003;21(1):92-98.
3. Bonner JA, Harari PM, Giralt J, et al. Radiotherapy plus cetuximab for locoregionally advanced head and neck cancer: 5-year survival data from a phase 3 randomised trial, and relation between cetuximab-induced rash and survival. *Lancet Oncol* 2010;11:21-28.
4. Denis F, Garaud P, Bardet E, et al. Final results of the 94-01 French Head and Neck Oncology and Radiotherapy Group randomized trial comparing radiotherapy alone with concomitant radiochemotherapy in advanced-stage oropharynx carcinoma. *J Clin Oncol* 2004;22:69-76.
5. Bourhis J, Sire C, Graff P, et al. Concomitant chemoradiotherapy versus acceleration of radiotherapy with or without concomitant chemotherapy in locally advanced head and neck carcinoma (GORTEC 99-02): an open-label phase 3 randomised trial. *Lancet Oncol* 2012;13:145-153.
6. Garden AS, Harris J, Vokes EE, et al. Preliminary results of Radiation Therapy Oncology Group 97-03: A randomized phase II trial of concurrent radiation and chemotherapy for advanced squamous cell carcinomas of the head and neck. *J Clin Oncol* 2004;22:2856-2864.
7. Taylor S, Murthy A, Vannetzel J, et al. Randomized comparison of neoadjuvant cisplatin and fluorouracil infusion followed by radiation versus concomitant treatment in advanced head and neck cancer. *J Clin Oncol* 1994;12:385-395.
8. Suntharalingam M, Haas ML, Conley BA, et al. The use of carboplatin and paclitaxel with daily radiotherapy in patients with locally advanced squamous cell carcinomas of the head and neck. *Int J Radiat Oncol Biol Phys* 2000;47:49-56.
9. Beckmann GK, Hoppe F, Pfreundner L, et al. Hyperfractionated accelerated radiotherapy in combination with weekly cisplatin for locally advanced head and neck cancer. *Head Neck* 2005;27:36-43.
10. Medina JA, Rueda A, de Pasos AS, et al. A phase II study of concomitant boost radiation plus concurrent weekly cisplatin for locally advanced unresectable head and neck carcinomas. *Radiother Oncol* 2006;79:34-38
11. Cooper JS, Pajak TF, Forastiere AA, et al. Postoperative concurrent radiotherapy and chemotherapy for high-risk squamous-cell carcinoma of the head and neck. *N Engl J Med* 2004;350:1937-1944
12. Bernier J, Dommenege C, Ozsahin M, et al. Postoperative irradiation with or without concomitant chemotherapy for locally advanced head and neck cancer. *N Engl J Med* 2004;350:1945-1952

