

高雄榮民總醫院

口腔癌診療原則

2025年01月15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:2024/5/29

本共識與上一版的差異

上一版	新版
<p>1. planning target volume在low to intermediate risk的劑量為44–50 Gy (2.0 Gy/fraction) to 54–63 Gy (1.6–1.8 Gy/fraction)</p>	<p>Global changes</p> <ol style="list-style-type: none">1. 3D conformal RT (3D-CRT) recommendations removed throughout the guidelines <p>OR-A (1 of 2)</p> <ol style="list-style-type: none">1. 將low to intermediate risk的劑量調為45–50 Gy (1.8 Gy/fraction) to 54–63 Gy (1.6–1.8 Gy/fraction) <p>The choice of systemic therapy <u>Useful in Certain Circumstances (First- and Subsequent-Line)</u></p> <ol style="list-style-type: none">1. Erdafitinib for FGFR mutations or fusions and disease progression with at least one line of prior systemic therapy and no availability of an alternative systemic therapy (category 2B)2. Fam-trastuzumab deruxtecan-nxki (for HER2+ (IHC 3+) solid tumors; subsequent line only with no satisfactory alternative treatment options) (category 2B)

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
- (* 與期別相關之主要檢查)
- Dental evaluation
 - Panorex ± teeth extraction
 - Multidisciplinary consultation
(± Fertility/reproductive, smoking cessation)
 - ± Swallowing evaluation
 - ± p16 status
 - Screening for HBV/HCV

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
- [Oral cancer after surgery]
詳見 Page 4
- [Inoperable status]
詳見 Page 5
- [M1]
詳見 Page 6

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**

Pathological features

Adjuvant Treatment

Primary treatment

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

Risk factor stratification (see page 4)

Definitive RT*, 註1

Residual disease

Surgery

Complete clinical response

Follow-up

Depth of invasion ≥ 4 mm可考慮Elective ND (依腫瘤厚度、位置、SLN biopsy結果而定) 或close follow-up ; T1-3, N0 mucosal lip cancer一般不考慮ND

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

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**Clinical T3, N0;
T1-3, N1-3; T4a-
resectable T4b,
any N; M0**

Pathological features

Adjuvant treatment

Primary treatment

**Resection of primary +
ND, unil. or bil.#**

Risk factor stratification (see page 4)

