

# 高雄榮民總醫院

## 下咽癌診療原則

2025年02月19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:2024/05/29

本共識與上一版的差異

上一版	新版
<ol style="list-style-type: none"><li>1. 診斷後應screening HBV(業已列為本院 guideline)</li><li>2. 多數T1N0及selected T2N0的患者，手術時不一定要同時接受同側甲狀腺切除</li><li>3. T1-4a, N1-3的患者，可視情況做單側或雙側頸部淋巴結廓清手術(Bil ND was recommended in post-cricoid and posterior pharyngeal wall; however, bilateral ND was still suggested in patients with pyriform sinus tumor)</li><li>4. Oral UFUR(2#BID or 1#TID)可作為取代iv-formed 5-FU之替代藥物</li><li>5. Nutrition support應優先考慮腸道營養(NG, PEG)</li></ol>	<p>2025 ver.1 無更改</p>

# Carcinoma of Hypopharynx

高雄榮民總醫院 臨床診療指引 Ver.1 修訂於 2025.02.19 Page 1 (Ref. 1,2)

## WORK-UP

- History & PE
- Biopsy & Pathology
- Image
  - MRI\* or CT of H&N\* or PET**
  - WBBS\* (if PET/CT not done)/ Abd.Sono\*/ CXR\***
- PES
- ± Chest CT(upper med.)  
(if PET/CT not done)
- ± Neck sono  
(**\*與期別相關之主要檢查**)
- Dental evaluation
  - Panorex ± teeth extraction
- Multidisciplinary consultation  
(Fertility/reproductive, smoking cessation)
- ± Swallowing/speech
- ± p16 status
- ± Pulmonary function if conservation surgery
- HBV/HCV screening

## STAGING & TREATMENT

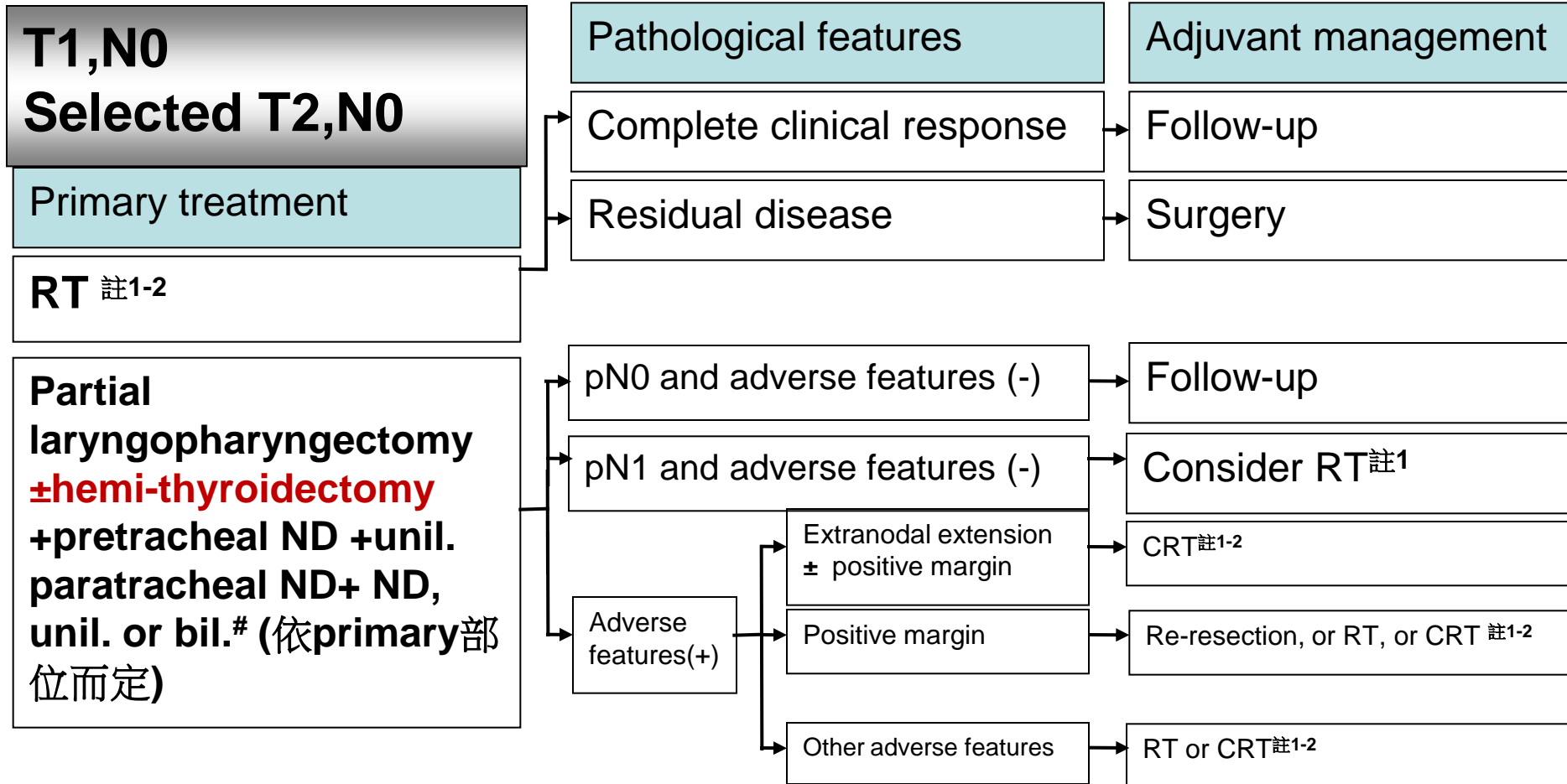
- [T1, N0 or Selected T2, N0, M0]  
*詳見 Page 2*
- [T2-3, any N; T1, N1-3, M0]  
*詳見 Page 3*
- [T4a, any N, M0]  
*詳見 Page 5*
- [T4b, any N, M0 or Inoperable status]  
*詳見 Page 6*
- M1  
*詳見 Page 7*