13. Bernier J, Cooper JS, Pajak TF, et al. Defining risk levels in locally advanced head and neck cancers: A comparative analysis of concurrent postoperative radiation plus chemotherapy trials of the EORTC (#22931) and radiotherapyOG (# 9501). *Head Neck* 2005;27:843-850.
14. Bachaud JM, Cohen-Jonathan E, Alzieu C, et al. Combined postoperative radiotherapy and weekly cisplatin infusion for locally advanced head and neck carcinoma: final report of a randomized trial. *Int J Radiat Oncol Biol Phys* 1996 Dec 1;36:999-1004.
15. Cooper JS, Zhang Q, Pajak TF, et al. Long-term follow-up of the radiotherapyOG 9501/intergroup phase III trial: postoperative concurrent radiation therapy and chemotherapy in high-risk squamous cell carcinoma of the head and neck. *Int J Radiat Oncol Biol Phys* 2012;84:1198-1205.
16. Jeremic B, Milicic B, Dagovic A, et al. Radiation Therapy With or Without Concurrent Low-Dose Daily Chemotherapy in Locally Advanced, Nonmetastatic Squamous Cell Carcinoma of the Head and Neck. *J Clin Oncol*, 2004, 22:3540-3548
17. RTOG 0522: a randomized phase III trial of concurrent accelerated radiation and cisplatin versus concurrent accelerated radiation, cisplatin, and cetuximab [followed by surgery for selected patients] for Stage III and IV head and neck carcinomas. *Clin Adv Hematol Oncol* 2007;5: 79-81
18. 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
19. Soo KC, Tan EH, Wee J, et al. Surgery and adjuvant radiotherapy vs concurrent chemoradiotherapy in stage III/IV nonmetastatic squamous cell head and neck cancer: a randomised comparison. *Br J Cancer*. 2005;93:279-286
20. Harari PM, Harris J, Kies MS, et al. Postoperative chemoradiotherapy and cetuximab for high-risk squamous cell carcinoma of the head and neck: Radiation Therapy Oncology Group radiotherapyOG-0234. *J Clin Oncol*. 2014;32:2486-2495
21. Fietkau R, Lautenschläger C, Sauer R, et al. Postoperative concurrent radio-chemotherapy versus radiotherapy in high-risk SCCA of the head and neck: Results of the German phase III trial ARO 96–32006 ASCO Annual Meeting Proceedings (Post-Meeting Edition)24,(18S) 2006: 5507
22. Vermorken JB, Remenar E, van Herpen C, et al; EORTC 24971/TAX 323 Study Group. Cisplatin, fluorouracil, and docetaxel in unresectable head and neck cancer. *N Engl J Med* 2007;357(17):1695-1704.
23. Posner MR, Hershock DM, Blajman CR, et al. Cisplatin and fluorouracil alone or with docetaxel in head and neck cancer. *N Engl J Med* 2007;357(17):1705-1715
24. Pointreau Y, Garaud P, Chapet S, et al. Randomized trial of induction chemotherapy with cisplatin and 5-fluorouracil with or without docetaxel for larynx preservation. *J Natl Cancer Inst* 2009;101:498-506

25. Hitt R, López-Pousa A, Martínez-Trufero J, et al. Phase III study comparing cisplatin plus fluorouracil to paclitaxel, cisplatin, and fluorouracil induction chemotherapy followed by chemoradiotherapy in locally advanced head and neck cancer. *J Clin Oncol* 2005;23:8636-8645.
26. Chitapanarux I, Lorvidhaya V, Kamnerdsupaphon P, et al. Chemoradiation comparing cisplatin versus carboplatin in locally advanced nasopharyngeal cancer: Randomised, non-inferiority, open trial. *Eur J Cancer* 2007;43:1399-1406
27. Haddad R, O'Neill A, Rabinowits G, et al. Induction chemotherapy followed by concurrent chemoradiotherapy (sequential chemoradiotherapy) versus concurrent chemoradiotherapy alone in locally advanced head and neck cancer (PARADIGM): a randomised phase 3 trial. *Lancet Oncol.* 2013;14:257-4264
28. Lefebvre JL, Pointreau Y, Rolland F, et al. Induction chemotherapy followed by either chemoradiotherapy or bioradiotherapy for larynx preservation: the TREMPIN randomized phase II study. *J Clin Oncol* 2013;31:853-859.
29. Hung-Ming Wang, Cheng-Su Wang, Jen-Shi Chen, et al. Cisplatin, tegafur, and leucovorin: A moderately effective and minimally toxic outpatient neoadjuvant chemotherapy for locally advanced squamous cell carcinoma of the head and neck. *Cancer* 2002; 94 (11): 2982-2995.
30. Wang HM, Hsu CL, Hsieh CH, et al. Concurrent chemoradiotherapy using cisplatin, tegafur, and leucovorin for advanced squamous cell carcinoma of the hypopharynx and oropharynx. *Biomed J* 2014;37(3):133-40.
31. Noronha V, Joshi A, Patil VM, et al. Once-a-Week versus once-every-3-weeks cisplatin chemoradiation for Locally advanced head and neck cancer: a phase III randomized noninferiority trial. *J Clin Oncol* 2017:Jco2017749457.