Induct. C/T 註3

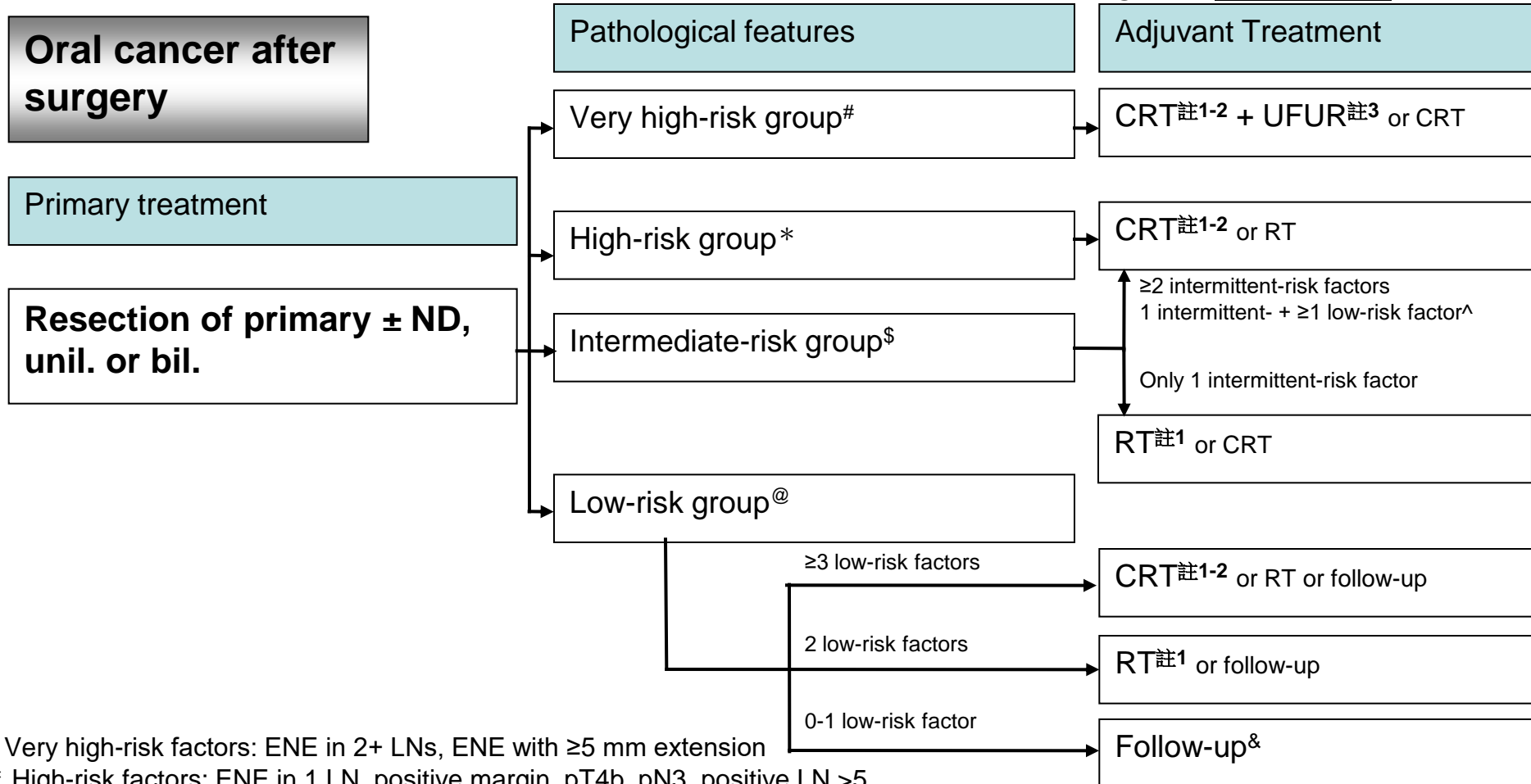
Clinical trials

Therapeutic neck dissection level 依cN status及腫瘤位置而定; T1-3, N0 mucosal lip cancer一般可不考慮ND

所有operable的病患皆建議接受手術，除非患者拒絕或不適合，inoperable cases(see page 5)

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Very high-risk factors: ENE in 2+ LNs, ENE with ≥5 mm extension

* High-risk factors: ENE in 1 LN, positive margin, pT4b, pN3, positive LN >5

\$ Intermediate-risk factors: pT3-4a, negative margin after re-resection for positive margin, tongue cancer with extrinsic muscle invasion, pN2 (positive LN ≤5), pN1 in lower neck, margin ≤2 mm (re-resection first), poorly differentiation + DOI ≥4 mm, 口腔癌第三期患者若MTR (margin/DOI<0.45)則可考慮輔助性CRT/RT, pT1 shallow lesion margin ≤2 mm可以選擇OBS

