高 雄 榮 民 總 醫 院
鼻咽癌診療原則

2024年05月29日 第一版

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：2023/03/02

本共識與上一版的差異

上一版	新版
1. 將[Clinical staging] T1- T2, N1, M0 or T3,N0, M0 的部分調整成 T0(EBV+)-T2, N1, M0 or T3,N0, M0，做CCRT 2. 治療的部分將 [Clinical T3-4,N1-3,M0 or any T,N2-3M0]只做CCRT的證據等級從category 3提升到 category 2B，但仍排在最後 3. 放射治療建議時間由6-7週改為7-8週 4. 在recurrent或persistent disease with distant metastases病人建議做NGS genomic profiling 5. M1 ECOG PS 3 的病人治療選項加上 Single-agent systemic therapy	Global Changes 1.修改質子治療的論述: Proton therapy may be considered when photon-based therapy causes compromise of standard radiation dosing to tumor or postoperative volumes 2.註腳修改:在Image-guided (US or CT) needle biopsy of cystic neck nodes 增加 For unresectable or metastatic disease where there is a plan for systemic therapy,a core biopsy would allow for ancillary immune-genomic testing. 3.Oral UFUR(2#BID or 1#TID)可作為取代iv-formed 5-FU之替代藥物 4.Nutrition support應優先考慮腸道營養(NG, PEG)

會議討論

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上一版	新版
1. 將[Clinical staging] T1- T2, N1, M0 or T3,N0, M0 的部分調整成 T0(EBV+)-T2, N1, M0 or T3,N0, M0，做CCRT 2. 治療的部分將 [Clinical T3-4,N1-3,M0 or any T,N2-3M0]只做CCRT的證據等級從category 3提升到 category 2B，但仍排在最後 3. 放射治療建議時間由6-7週改為7-8週 4. 在recurrent或persistent disease with distant metastases病人建議做NGS genomic profiling 5. M1 ECOG PS 3 的病人治療選項加上 Single-agent systemic therapy	NASO-B 1.在復發、無法切除或轉移的疾病系統性治療部分提升 Cisplatin/gemcitabine + PD-1 inhibitor (eg, pembrolizumab or nivolumab)的位階

Nasopharyngeal cancer
Clinical staging AJCC 8th

Nasopharyngeal cancer TNM staging AJCC UICC 8th edition

Primary tumor (T)	
T category	**T criteria**
TX	Primary tumor cannot be assessed
T0	No tumor identified, but EBV-positive cervical node(s) involvement
Tis	Tumor *in situ*
T1	Tumor confined to nasopharynx, or extension to oropharynx and/or nasal cavity without parapharyngeal involvement
T2	Tumor with extension to parapharyngeal space, and/or adjacent soft tissue involvement (medial pterygoid, lateral pterygoid, prevertebreal muscles)
T3	Tumor with infiltration of bony structures at skull base, cervical vertebra, pterygoid structures, and/or paranasal sinuses
T4	Tumor with intracranial extension, involvement of cranial nerves, hypopharynx, orbit, parotid gland, and/or extensive soft tissue infiltration beyond the lateral surface of the lateral pterygoid muscle
Regional lymph nodes (N)	
N category	**N criteria**
NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Unilateral metastasis in cervical lymph node(s) and/or unilateral or bilateral metastasis in retropharyngeal lymph node(s), 6 cm or smaller in greatest dimension, above the caudal border of cricoid cartilage
N2	Bilateral metastasis in cervical lymph node(s), 6 cm or smaller in greatest dimension, above the caudal border of cricoid cartilage
N3	Unilateral or bilateral metastasis in cervical lymph node(s), larger than 6 cm in greatest dimension, and/or extension below the caudal border of cricoid cartilage
Distant metastasis (M)	
M category	**M criteria**
M0	No distant metastasis
M1	Distant metastasis

rognostic stage groups

hen T is...	**And N is...**	**And M is...**	**Then the stage group is...**
Tis	N0	M0	0
T1	N0	M0	I
T1, T0	N1	M0	II
T2	N0	M0	II
T2	N1	M0	II
T1, T0	N2	M0	III
T2	N2	M0	III
T3	N0	M0	III
T3	N1	M0	III
T3	N2	M0	III
T4	N0	M0	IVA
T4	N1	M0	IVA
T4	N2	M0	IVA
Any T	N3	M0	IVA
Any T	Any N	M1	IVB

tumor, node, metastasis; AJCC: American Joint Committee on Cancer; UICC: Union for International Cancer Control; EBV: Epstein-virus.