## Recurrent, Unresectable, or Metastatic (incurable) Regimens

### 1<sup>st</sup> Line Therapy

#### Combination Therapy

藥品名*	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Cetuximab	400* → 250	1	QW		1
Cisplatin	100	1	Q3W	Max 6	
5-FU	1000	1-4	Q3W	Max 6	

\*1<sup>st</sup> dose 400 mg/m<sup>2</sup> then followed by 250 mg/m<sup>2</sup>

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Cetuximab	400* → 250	1	QW		1
Carboplatin	AUC 5	1	Q3W	Max 6	
5-FU	1000	1-4	Q3W	Max 6	

\*1<sup>st</sup> dose 400 mg/m<sup>2</sup> then followed by 250 mg/m<sup>2</sup>

#### Immunotherapy

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Pembrolizumab	200 mg	1	Q3W	34 (24 mo)	18
Cisplatin	100	1	Q3W	6	
5-FU	1000	1-4	Q3W	6	

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Pembrolizumab	200 mg	1	Q3W	34 (24 mo)	18
Carboplatin	AUC 5	1	Q3W	6	
5-FU	1000	1-4	Q3W	6	

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Pembrolizumab	200 mg	1	Q3W	34 (24 mo)	18, 19

#### Other combination therapy

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Docetaxel	65	1	Q3W		2
Carboplatin	AUC 6	1	Q3W		

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Paclitaxel	175	1	Q3W		3
Cisplatin	75	1	Q3W		

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Paclitaxel	175	1	Q3W		3
Carboplatin	AUC 6	1	Q3W		



藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Cetuximab	200* → 125	1	QW		4
Cisplatin	100	1	Q4W	2-6	

\*1<sup>st</sup> dose 200 mg/m<sup>2</sup> then followed by 125 mg/m<sup>2</sup>

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Cisplatin	100	1	Q3W	Min 6	3, 5
5-FU	1000	1-4	Q3W	Min 6	

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Cetuximab	400→250→500*	1	QW→QW→Q2W*		6
Docetaxel	75	1	Q3W	4	
Cisplatin	75	1	Q3W	4	

\*1<sup>st</sup> dose 400 mg/m<sup>2</sup> and 2<sup>nd</sup> dose 250 mg/m<sup>2</sup> QW then followed by 500 mg/m<sup>2</sup> Q2W

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Cetuximab	400→250→500*	1	QW→QW→Q2W*		15
Docetaxel	75	1	Q3W	4	
Carboplatin	AUC 5	1	Q3W	4	

\*1<sup>st</sup> dose 400 mg/m<sup>2</sup> and 2<sup>nd</sup> dose 250 mg/m<sup>2</sup> QW then followed by 500 mg/m<sup>2</sup> Q2W

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Paclitaxel	175	1	Q3W	2	16, 17
Cisplatin	75	1	Q3W	2	
Followed by					
Cetuximab	400* → 250	1	QW		
Cisplatin	75	1	Q3W	4	

\*1<sup>st</sup> dose 400 mg/m<sup>2</sup> then followed by 250 mg/m<sup>2</sup>

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Paclitaxel	175	1	Q3W	2	16, 17
Carboplatin	AUC 6	1	Q3W	2	
Followed by					
Cetuximab	400* → 250	1	QW		
Carboplatin	AUC 6	1	Q3W	4	

\*1<sup>st</sup> dose 400 mg/m<sup>2</sup> then followed by 250 mg/m<sup>2</sup>

## Single Agents

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Cisplatin	100	1	Q3-4W		7, 8

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Paclitaxel	80	1	QW	6	9

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Docetaxel	100	1	Q3W		10

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
5-FU	1000	1	Q3W		8

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Methotrexate	40	1	QW		11, 12

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Cetuximab	400* → 250	1	QW	Min 7	13

\*1<sup>st</sup> dose 400 mg/m<sup>2</sup> then followed by 250 mg/m<sup>2</sup>

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Capecitabine	1250 PO BID	1-14	Q3W	Min 2	14