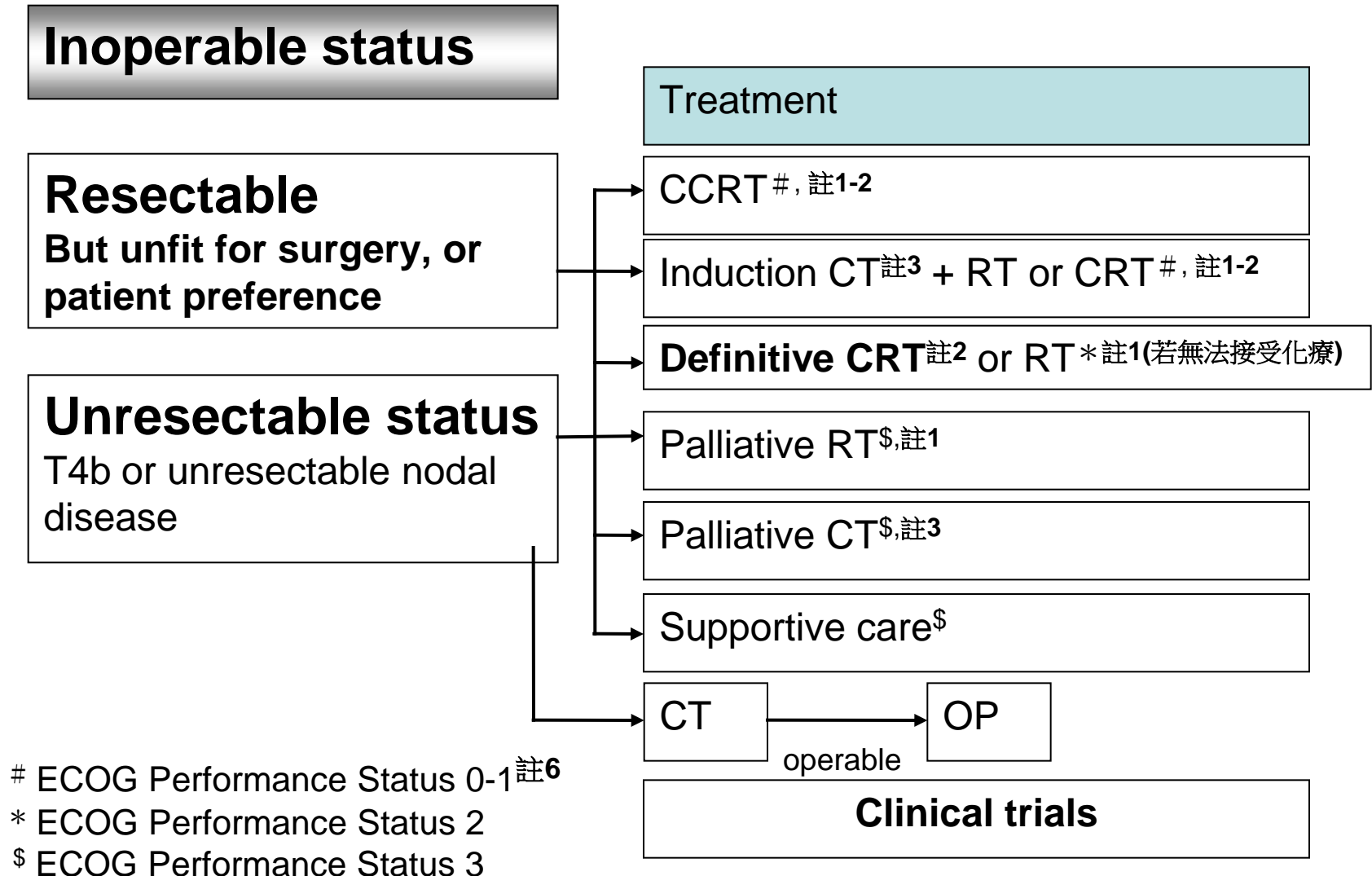
@ Low-risk factors: pN1, perineural invasion, lymphovascular invasion, DOI ≥10 mm, poorly differentiation, margin 3-4 mm

^ Exception: pT3N1可以只做RT,

& 若只有一個low-risk factor但為perineural invasion且無接受過neck dissection，則建議RT.