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Carcinoma of Nasopharynx

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WORK-UP

- History & PE & NP scopy
- NP biopsy ± Neck FNA
- Image

→ MRI* or CT* of H&N or PET/CT
→ Chest X-ray * (if PET/CT not done)
→ Bone scan * (if PET/CT not done)
→ Abd. Sono *
→ ± PET scan ± Chest CT

- EBV status: viral load, ± EB-EA/NA, ± EB-VCA IgG/IgA
- Dental evaluation

→ Panorex ± teeth extraction

- Hearing evaluation

→ PTA, tympanogram

- Multidisciplinary consultation

(± Fertility/reproductive, smoking cessation, ophthalmologic, nutrition,speech, swallowng and endocrine evaluation if indicated)

- Screening for HBV/HCV

(* 期別之相關之主要檢查)

STAGING & TREATMENT

- [c**T1,N0,M0**]
  詳見 *Page 2*
- [**cT2,N0,M0**]
  詳見 *Page 2*
- [**cT0(EBV+)-2, N1, M0 or cT3, N0, M0**]
  詳見 *Page 3*
- [**T3, N1, M0 or T4, N0-1, M0, Any T, N2-3, M0**]
  詳見 *Page 4*
- [**M1**]
  詳見 Page 5

FOLLOW-UP

- [Post-Tx within 6 months]

→Post-Tx baseline MRI and/or CT, EBV viral load,
→Every 2-3 months: PE, NP scopy± Neck Sono

- [0.5-3 years]

→Every 3-4 months: PE, NP scopy+/- EBV viral load,
→Every 1 yr: ± EB-EA/NA ± EB-VCA IgG/IgA, MRI and/or CT, CxR, WBBS & Abd. Sono as indicated, ±TSH, free T4*

- [3-5 years] → Every 4-6 months: PE, NP scopy
- [5 years later]

→ Every 6-12 months: PE, NP scopy
(*if RT, 6-12 months)
(AM cortisol, GH, free T4, prolactin, IGF-2, LH, FSH, ACTH, TSH, testosterone levels if RT to the skull base)

Carcinoma of Nasopharynx

Clinical T1,N0,M0

Primary treatment

Definitive RT to nasopharynx and elective RT to neck → Follow-up

Clinical T2,N0,M0

Primary treatment

Definitive RT ± concurrent systemic therapy if high-risk features @ → Follow-up

@Bulky tumor volume, high serum EBV DNA copy number

Carcinoma of Nasopharynx

Clinical T0(EBV+)-2, N1, M0 or T3, N0, M0

Primary treatment

CCRT ± induction or adjuvant CT註1-3 if high risk features@

若只打1cycle且與後續CCRT間隔小於2weeks，視為CCRT only

Response and salvage treatment

Complete clinical response → Follow-up

Residual disease or clinically suspicious residue → Surgery if operable＊ # / Adjuvant CT 註3

@Bulky tumor volume, high serum EBV DNA copy number
#Salvage neck dissection is indicated if residual neck disease.
＊Salvage nasopharyngectomy is indicated for operable residual primary tumor