\*三院有個別版本

## 參考文獻

1. Vermorken JB, Mesia R, Rivera F, et al. Platinum-based chemotherapy plus cetuximab in head and neck cancer. *N Engl J Med* 2008;359:1116-1127.
2. Samlowski WE, Moon J, Kuebler JP, et al. Evaluation of the combination of docetaxel/carboplatin in patients with metastatic or recurrent squamous cell carcinoma of the head and neck (SCCHN): a Southwest Oncology Group Phase II study. *Cancer Invest* 2007;25:182-188.
3. 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.
4. 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.
5. 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.
6. Guigay J, Fayette J, Dillies A-F, et al. Cetuximab, docetaxel, and cisplatin (TPEX) as first-line treatment in patients with recurrent or metastatic (R/M) squamous cell carcinoma of the head and neck (SCCHN): Final results of phase II trial GORTEC 2008-03 [abstract]. *J Clin Oncol* 2012;30(Suppl 15):Abstract 5505.
7. Burthess B, Goldwasser MA, Flood W, et al. Phase III Randomized Trial of Cisplatin Plus Placebo Compared With Cisplatin Plus Cetuximab in Metastatic/Recurrent Head and Neck Cancer: An Eastern Cooperative Oncology Group Study. *J Clin Oncol* 2005;23:8646-8654.

8. Jacobs C, Lyman G, Velez-Garcia 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.
9. Grau JJ, Caballero M, Verger E, et al. Weekly paclitaxel for platin-resistant stage IV head and neck cancer patients. *Acta OtoLaryngol* 2009;129:1294-1299.
10. 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. *Ann Oncol* 1994;5:533-537.
11. Stewart JS, Cohen EE, Licitra L, et al. Phase III study of gefitinib compared with intravenous methotrexate for recurrent squamous cell carcinoma of the head and neck [corrected]. *J Clin Oncol* 2009;27:1864-1871
12. 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 Aug;10(8):1245-51.
13. Vermorken JB, Trigo J, Hitt R, et al. Open-label, uncontrolled, multicenter phase II study to evaluate the efficacy and toxicity of cetuximab as a single agent in patients with recurrent and/or metastatic squamous cell carcinoma of the head and neck who failed to respond to platinum-based therapy. *J Clin Oncol*. 2007 Jun 1;25(16):2171-7.
14. Martinez-Trufero J, Isla D, Adansa JC, et al. Phase II study of capecitabine as palliative treatment for patients with recurrent and metastatic squamous head and neck cancer after previous platinum-based treatment. *Br J Cancer* 2010;102:1687-1691.
15. Joel Guigay UK, Ricard Mesia, Nadejda Vintonenko, Jean Bourhis, Anne Auperin. TPEXtreme randomized trial: TPEX versus Extreme regimen in 1st line recurrent/metastatic head and neck squamous cell carcinoma. *Journal of Clinical Oncology* 2015.
16. Price KA, Cohen EE. Current treatment options for metastatic head and neck cancer. *Curr Treat Options Oncol* 2012;13:35-46.
17. Herbst RS, Arquette M, Shin DM, et al. Phase II multicenter study of the epidermal growth factor receptor antibody cetuximab and cisplatin for recurrent and refractory squamous cell carcinoma of the head and neck. *J Clin Oncol* 2005;23:5578-5587.
18. Rischin D, Harrington KJ, Greil R, et al. Protocol-specified final analysis of the phase 3 KEYNOTE-048 trial of pembrolizumab (pembro) as first-line therapy for recurrent/metastatic head and neck squamous cell carcinoma (R/M HNSCC). *J Clin Oncol* 2019;37(suppl)6000-6000.
19. Burtneß B, Harrington KJ, Greil R, et al. KEYNOTE-048: Phase 3 study of first-line pembrolizumab (P) for recurrent/metastatic head and neck squamous cell carcinoma (R/M HNSCC). *ESMO 2018 Congress*.

## Nasopharynx Carcinoma

### Chemoradiation Followed by Adjuvant Chemotherapy

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Cisplatin	100	1	Q3W	3 with RT	1
Followed by					
Cisplatin	80	1	Q4W	3 after RT	
5-FU	1000	1-4	Q4W	3 after RT	

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Carboplatin	AUC 6	1	Q3W	3-5 with RT	2
Followed by					
Carboplatin	AUC 5	1	Q3W	2 after RT	
5-FU	1000*	1-4	Q3W	2 after RT	

\*Continuous infusion for 24 h

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Cisplatin	40	1	QW	7	3

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Cisplatin	50	1	Q2W	6	11
UFUR	800 mg* PO	1-14	Q2W		
Leucovorin	60 mg PO	1-14	Q2W		

