

# 高雄榮民總醫院

## 口腔癌診療原則

2024年05月01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:2023/3/22

本共識與上一版的差異

上一版	新版
<ol style="list-style-type: none"><li>1. Subsite 處將anterior tongue 改成 oral tongue</li><li>2. Adverse features 改成 adverse pathologic features</li><li>3. T1-2術後 Positive Margin治療從 Re-resection or RT 改成 Re-resection + RT if negative margin</li><li>4. M1 ECOG PS 3 的病人治療選項加上 Single-agent systemic therapy</li><li>5. 在recurrent or persistent disease with distant metastases病人建議做NGS genomic profiling</li></ol>	<ol style="list-style-type: none"><li>1. 診斷後應screening HBV(業已列為本院guideline)</li><li>2. 所有tumor resectable的病患皆建議接受手術，除非患者拒絕或不適合接受手術(業已列為本院guideline)</li><li>3. 口腔癌第三期患者若MTR (margin/DOI&lt;0.45)則可考慮輔助性CRT/RT</li><li>4. Inoperable ECOG PS 2 的病患建議優先考慮CRT</li><li>5. Oral UFUR(2#BID or 1#TID)可作為取代iv-formed 5-FU之替代藥物</li><li>6. Nutrition support應優先考慮腸道營養(NG, PEG)</li></ol>

# Carcinoma of Oral Cavity

高雄榮民總醫院 臨床診療指引 Ver.1 修訂於 2024.05.01 Page 1 (Ref. 1)

## 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
- **Screening for HBV/HCV**  
(\* 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
- [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)

# Carcinoma of Oral Cavity

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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