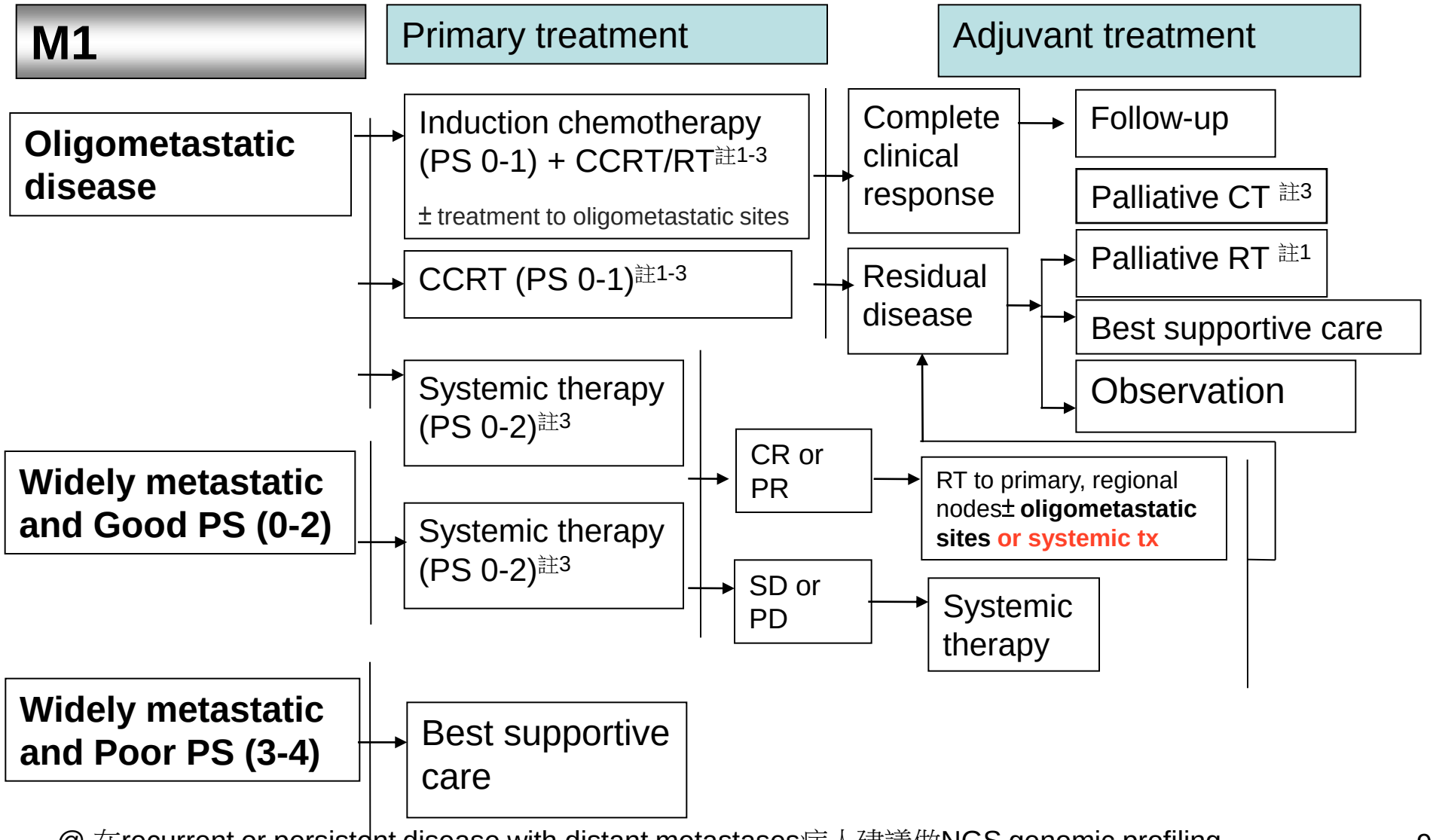
Carcinoma of Nasopharynx

Clinical T3, N1, M0 or T4, N0-1, M0, Any T, N2-3, M0

Primary treatment	Response and salvage treatment
Clinical trials	Complete clinical response → Follow-up
Induction CT+CCRT 註1-3 若只打1cycle且與後續CCRT間隔小於2weeks，視為CCRT only	Residual disease or clinically suspicious residue → Surgery if operable* #
CCRT ± Adjuvant CT 註1-3 High risk for distant failure (ex. cT4 or cN3 or 視病情需求) 建議加打 2-3 cycles of adjuvant CT。	→ Adjuvant CT 註3
RT 註1 Poor medical condition or patient's preference。	

