高 雄 榮 民 總 醫 院
口腔癌診療原則

2021年04月28日 第一版

頭頸癌醫療團隊擬訂

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：2020/05/06

本共識與上一版的差異

上一版	新版
1. 在Workup加入± Neck FNA以及± Chest CT 2. 在Follow up 加入±TSH for irradiated neck 3. 在Clinical T1-2, N0, M0治療中加入SLN biopsy 4. 在Recurrent, unresectable, metastatic的化療Regimen提升immunotherapy順序，並加入合併使用化療的選項	1.Workup中加入上消化道內視鏡檢查(PES) 2. Workup中的Multidisciplinary consultation加上會診項目Fertility/reproductive, smoking cessation 3.Follow-up的Every 1 year排的檢查項目加上 As clinically indicated 4. [Clinical T1-2, N0, M0]，if positive margin，adjuvant treatment的Re-resection和 RT之間加上”or” 5. [Clinical T3, N0; T1-3, N1-3; T4a-resectable T4b, any N; M0]，if positive margin，adjuvant treatment的re-resection or RT改成re-resection and RT 6. [Recurrent, unresectable, metastatic]化療regimen，把immunotherapy順序往前調升，將EXTREME Regimen順序後移。 7.M1的部分，PS2、PS3增加Palliative RT 或 palliative surgery

Carcinoma of Oral Cavity

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WORK-UP

- History& PE

(pack yr smoked)

- Biopsy & Pathology
- Image

→ MRI*or CT of H&N* or PET

→ Chest X-ray ± Chest CT

→ Bone scan* (if PET/CT not done)

→ Abd. Sono*

→ ± Neck Sono

→ ± PES

- Dental evaluation

→ Panorex

→ ± teeth extraction

- Multidisciplinary consultation

(± Fertility/reproductive, smoking cessation)

± Swallowing evaluation

•± p16 status

(* 期別之相關之主要檢查)

STAGING & TREATMENT

- [T1-2, N0, M0]

詳見 *Page 2*

- [T3, N0; T1-3, N1-3; T4a-resectable T4b, any N, M0]

詳見 *Page 3*

- [Inoperable status]

詳見 Page 4

- [M1]

詳見Page 5

FOLLOW-UP

- [Post-Tx within 6 months]

→ Every 1-2 months: PE

→ Baseline MRI or CT

→ ± Neck Sono

- [0.5-3 years after Tx]

→ Every 2-3 months: PE

→ Every 1 year: H & N MRI or CT, CxR, Bone scan & Abd. Sono ± Neck Sono As clinically indicated

±TSH, free T4*

As clinically indicated

- [3-5 years after Tx]

→ Every 4-6 months: PE

- [5 years later after Tx]

→ Every 6-12 months: PE

(*if RT, every 6-12 months)

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Clinical T1-2, N0, M0

Primary treatment

Resection of primary ± ND, unil. or bil.# ± SLN biopsy

Pathological features	Adjuvant Treatment
Adverse features*(-), N0	Follow-up
Adverse features *(-), N1	RT註1 or follow-up
Positive margin	Re-resection, or RT or CRT註1-2 (T2 only)
ENE(Extranodal extension)	CRT or RT註1-2 or follow-up
Other adverse features(+)	RT or CRT註1-2 or follow-up

Definite RT$, 註1

Residual disease	Surgery
Complete clinical response	Follow-up

#Depth of invasion≧4mm可考慮Elective ND(依腫瘤厚度、位置、SLN biopsy結果而定)或close follow up

*Adverse features: extranodal extension, positive or close margins, pT3 or pT4 primary, pN2 or pN3 nodal disease, nodal disease in level IV or V, perineural invasion, vascular invasion, lymphatic invasion