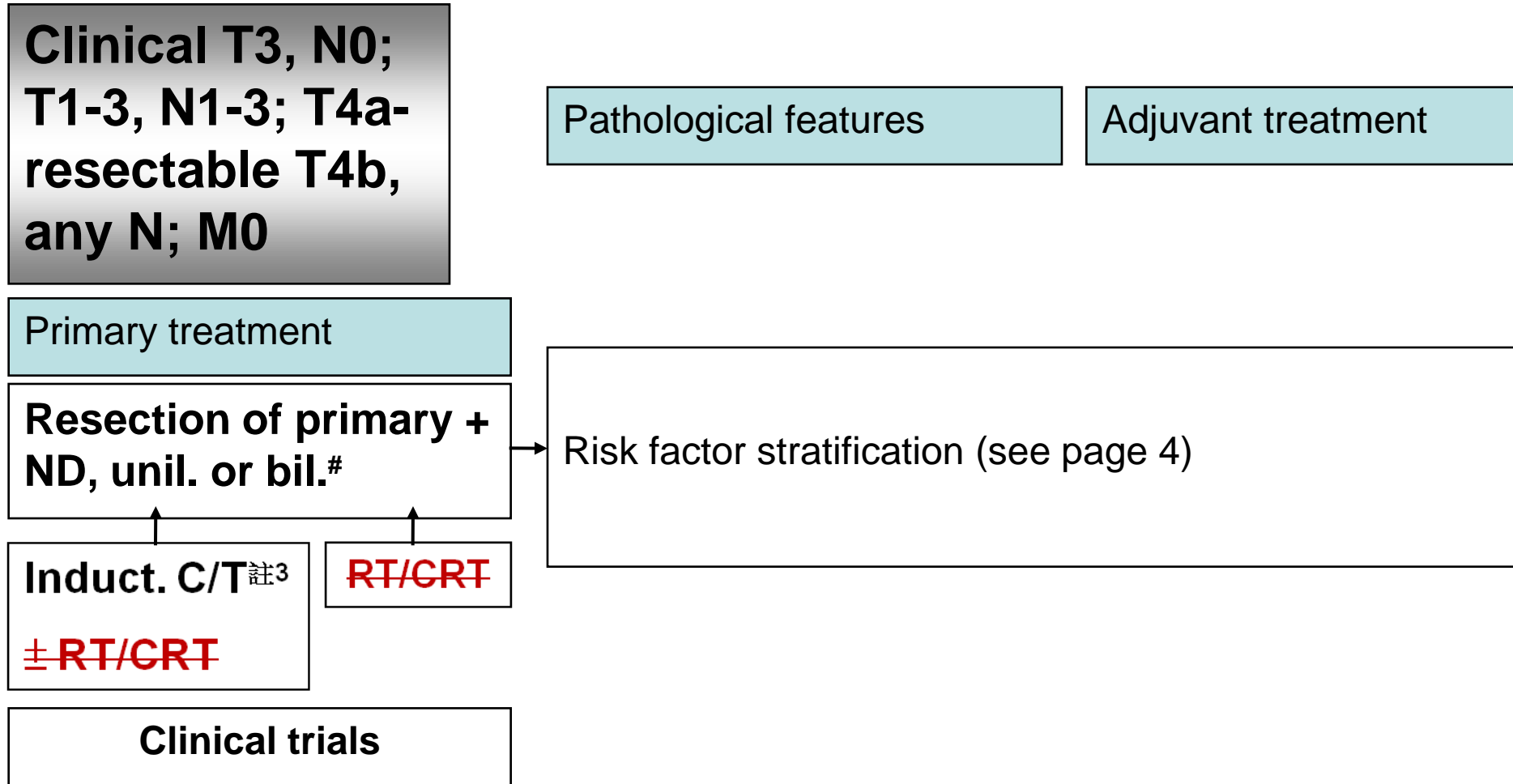
Follow-up

# Depth of invasion  $\geq 4$  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

# Carcinoma of Oral Cavity

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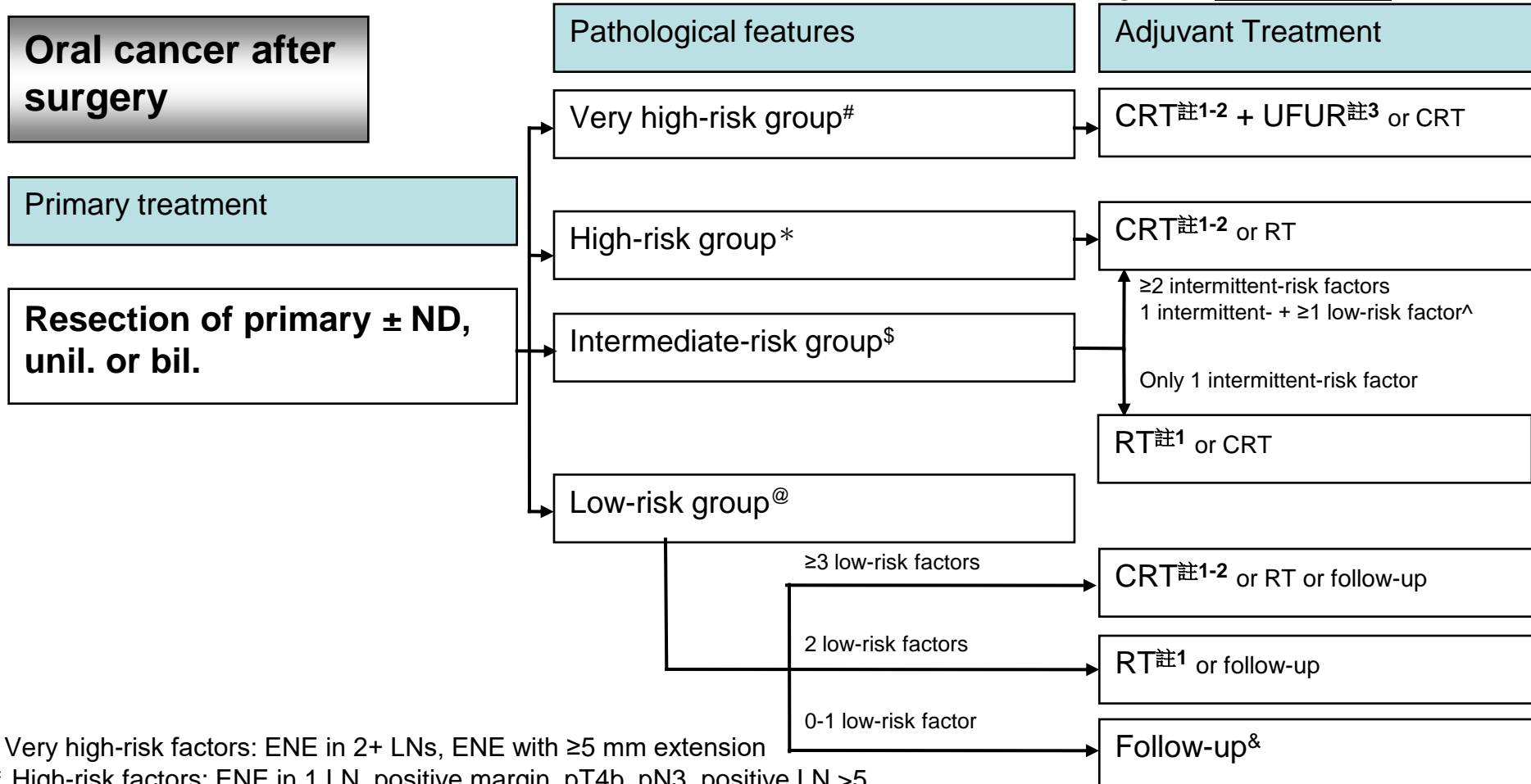