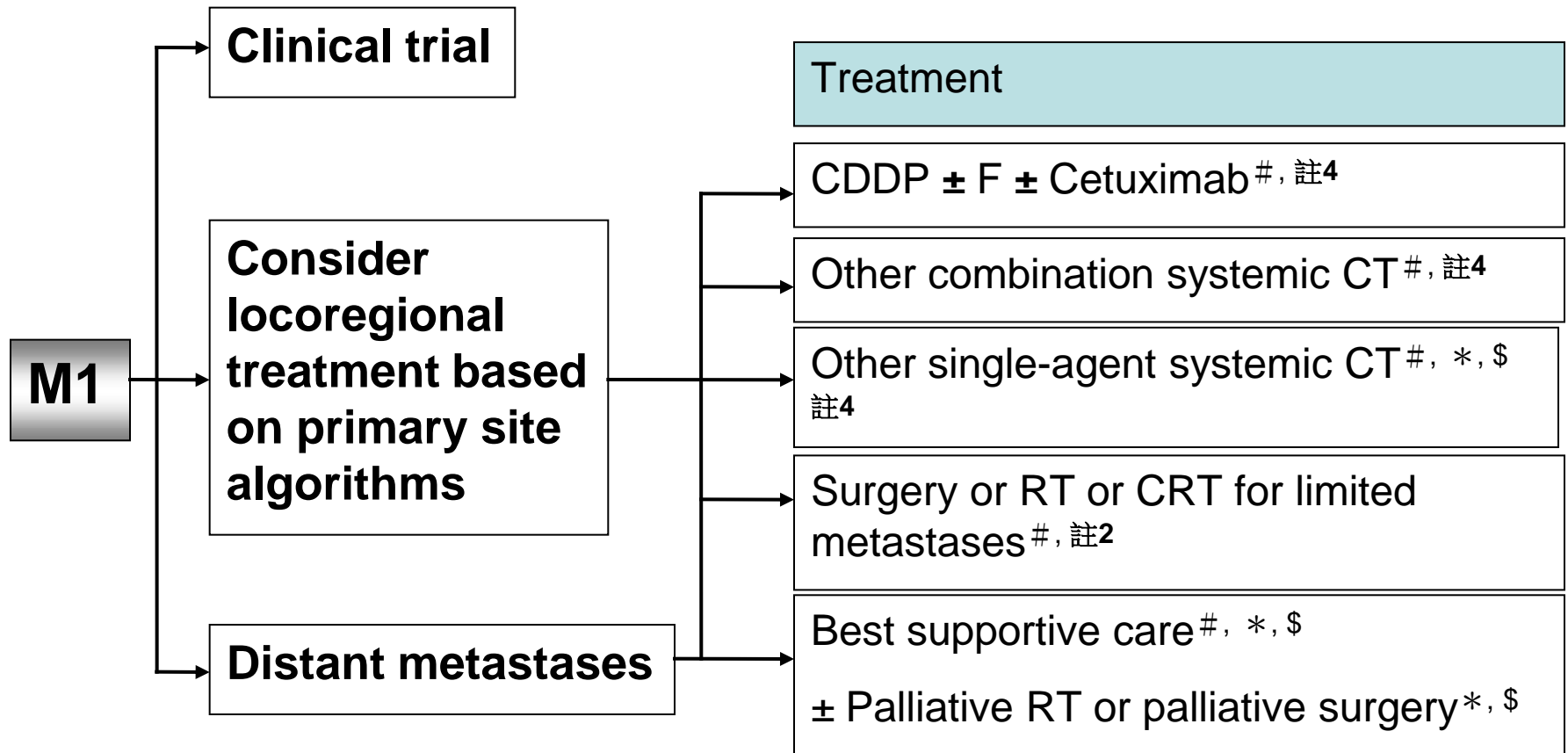
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ECOG Performance Status 0-1 註6

* ECOG Performance Status 2

\$ ECOG Performance Status 3

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

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註1

Principles of Radiotherapy

Definitive Radiotherapy

- Primary and gross adenopathy : 66 - 70 Gy (2.0-2.2 Gy/fraction)
- Neck uninvolved nodal stations : 45 - 63 Gy (1.6-1.8 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 : 45 - 63 Gy (1.6-1.8 Gy/fractions)

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 2025.01.15 Page 8 (Ref. 15-20)

Principles of Chemotherapy

Concurrent with RT

Regimen 1: q3w CDDP ± Cetuximab^{註5} + RT

- 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^{註5} + RT

- 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^{註5} ± Cetuximab^{註5} + RT

- 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^{註5} + RT

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

Regimen5 : Carboplatin + 5-FU + Hydroxyurea (CCr < 60) + RT

- Carboplatin (AUC x 1.25mg) D1-D4
- Fluorouracil (5-FU) (850mg/m²) D1-D4
- Hydroxyurea 1CAP BID D1-D5

Regimen6 : Cisplatin + 5-FU + Hydroxyurea + RT

- Cisplatin(20mg/ m²) D1-D4
- Fluorouracil (5-FU) (850mg/m²) D1-D4
- Hydroxyurea 1CAP BID D1-D5