$RT: external beam RT(EBRT)± brachytherapy alone

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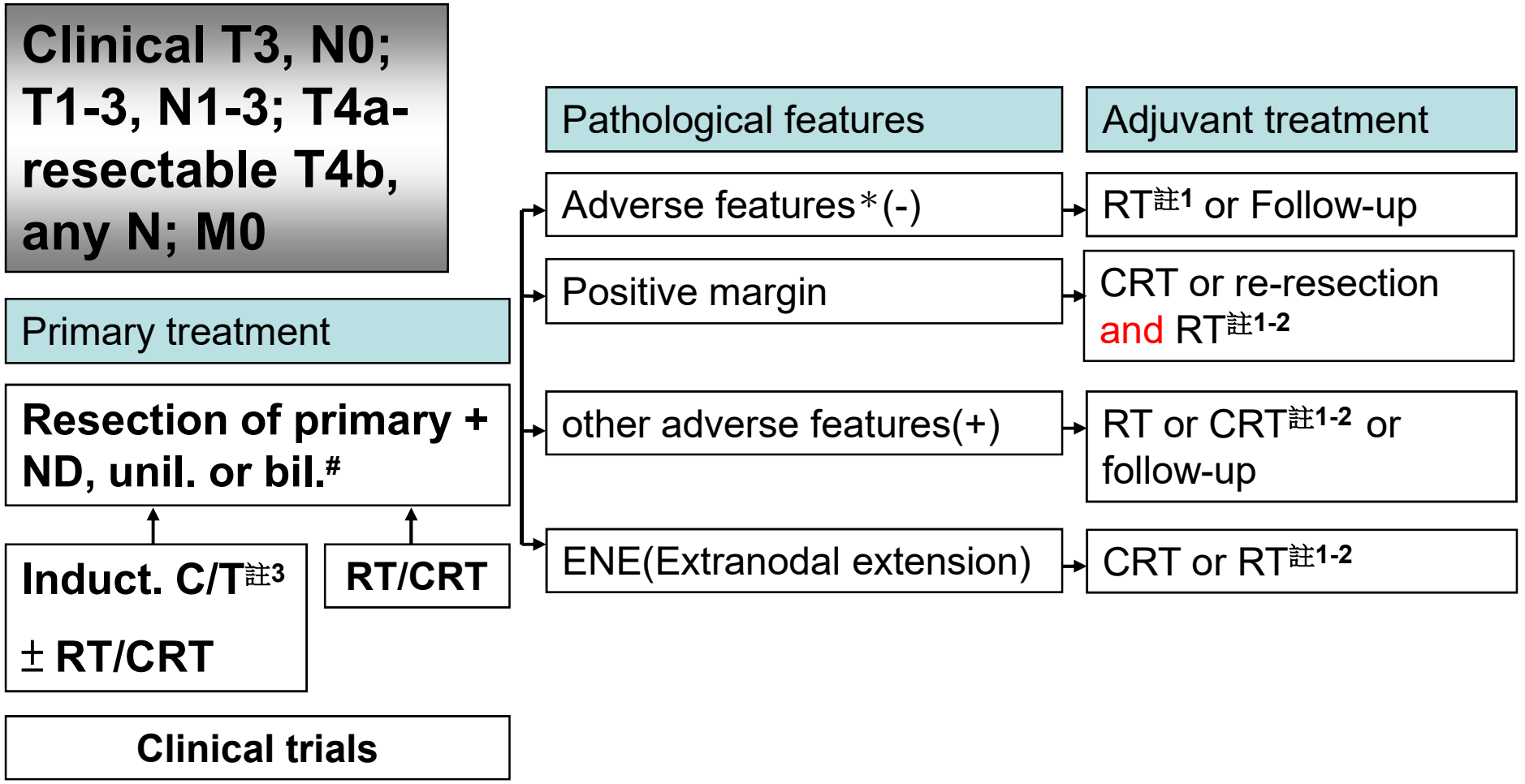

＃Therapeutic neck dissection, level依cN status及腫瘤位置而定

＊Adverse features：Extranodal extension, positive or close margins, pT3 or pT4 primary, N2 or N3 nodal disease, nodal disease in levels IV or V, perineural invasion, lymphovascular invasion