# Therapeutic neck dissection level依cN status及腫瘤位置而定; T1-3, N0 mucosal lip cancer一般可不考慮ND

# 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 10)

# Carcinoma of Oral Cavity

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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RT0.

# Carcinoma of Oral Cavity

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**Inoperable status**

**Resectable**

**But unfit for surgery, or  
patient preference**

**Unresectable status**

T4b or unresectable nodal  
disease

Treatment

CCRT#, 註1-2

Induction CT<sup>註3</sup> + RT or CRT#, 註1-2

**Definitive CRT<sup>註2</sup> or RT\*<sup>註1</sup>(若無法接受化療)**

Palliative RT<sup>\$, 註1</sup>

Palliative CT<sup>\$, 註3</sup>

Supportive care<sup>\$</sup>

CT

operable

OP

**Clinical trials**

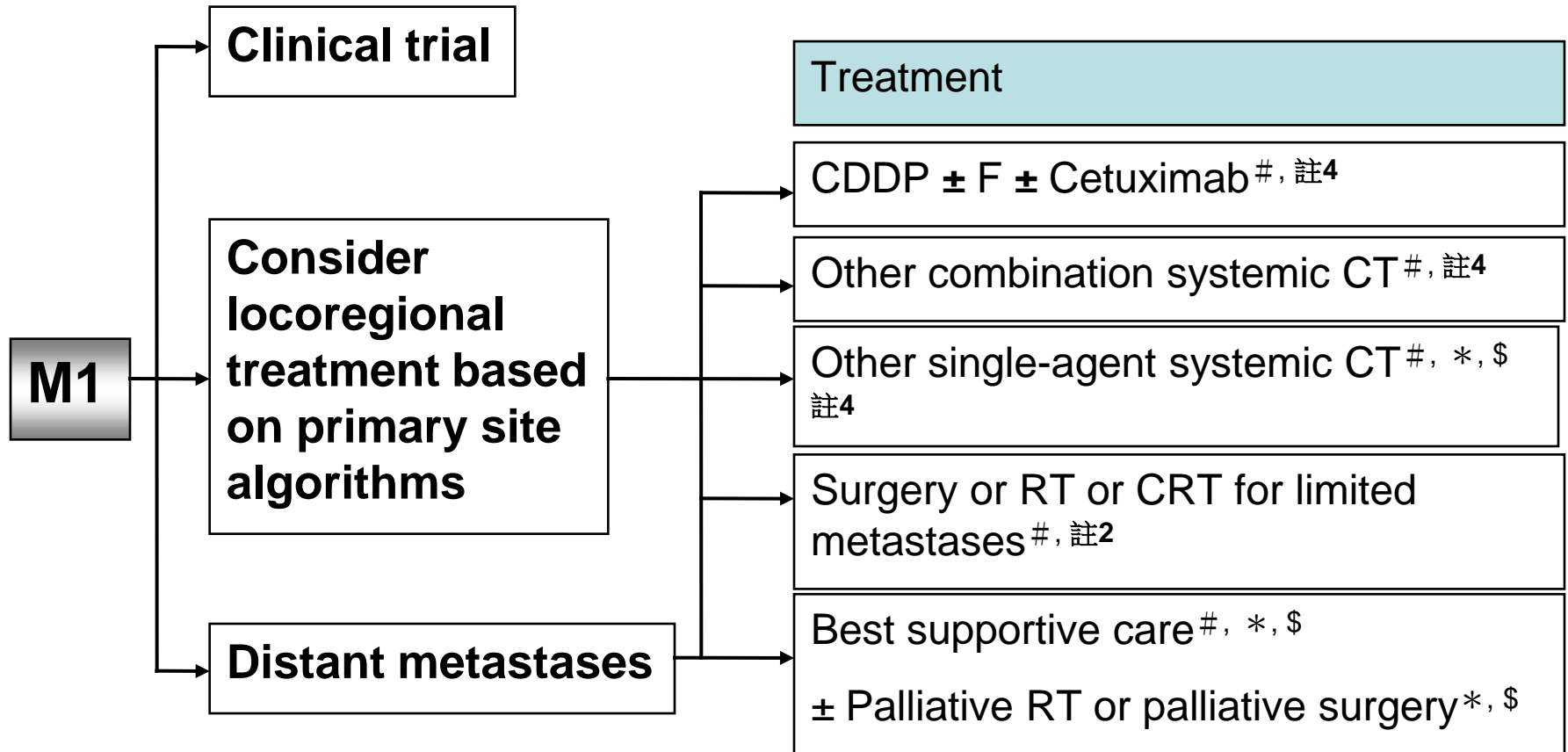
# ECOG Performance Status 0-1<sup>註6</sup>