#Salvage neck dissection is indicated if residual neck disease.
*Salvage nasopharyngectomy is indicated for operable residual primary tumor

Carcinoma of Nasopharynx



@ 在recurrent or persistent disease with distant metastases病人建議做NGS genomic profiling

Carcinoma of Nasopharynx

註1 高雄榮民總醫院 臨床診療指引 Ver.1 修訂於2024.05.29 *Page 6 (**Ref. 1,5,6**)*

Principles of Radiotherapy

Definitive Radiotherapy

•Primary and gross adenopathy：66 - 74 Gy (2.0-2.2 Gy/fraction)(in 7-8 weeks)

•Neck uninvolved nodal stations：

-Low risk-44-54 Gy (2 Gy/fraction)

-Intermediate risk: 54-63 Gy (1.6-2.0 Gy/fraction)

•Suspicious Neck lymph nodes：58.8-63.8Gy (2.2 Gy/fractions) (optional)

•Adaptive radiotherapy：direct CCRT, BW change more than 3-5 kg, high initial stage etc.(optional)

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 loco-regional control.

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註2 高雄榮民總醫院 臨床診療指引 Ver.1 修訂於2024.05.29 *Page 7* (***Ref. 1,5-9)***

Principles of Chemotherapy

Concurrent with RT

Regimen 1: q3w CDDP ± Cetuximab + RT 註5
- Cisplatin (80-100mg/ m^2) q3w during R/T
- Cetuximab(400mg/ m^2) loading dose first week, then Cetuximab(250mg/ m^2) maintain dose D1 + Cisplatin (80-100mg/ m^2) q3w D2 during R/T

Regimen 2: Weekly CDDP ± Cetuximab + RT 註5
- Cisplatin (30-40mg/ m^2) weekly during R/T
- Cetuximab(400mg/ m^2) loading dose first week, and then Cisplatin (30-40mg/ m^2) weekly D1 + Cetuximab(250mg/ m^2) maintain dose D2 during R/T

Regimen 3: q3w Carboplatin ± Cetuximab + RT 註5
- Carboplatin (AUC x 5mg) q3w during R/T
- Cetuximab(400mg/ m^2) loading dose first week, then Cetuximab(250mg/ m^2) maintain dose D1 + Carboplatin (AUC x 5mg) q3w D2 during R/T

Regimen 4: Weekly Cetuximab + RT 註5
- Cetuximab(400mg/ m^2) loading dose first week, then Cetuximab(250mg/ m^2) maintain dose during RT

Carcinoma of Nasopharynx

註3 高雄榮民總醫院 臨床診療指引 Ver.1 修訂於2024.05.29 *Page 8 (**Ref. 5-8**)*

Regimens of Chemotherapy

Induction or adjuvant, *建議2-3cycles*

Regimen 1 : q3w G[註5] P
- Gemcitabine (1000mg/ m^2) D1, 8
- Cisplatin (80mg/ m^2) D1

Regimen 2 : q3w G[註5] Carboplatin
- Gemcitabine (1000mg/ m^2) D1, 8
- Carboplatin (AUC x 5mg) D1

Regimen 3 : q3-4 weeks T + P ± F (5-FU or UFUR) ± weekly Cetuximab[註5]
- Taxotere(60 mg/ m^2) D1 [註5]
- Cisplatin(60-75 mg/ m^2) D1
- Fluorouracil (5-FU)(600-750mg/ m^2) D2-D5 or **UFUR**
- Cetuximab (400mg/ m^2) loading dose first week, then Cetuximab (250mg/ m^2) maintain dose

Regimen 4 : q3-4 weeks T + Carboplatin ± F (5-FU or UFUR) ± weekly Cetuximab[註5]
- Taxotere(60 mg/ m^2) D1 [註5]
- Carboplatin (AUC x 5mg) D1
- Fluorouracil (5-FU)(600-750mg/ m^2) D2-D5 or **UFUR**
- Cetuximab (400mg/ m^2) loading dose first week, then Cetuximab (250mg/ m^2) maintain dose