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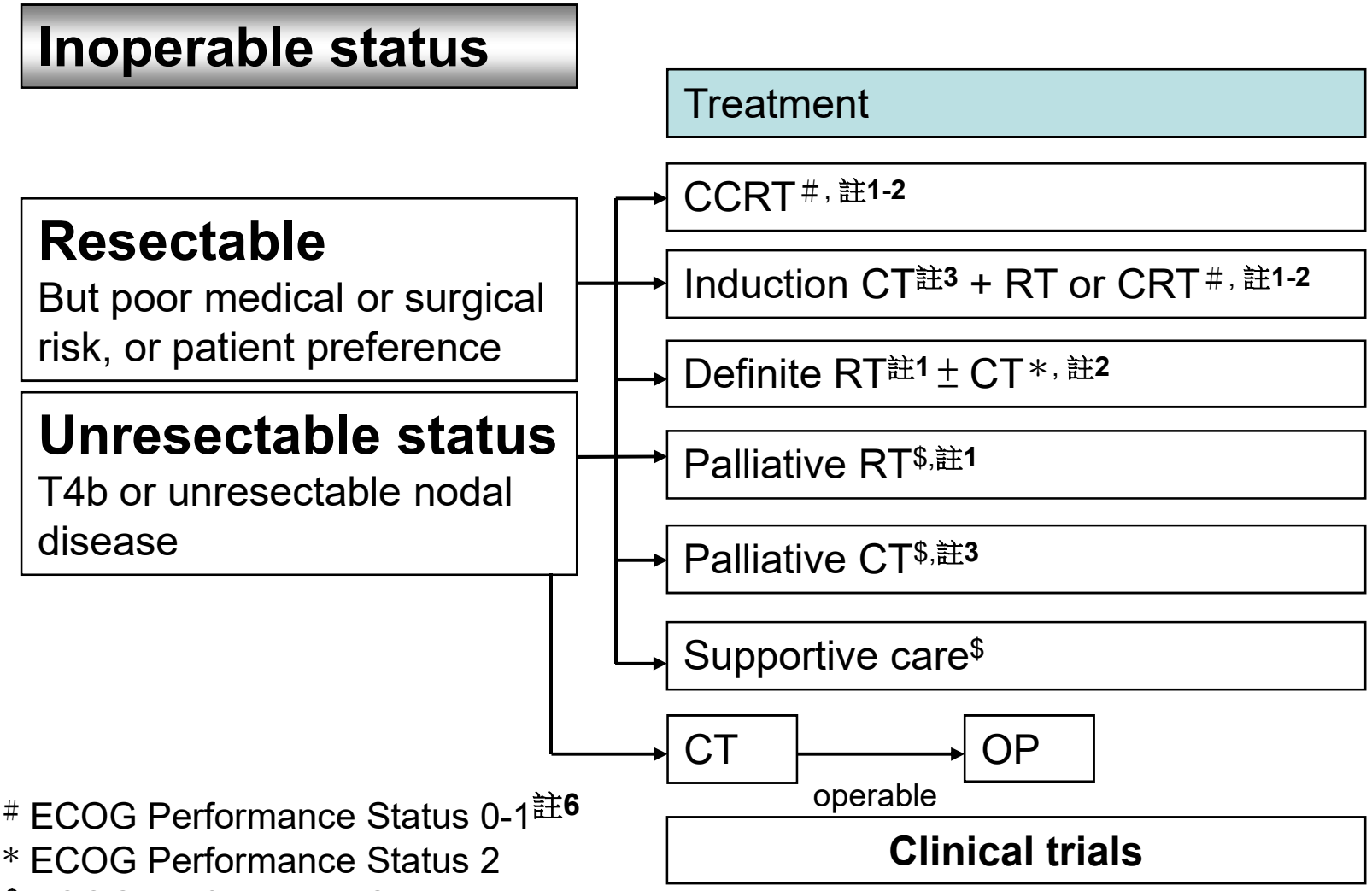

ECOG Performance Status 0-1註6
* ECOG Performance Status 2
$ ECOG Performance Status 3