\*Or 300 mg/m<sup>2</sup>

### Induction (Category 3)/Sequential Chemotherapy

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Docetaxel	70	1	Q3W	3	4
Cisplatin	75	1	Q3W	3	
5-FU	1000*	1-4	Q3W	3	
Followed by					
Cisplatin	100	1	Q3W	With RT	

藥品名*	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Docetaxel	60	1	Q3W	3	12
Cisplatin	60	1	Q3W	3	
5-FU	600	1-5	Q3W	3	
Followed by					
Cisplatin	100	1	Q3W	With RT	

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Docetaxel	75	1	Q3W	2	5
Cisplatin	75	1	Q3W	2	
Followed by					
Cisplatin	40	1	QW	With RT	

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Cisplatin	100	1	Q3W	3	6
5-FU	1000*	1-4	Q3W	3	

\*Continuous infusion for 24 h

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Epirubicin	75	1	Q3W	3	7
Paclitaxel	175	1	Q3W	3	
Cisplatin	75	2	Q3W	3	
Followed by					
Paclitaxel	60	1	QW	During RT	

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Cisplatin	40	1	QW	7 during RT	8

### Adjuvant CT (post RT or CCRT completion on day 29) (category 2B)

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Cisplatin	80	1	Q4W	3	9
5-FU	1000	1-4	Q4W	3	

### Following induction, agents to be used with concurrent chemoradiation typically include weekly cisplatin or carboplatin

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Cisplatin	40	1	QW	7	10

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Carboplatin	AUC 2	1	QW	6 (Max 7)	13

\*三院有個別版本

#### 參考文獻

1. Al-Sarraf M, LeBlanc M, Giri PG, Fu KK, et al. Chemoradiotherapy versus radiotherapy in patients with advanced nasopharyngeal cancer: phase III randomized Intergroup study 0099. J Clin Oncol. 1998 ;16:1310-1317.
2. Dechaphunkul T, Pruegsanusak K, Sangthawan D, et al. Concurrent chemoradiotherapy with carboplatin followed by carboplatin and 5-fluorouracil in locally advanced nasopharyngeal carcinoma. Head Neck Oncol. 2011;3:30.

3. Chen L, Hu CS, Chen XZ, et al. Concurrent chemoradiotherapy plus adjuvant chemotherapy versus concurrent chemoradiotherapy alone in patients with locoregionally advanced nasopharyngeal carcinoma: a phase 3 multicentre randomised controlled trial. *Lancet Oncol*. 2012;13:163-171.
4. Bae WK, Hwang JE, Shim HJ, et al. Phase II study of docetaxel, cisplatin, and 5-FU induction chemotherapy followed by chemoradiotherapy in locoregionally advanced nasopharyngeal cancer. *Cancer Chemother Pharmacol*. 2010;65:589-595.
5. Hui EP, Ma BB, Leung SF, et al. Randomized phase II trial of concurrent cisplatin-radiotherapy with or without neoadjuvant docetaxel and cisplatin in advanced nasopharyngeal carcinoma. *J Clin Oncol*. 2009;27:242-249.
6. Posner MR, Hershock DM, Blajman CR, et al. Cisplatin and fluorouracil alone or with docetaxel in head and neck cancer. *N Engl J Med* 2007;357(17):1705-1715.
7. Fountzilas G, Tolis C, Kalogera-Fountzila A, et al. Induction chemotherapy with cisplatin, epirubicin, and paclitaxel (CEP), followed by concomitant radiotherapy and weekly paclitaxel for the management of locally advanced nasopharyngeal carcinoma.
8. A Hellenic Cooperative Oncology Group phase II study. *Strahlenther Onkol*. 2005;181:223-230.
9. Muhyi al-Sarraf, Martine Leblanc, et al. Chemoradiotherapy versus radiotherapy in patients with advanced nasopharyngeal cancer: phase III randomized Intergroup study 0099. *J Clin Oncol* 1998; 16: 1310-1317.
10. Chan AT, Leung SF, Ngan RK, et al. Overall survival after concurrent cisplatin-radiotherapy compared with radiotherapy alone in locoregionally advanced nasopharyngeal carcinoma. *J Natl Cancer Inst*. 2005 Apr 6;97(7):536-539.
11. Concurrent chemoradiotherapy using biweekly cisplatin/tegafur plus uracil/leucovorin in stage III nasopharyngeal carcinoma. *J Clin Oncol*. 2005 23(16): 5510
12. 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: 1509–20.
13. Ou D, Blanchard P, Khoury CE, et al. Induction chemotherapy with docetaxel, cisplatin and fluorouracil followed by concurrent chemoradiotherapy or chemoradiotherapy alone in locally advanced non-endemic nasopharyngeal carcinoma. *Oral Oncology* 62 (2016) 114–121.