Carcinoma of Nasopharynx

註3 高雄榮民總醫院 臨床診療指引 Ver.1 修訂於2024.05.29 *Page 9* (***Ref. 5-12)***

Regimens of Chemotherapy

Induction or adjuvant, *建議2-3cycles*

Regimen 5: q3-4 weeks CDDP ± F (5-FU or UFUR) ± weekly Cetuximab 註5

- Cisplatin(80-100mg/ m^2) D1 or Cisplatin (20mg/ m^2) D1-D5
- Fluorouracil (5-FU) (1000mg/ m^2) D2-D5 or **UFUR**
- Cetuximab(400mg/ m^2) loading dose first week, then weekly Cetuximab (250mg/ m^2)

Regimen 6: q3-4 weeks Carboplatin ± F (5-FU or UFUR) ± weekly Cetuximab 註5

- Carboplatin (AUC x 5mg) D1
- Fluorouracil (5-FU) (1000mg/ m^2) D2-D5 or **UFUR**
- Cetuximab(400mg/ m^2) loading dose first wk, then weekly Cetuximab (250mg/ m^2)

Regimen 7: oral Fluorouracil

- Ufur cap (tegafur 100mg+uracil 224mg) 2# BID-TID

(作為取代 IV form 5-FU之替代藥物)

Carcinoma of Nasopharynx

註4 高雄榮民總醫院 臨床診療指引 Ver.1 修訂於2024.05.29 *Page 10 (**Ref. 13-30**)*

Regimens of Chemotherapy

Recurrent or metastatic disease

Regimen 1 (First line): q3w G[註5] ± P
- Gemcitabine (1000mg/ m^2) D1, 8
- Cisplatin (80mg/ m^2) D1

Regimen 2: q3w G ± P + Pembrolizumab / Nivolumab(q2w) [31, 32, 註5]
- Gemcitabine (1000mg/ m^2) D1, 8
- Cisplatin (80mg/ m^2) D1
- Pembrolizumab(200mg) D1 / Nivolumab(3mg/kg) D1

Regimen 3: q4w GGG[註5] ±P
- Gemcitabine (1000mg/ m^2) D1, 8, 15
- Cisplatin (50-60mg/ m^2) D22

Regimen 4: q3w G[註5] ± Carboplatin
- Gemcitabine (1000mg/ m^2) D1, 8
- Carboplatin (AUC x 5mg) D1

Carcinoma of Nasopharynx

註4 高雄榮民總醫院 臨床診療指引 Ver.1 修訂於2024.05.29 *Page 11* (***Ref. 13-30***)

Regimens of Chemotherapy

Recurrent or metastatic disease

Regimen 5: q3-4 weeks P ± F
- Cisplatin(80-100mg/ m2) D1 or Cisplatin (20mg/ m2) D1-D5
- Fluorouracil (5-FU) (600-1000 mg/m2) D2-D5

Regimen 6: q3-4 weeks Carboplatin ± F
- Carboplatin (AUC x 5mg) D1
- Fluorouracil (5-FU) (1000mg/ m^2) D2-D5

Regimen 7: q3-4 weeks T ± P
- Taxotere(60 mg/ m^2) D1 註5
- Cisplatin(60-75 mg/ m^2) D1

Regimen 8: q3-4 weeks T ± Carboplatin
- Taxotere(60 mg/ m^2) D1 註5
- Carboplatin (AUC x 5mg) D1

Carcinoma of Nasopharynx

註4 高雄榮民總醫院 臨床診療指引 Ver.1 修訂於2024.05.29 *Page 12 (**Ref. 13-30**)*

Regimens of Chemotherapy

Recurrent or metastatic disease

Regimen 9: q3-4 weeks Carboplatin ± weekly Cetuximab 註5
- Carboplatin (AUC x 5mg) D1
- Cetuximab(400mg/ m^2) loading dose first week, then weekly Cetuximab (250mg/ m^2)

Regimen 10: weekly Methotrexate
- Methotrexate (40-60mg/ m^2)