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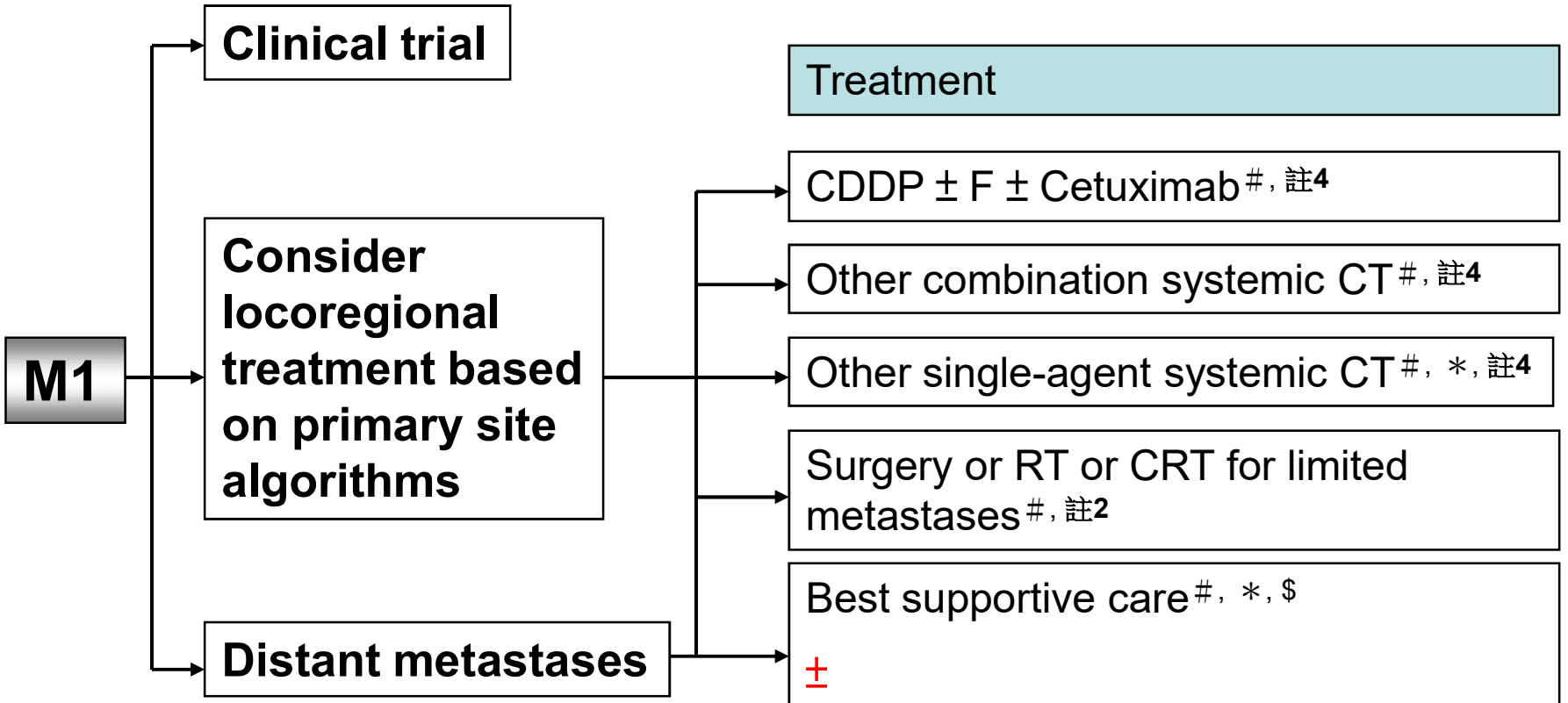

ECOG Performance Status 0-1註6
* ECOG Performance Status 2
$ ECOG Performance Status 3

Carcinoma of Oral Cavity

註1

Principles of Radiotherapy

Definitive Radiotherapy

- Primary and gross adenopathy：66 - 74 Gy (1.8-2.0 Gy/fraction)
- Neck uninvolved nodal stations：44 - 64 Gy (1.6-2.0 Gy/fractions)

Postoperative Radiotherapy

- Preferred interval between operation and radiotherapy is ≤ 6 weeks.
- Primary：60-66 Gy (1.8-2.0 Gy/fraction)
- Neck involved nodal stations：60 - 66 Gy (1.8-2.0 Gy/fraction)
- Neck uninvolved nodal stations：44 - 64 Gy (1.6-2.0 Gy/fraction)

Palliative RT

- Indicated in：relieve local symptoms, prevent debilitation such as spinal cord compression and pathological fracture, achieve durable locoregional control.

CCRT or RT

- RT alone if：old age, impaired renal function, poor condition or refused chemotherapy

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註2 高雄榮民總醫院 臨床診療指引 Ver.1 修訂於2021.04.28 *Page 7 (**Ref. 8-13**)*

Principles of Chemotherapy

Concurrent with RT

Regimen 1: q3w CDDP ± Cetuximab[註5] + RT
•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[註5] + RT
•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[註5] ± Cetuximab[註5] + RT
•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[註5] + RT
•Cetuximab(400mg/ m^2) loading dose first week, then Cetuximab(250mg/ m^2) maintain dose during RT

Regimen5 : Carboplatin + 5-FU + Hydroxyurea (CCr < 60) + RT
•Carboplatin (AUC x 1.25mg) D1-D4
•Fluorouracil (5-FU) (850mg/m^2) D1-D4
•Hydroxyurea 1CAP BID D1-D5

Regimen6 : Cisplatin + 5-FU + Hydroxyurea + RT
•Cisplatin(20mg/ m^2) D1-D4
•Fluorouracil (5-FU) (850mg/m^2) D1-D4
•Hydroxyurea 1CAP BID D1-D5

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註3 高雄榮民總醫院 臨床診療指引 Ver.1 修訂於2021.04.28 *Page 8 (**Ref. 8-13**)*