\* ECOG Performance Status 2

\$ ECOG Performance Status 3

# Carcinoma of Oral Cavity

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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

# Carcinoma of Oral Cavity

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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  $\leq 6$  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

# Carcinoma of Oral Cavity

註2 高雄榮民總醫院 臨床診療指引 Ver.1 修訂於 2024.05.01 Page 8 (Ref. 15-20)

## Principles of Chemotherapy

### Concurrent with RT

#### Regimen 1: q3w CDDP ± Cetuximab<sup>註5</sup> + RT

- Cisplatin (80-100mg/ m<sup>2</sup>) q3w during R/T
- Cetuximab(400mg/ m<sup>2</sup>) loading dose first week, then Cetuximab(250mg/ m<sup>2</sup>) maintain dose D1 + Cisplatin (80-100mg/ m<sup>2</sup>) q3w D2 during R/T

#### Regimen 2: Weekly CDDP ± Cetuximab<sup>註5</sup> + RT

- Cisplatin (30-40mg/ m<sup>2</sup>) weekly during R/T
- Cetuximab(400mg/ m<sup>2</sup>) loading dose first week, and then Cisplatin (30-40mg/ m<sup>2</sup>) weekly D1 + Cetuximab(250mg/ m<sup>2</sup>) maintain dose D2 during R/T

#### Regimen 3: q3w Carboplatin<sup>註5</sup> ± Cetuximab<sup>註5</sup> + RT

- Carboplatin (AUC x 5mg) q3w during R/T
- Cetuximab(400mg/ m<sup>2</sup>) loading dose first week, then Cetuximab(250mg/ m<sup>2</sup>) maintain dose D1 + Carboplatin (AUC x 5mg) q3w D2 during R/T

#### Regimen 4: Weekly Cetuximab<sup>註5</sup> + RT

- Cetuximab(400mg/ m<sup>2</sup>) loading dose first week, then Cetuximab(250mg/ m<sup>2</sup>) maintain dose during RT

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

- Carboplatin (AUC x 1.25mg) D1-D4
- Fluorouracil (5-FU) (850mg/m<sup>2</sup>) D1-D4
- Hydroxyurea 1CAP BID D1-D5

#### Regimen6 : Cisplatin + 5-FU + Hydroxyurea + RT

- Cisplatin(20mg/ m<sup>2</sup>) D1-D4
- Fluorouracil (5-FU) (850mg/m<sup>2</sup>) D1-D4
- Hydroxyurea 1CAP BID D1-D5