Regimen 11: q3 weeks Pembrolizumab
- Pembrolizumab(200mg) D1

Regimen 12: q2 weeks Nivolumab
- Nivolumab(3mg/kg) D1

Regimen 13: weekly Cetuximab 註5
- Cetuximab (400mg/ m^2) loading dose first week, then Cetuximab (250mg/ m^2) maintain dose

Carcinoma of Nasopharynx

註4 高雄榮民總醫院 臨床診療指引 Ver.1 修訂於2024.05.29 *Page 13 (**Ref. 13-30**)*

Regimens of Chemotherapy

Recurrent or metastatic disease

Regimen 14: oral Fluorouracil

•Ufur cap (tegafur 100mg+uracil 224mg) 2# BID-TID
(作為取代 IV form 5-FU之替代藥物)

Regimen 15: FL

•Leucovorin (250 mg/ m2) D1
•Fluorouracil (5-FU) (2500 mg/ m^2) D1

Regimen 16: P-FL

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

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註5 高雄榮民總醫院 臨床診療指引 Ver.1 修訂於2024.05.29 *Page 14*

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，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。

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。

- 限無法接受局部治療之復發及/或轉移性頭頸部鱗狀細胞癌，且未曾申報 cetuximab 之病患使用。需經事前審查核准後使用，使用總療程以18週為限，每9週申請一 次，需無疾病惡化情形方得繼續使 用。 (106/4/1)

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

註5 高雄榮民總醫院 臨床診療指引 Ver.1 修訂於2024.05.29 *Page 15*

特殊用藥健保給付規定

Pembrolizumab、Nivolumab

•一線:先前未曾接受全身性治療且無法手術切除之復發性或轉移性(第三期或第四期)頭頸部鱗狀細胞癌成人患者)(不含鼻咽癌) (CPS≧20)

• 二線:先前已使用過 platinum 類化學治療失敗後，又有疾病惡化的復發或轉移性(第三期或第四期)頭頸部鱗狀細胞癌成人患者(不含鼻咽癌) 。

•本類藥品與 cetuximab 僅能擇一使用，且治療失敗時不可互換。

• 符合下列條件：

1.病人身體狀況良好(ECOG≦1)

2.NYHA (the New York Heart Association) Functional Class I 或 II

3.GOT<60U/L及GPT<60U/L，且T-bilirubin<1.5mg/dL；Creatinine<1.5mg/dL，且 eGFR>60mL/min/1.73m2

4.PD-L1 表現量一線:CPS≧20; 二線:TPS≧50%, TC≧10%

• 初次申請以12 週為限，申請時需檢附以下資料：病理或細胞檢查報告、生物標記(PD-L1)表現量檢測報告、病人身體狀況良好(ECOG≦1)及心肺與肝腎功能之評估資料、符合 i-RECIST 定義之影像檢查及報告(上述影像檢查之給付範圍不包括PET)、先前已接受過之治療與完整用藥資料、使用免疫檢查點抑制劑之治療計畫(treatment protocol)。

•用藥後每 12 週評估一次，以 i-RECIST 或 mRECIST 標準評定反應，依下列原則給付：

I. 有療效反應者(PR 及 CR)得繼續使用；

II. 出現疾病惡化(PD)或出現中、重度或危及生命之藥物不良反應時，應停止使用；

III. 疾病呈穩定狀態者(SD)，可持續再用藥 4 週，並於 4 週後再次評估，經再次評估若為 PR、CR 者，得再繼續使用 12 週。若仍為 SD 或已 PD 者，應停止使用。

Carcinoma of Nasopharynx

特殊用藥健保給付規定

Gemcitabine

限用於：

1.晚期或無法手術切除之非小細胞肺癌及胰臟癌病患。

2.晚期膀胱癌病患。

3.Gemcitabine與paclitaxel併用，可使用於曾經使用過anthracycline之局部復發且無法手術切除或轉移性之乳癌病患。

4.用於曾經使用含鉑類藥物(platinum-based) 治療後復發且間隔至少6個月之卵巢癌，作為第二線治療。

5.無法手術切除或晚期或復發之膽道癌(含肝內膽管)病患。

備註：頭頸癌與鼻咽癌目前無健保給付

Carcinoma of Nasopharynx

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