## Recurrent, Unresectable, or Metastatic (incurable) Regimens

### 1<sup>st</sup> Line Therapy

#### Preferred regimen

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Cisplatin	20-30*	1-3	Q3W	Max 6	5
Gemcitabine	1000	1, 8	Q3W	Max 6	

\*80 mg/m<sup>2</sup> in divided doses on 3 days

#### Other recommended regimen

#### Combination therapy

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Docetaxel	65	1	Q3W		1
Carboplatin	AUC 6	1	Q3W		

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Paclitaxel	175	1	Q3W	Min 6	2
Cisplatin	75	1	Q3W	Min 6	

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Carboplatin	AUC 6	1	Q3W	Min 6	2
Paclitaxel	175	1	Q3W	Min 6	

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Cisplatin	100	1	Q3W	Min 6	2, 3
5-FU	1000*	1-4	Q3W	Min 6	

\*Continuous infusion for 24 h

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Carboplatin	AUC 5	1	Q3W	Max 8	4
Cetuximab	400* → 250	1	QW		

\*1<sup>st</sup> dose 400 mg/m<sup>2</sup> then followed by 250 mg/m<sup>2</sup>

#### Single agents

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Cisplatin	100	1	Q3-4W	Min 4	6, 7

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Carboplatin	AUC 6	1	Q3W		14

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Paclitaxel	80	1	QW	6	8

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Docetaxel	100	1	Q3W		9

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
5-FU	1000	1	Q3W		7

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Methotrexate	40	1	QW		10, 11

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Gemcitabine	1000	1, 8, 15	Q4W		12

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Capecitabine	1250 PO BID	1-14	Q3W	Min 2	13

## 參考文獻

1. Samlowski WE, Moon J, Kuebler JP, et al. Evaluation of the combination of docetaxel/carboplatin in patients with metastatic or recurrent squamous cell carcinoma of the head and neck (SCCHN): a Southwest Oncology Group Phase II study. *Cancer Invest* 2007;25:182-188.
2. 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.
3. 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.
4. 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.
5. 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.
6. Burdese B, Goldwasser MA, Flood W, et al. Phase III Randomized Trial of Cisplatin Plus Placebo Compared With Cisplatin Plus Cetuximab in Metastatic/Recurrent Head and Neck Cancer: An Eastern Cooperative Oncology Group Study. *J Clin Oncol* 2005;23:8646-8654.
7. Jacobs C, Lyman G, Velez-Garcia 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.



8. Grau JJ, Caballero M, Verger E, et al. Weekly paclitaxel for platin-resistant stage IV head and neck cancer patients. *Acta OtoLaryngol* 2009;129:1294-1299.
9. 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. *Ann Oncol* 1994;5:533-537.
10. Stewart JS, Cohen EE, Licitra L, et al. Phase III study of gefitinib compared with intravenous methotrexate for recurrent squamous cell carcinoma of the head and neck [corrected]. *J Clin Oncol* 2009;27:1864-1871
11. 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 Aug;10(8):1245-51.
12. 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;61:33-8. Epub 2007 Mar 20.
13. Martinez-Trufero J, Isla D, Adansa JC, et al. Phase II study of capecitabine as palliative treatment for patients with recurrent and metastatic squamous head and neck cancer after previous platinum-based treatment. *Br J Cancer* 2010;102:1687-1691.
14. 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.