#### Regimen 7: Doxetaxel + RT

- Doxetaxel (60g/m<sup>2</sup>) D1, if cisplatin not eligible

# Carcinoma of Oral Cavity

註3

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## Regimens of Chemotherapy

Induction or adjuvant, 建議2-3cycles

**Regimen 1 : q3-4 weeks T<sup>註5</sup> + P ± F (5-FU or UFUR) ± weekly Cetuximab<sup>註5</sup>**

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

**Regimen 2: q3-4 weeks Platinum ± F (5-FU or UFUR) ± weekly Cetuximab<sup>註5</sup>**

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

**Regimen 3: weekly Cetuximab<sup>註5</sup>**

- Cetuximab (400mg/ m<sup>2</sup>) loading dose first week, then Cetuximab (250mg/ m<sup>2</sup>) 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 2024.05.01 Page 10 (Ref. 15-20)

## 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)

# Carcinoma of Oral Cavity

註4

高雄榮民總醫院 臨床診療指引 Ver1 修訂於 2024.05.01 Page 11 (Ref. 21-29)

## Regimens of Chemotherapy

### Recurrent, unresectable, metastatic

#### Regimen 1 (First line): q3 weeks Pembrolizumab<sup>註5</sup> ± Platinum ± F

- Pembrolizumab(200mg) D1
- Cisplatin(80-100mg/m<sup>2</sup>) D1 or Cisplatin (20mg/ m<sup>2</sup>) D1-D5 or Carboplatin (AUC x 5mg) D1
- Fluorouracil (5-FU) (600-1000 mg/m<sup>2</sup>) D2-D5

#### Regimen 2 (First line): q3 weeks Pembrolizumab<sup>註5</sup>

- Pembrolizumab(200mg) D1 (if CPS ≥ 1)

#### Regimen 3 (Subsequent line): q2 weeks Nivolumab<sup>註5</sup>

- Nivolumab(3mg/kg) D1

#### Regimen 4 (Subsequent line): q3 weeks Pembrolizumab<sup>註5</sup>

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

#### Regimen 5: q3-4 weeks Platinum ± F ± weekly Cetuximab<sup>註5</sup>

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

#### Regimen 6: q3 weeks Pembrolizumab<sup>註5</sup> + Platinum + Doxetacel

- Pembrolizumab(200mg) D1
- Cisplatin(80-100mg/ m<sup>2</sup>) D1 or Cisplatin (20mg/ m<sup>2</sup>) D1-D5 or Carboplatin (AUC x 5mg) D1
- Taxotere(60 mg/ m<sup>2</sup>)

# Carcinoma of Oral Cavity

註4

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## Regimens of Chemotherapy

### Recurrent, unresectable, metastatic

#### **Regimen 6: q3-4 weeks T ± P ± weekly Cetuximab**<sup>註5</sup>

- Taxotere(60 mg/ m<sup>2</sup>) D1
- Cisplatin(60-75 mg/ m<sup>2</sup>) D1
- Cetuximab(400mg/ m<sup>2</sup>) loading dose first week, then weekly Cetuximab (250mg/ m<sup>2</sup>)

#### **Regimen 7: q3-4 weeks T ± Carboplatin ± weekly Cetuximab**<sup>註5</sup>

- Taxotere(60 mg/ m<sup>2</sup>) D1
- Carboplatin (AUC x 5mg) D1
- Cetuximab(400mg/ m<sup>2</sup>) loading dose first week, then weekly Cetuximab (250mg/ m<sup>2</sup>)

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

- Cisplatin (60 mg/ m<sup>2</sup>) D1
- Epirubicin (50 mg/ m<sup>2</sup>) D1
- Fluorouracil (5-FU) (2000 mg/m<sup>2</sup>) D1

#### **Regimen 9: q2 weeks Bevacizumab**

- Bevacizumab (200 mg/ m<sup>2</sup>) D1

#### **Regimen 10: weekly Gemcitabine**

- Gemcitabine (1000 mg/m<sup>2</sup>) D1

# Carcinoma of Oral Cavity

註5

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## 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  $\geq 70$  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。

# Carcinoma of Oral Cavity

註5

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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/1.73m<sup>2</sup>
- 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。

# Carcinoma of Oral Cavity

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	

# Carcinoma of Oral Cavity

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