Regimens of Chemotherapy

***Induction or adjuvant,** 建議2-3cycles*

Regimen 1 : q3-4 weeks T註5 + P ± F ± weekly Cetuximab註5

- Taxotere(60 mg/ m^2) D1
- Cisplatin(60-75 mg/ m^2) D1
- Fluorouracil (5-FU) (600-750mg/m^2) D2-D5
- Cetuximab (400mg/ m^2) loading dose first week, then Cetuximab (250mg/ m^2) maintain dose

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

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

Regimen 3: weekly Cetuximab註5

- Cetuximab (400mg/ m^2) loading dose first week, then Cetuximab (250mg/ m^2) maintain dose

Carcinoma of Oral Cavity

註3 高雄榮民總醫院 臨床診療指引 Ver.1 修訂於2021.04.28 *Page 9 (**Ref. 8-13**)*

Regimens of Chemotherapy

***Induction or adjuvant,** 建議2-3cycles*

Regimen 4: oral Fluorouracil

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

(Salvage or palliative CT中作為取代iv-formed 5-FU之替代藥物)

Regimen 5: weekly Methotrexate

•Methotrexate (40-60mg/ m2)

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註4 高雄榮民總醫院 臨床診療指引 Ver.1 修訂於2021.04.28 *Page 10 (**Ref. 14-22**)*

Regimens of Chemotherapy

Recurrent, unresectable, metastatic

Regimen 1 (First line): q3 weeks Pembrolizumab註5 ± Platinum ± F

- Pembrolizumab(200mg) D1 (if CPS≧1)
- Cisplatin(80-100mg/m^2) D1 or Cisplatin (20mg/ m^2) D1-D5 or Carboplatin (AUC x 5mg) D1
- Fluorouracil (5-FU) (600-1000 mg/m^2) D2-D5

Regimen 2 (First line): q3 weeks Pembrolizumab註5

- Pembrolizumab(200mg) D1 (if CPS≧1)

Regimen 3 (Subsequent line): q2 weeks Nivolumab註5

- Nivolumab(3mg/kg) D1

Regimen 4 (Subsequent line): q3 weeks Pembrolizumab註5

- Pembrolizumab(200mg) D1 (if disease progression on or after platinum therapy)

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

- Cisplatin(80-100mg/ m^2) D1 or Cisplatin (20mg/ m^2) D1-D5 or Carboplatin (AUC x 5mg) D1
- Fluorouracil (5-FU) (600-1000 mg/m^2) D2-D5
- Cetuximab(400mg/ m^2) loading dose first week, then weekly Cetuximab (250mg/ m^2)

Carcinoma of Oral Cavity

Regimens of Chemotherapy

Recurrent, unresectable, metastatic

Regimen 6: q3-4 weeks T ± P ± weekly Cetuximab[註5]
- Taxotere(60 mg/ m^2) D1
- Cisplatin(60-75 mg/ m^2) D1
- Cetuximab(400mg/ m^2) loading dose first week, then weekly Cetuximab (250mg/ m^2)

Regimen 7: q3-4 weeks T ± Carboplatin ± weekly Cetuximab[註5]
- Taxotere(60 mg/ m^2) D1
- Carboplatin (AUC x 5mg) D1
- Cetuximab(400mg/ m^2) loading dose first week, then weekly Cetuximab (250mg/ m^2)

Regimen 8: Cisplatin + Epirubicin+ 5-FU+ Leucovorin
- Cisplatin (60 mg/ m^2) D1
- Epirubicin (50 mg/ m^2) D1
- Fluorouracil (5-FU) (2000 mg/m2) D1

Regimen 9: q2 weeks Bevacizumab
- Bevacizumab (200 mg/ m^2) D1

Regimen 10: weekly Gemcitabine
- Gemcitabine (1000 mg/m^2) D1

Carcinoma of Oral Cavity

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 Oral Cavity

特殊用藥健保給付規定

Pembrolizumab、Nivolumab

• 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頭頸部鱗狀細胞癌成人患者。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 TPS≧50%

• 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 Oral Cavity

Eastern Cooperative Oncology Group (ECOG) Performance Status

Grade	Description	Suggestion
0	Normal activity fully ambulatory (無症狀)	按照標準化療評估及療程。
1	Symptoms, but nearly fully ambulatory (有症狀，完全步行，但對生活無影響)	按照標準化療評估及療程。
2	Some bed time, but needs to be in bed less than 50% of normal daytime (躺在床上的時間<50%)	按照標準化療評估及療程。
3	Needs to be in bed more than 50% of normal daytime (躺在床上的時間>50%)	可視情況考慮停止化學治療。
4	Unable to get out of bed (長期完全臥床)	建議停止化學治療。
5	Dead	

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