Regimen 7: Doxetaxel + RT

- Doxetaxel (60g/m²) D1, if cisplatin not eligible

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註3

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Regimens of Chemotherapy

Induction or adjuvant, 建議2-3cycles

Regimen 1 : q3-4 weeks T^{註5} + P ± F (5-FU or UFUR) ± weekly Cetuximab^{註5}

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

Regimen 2: q3-4 weeks Platinum ± F (5-FU or UFUR) ± weekly Cetuximab^{註5}

- Cisplatin(80-100mg/ m²) D1 or Cisplatin (20mg/ m²) D1-D5 or Carboplatin (AUC x 5mg) D1
- Fluorouracil (5-FU) (1000mg/ m²) D2-D5 or **UFUR**
- Cetuximab(400mg/ m²) loading dose first week, then weekly Cetuximab (250mg/ m²)

Regimen 3: weekly Cetuximab^{註5}

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

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註3

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Regimens of Chemotherapy

Induction or adjuvant, 建議2-3cycles

Regimen 4: oral Fluorouracil

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

Regimen 5: weekly Methotrexate

- Methotrexate (40-60mg/ m2)

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註4

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Regimens of Chemotherapy

Recurrent, unresectable, metastatic

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

- Pembrolizumab(200mg) D1
- Cisplatin(80-100mg/m²) D1 or Cisplatin (20mg/ m²) D1-D5 or Carboplatin (AUC x 5mg) D1
- Fluorouracil (5-FU) (600-1000 mg/m²) 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/ m²) D1 or Cisplatin (20mg/ m²) D1-D5 or Carboplatin (AUC x 5mg) D1
- Fluorouracil (5-FU) (600-1000 mg/m²) D2-D5
- Cetuximab(400mg/ m²) loading dose first week, then weekly Cetuximab (250mg/ m²)

Regimen 6: q3 weeks Pembrolizumab^{註5} + Platinum + Doxetacel

- Pembrolizumab(200mg) D1
- Cisplatin(80-100mg/ m²) D1 or Cisplatin (20mg/ m²) D1-D5 or Carboplatin (AUC x 5mg) D1
- Taxotere(60 mg/ m²)

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註4

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Regimens of Chemotherapy

Recurrent, unresectable, metastatic

Regimen 6: q3-4 weeks T ± P ± weekly Cetuximab^{註5}

- Taxotere(60 mg/ m²) D1
- Cisplatin(60-75 mg/ m²) D1
- Cetuximab(400mg/ m²) loading dose first week, then weekly Cetuximab (250mg/ m²)

Regimen 7: q3-4 weeks T ± Carboplatin ± weekly Cetuximab^{註5}

- Taxotere(60 mg/ m²) D1
- Carboplatin (AUC x 5mg) D1
- Cetuximab(400mg/ m²) loading dose first week, then weekly Cetuximab (250mg/ m²)

Regimen 8: Cisplatin + Epirubicin + 5-FU+ Leucovorin

- Cisplatin (60 mg/ m²) D1
- Epirubicin (50 mg/ m²) D1
- Fluorouracil (5-FU) (2000 mg/m²) D1

Regimen 9: q2 weeks Bevacizumab

- Bevacizumab (200 mg/ m²) D1

Regimen 10: weekly Gemcitabine

- Gemcitabine (1000 mg/m²) D1

Regimen 11: Erdafitinib for FGFR mutations or fusions and disease progression with at least one line of prior systemic therapy and no availability of an alternative systemic therapy (category 2B)

Regimen 12: Fam-trastuzumab deruxtecan-nxki (for HER2+ (IHC 3+) solid tumors; subsequent line only with no satisfactory alternative treatment options) (category 2B)

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註5 高雄榮民總醫院 臨床診療指引 Ver.1 修訂於 2025.01.15 Page 13

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，且符合下列條件之一：
 1. 年齡 ≥ 70 歲
 2. $\text{Ccr} < 50\text{ml/min}$
 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。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。

Carboplatin

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

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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 \leq 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 \geq 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 \leq 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。

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註6

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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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