## FOLLOW-UP

- [Post-Tx within 3-6 months]
  - Baseline MRI or CT (PET)
  - Every 1-2 months: PE
- [2nd year after Tx]
  - Every 2-3 months: PE
- [3-5 years after Tx]
  - Every 4-8 months: PE
- [5 years after Tx]
  - Every 12 months: PE
- Every year:  
H & N MRI or CT, CxR, Bone scan & Abd. Sono, Neck Sono, PES, TSH, free T4(if RT, 6-12 months) As clinically indicated

# Carcinoma of Hypopharynx

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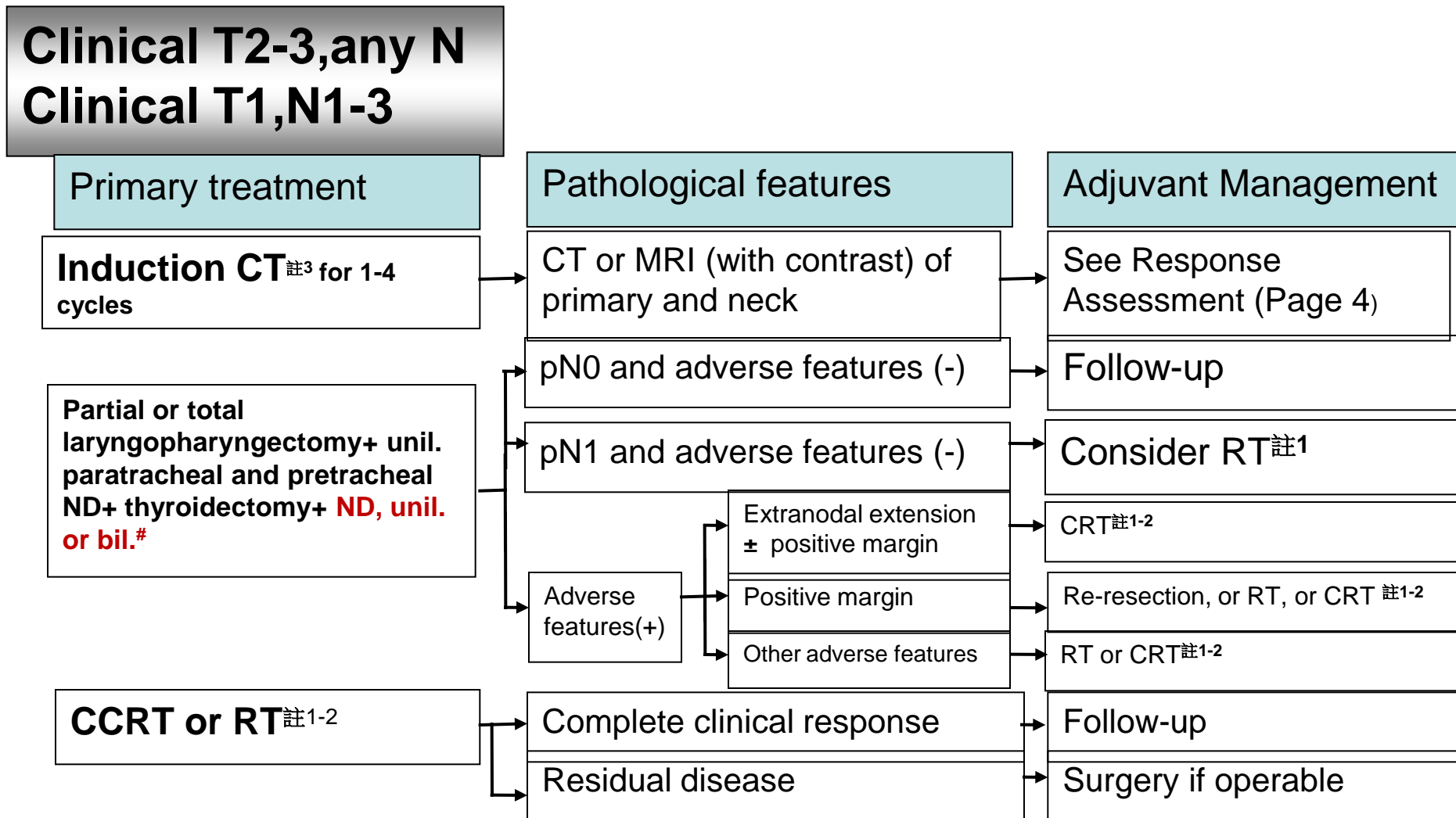


# Bil ND was recommended in post-cricoid and posterior pharyngeal wall; however, bilateral ND was still suggested in patients with pyriform sinus tumor

\* Adverse features : Extranodal extension, positive or close margins, pT3 or pT4 primary, pN2 or pN3 nodal disease, perineural invasion, lymphovascular invasion

# Carcinoma of Hypopharynx

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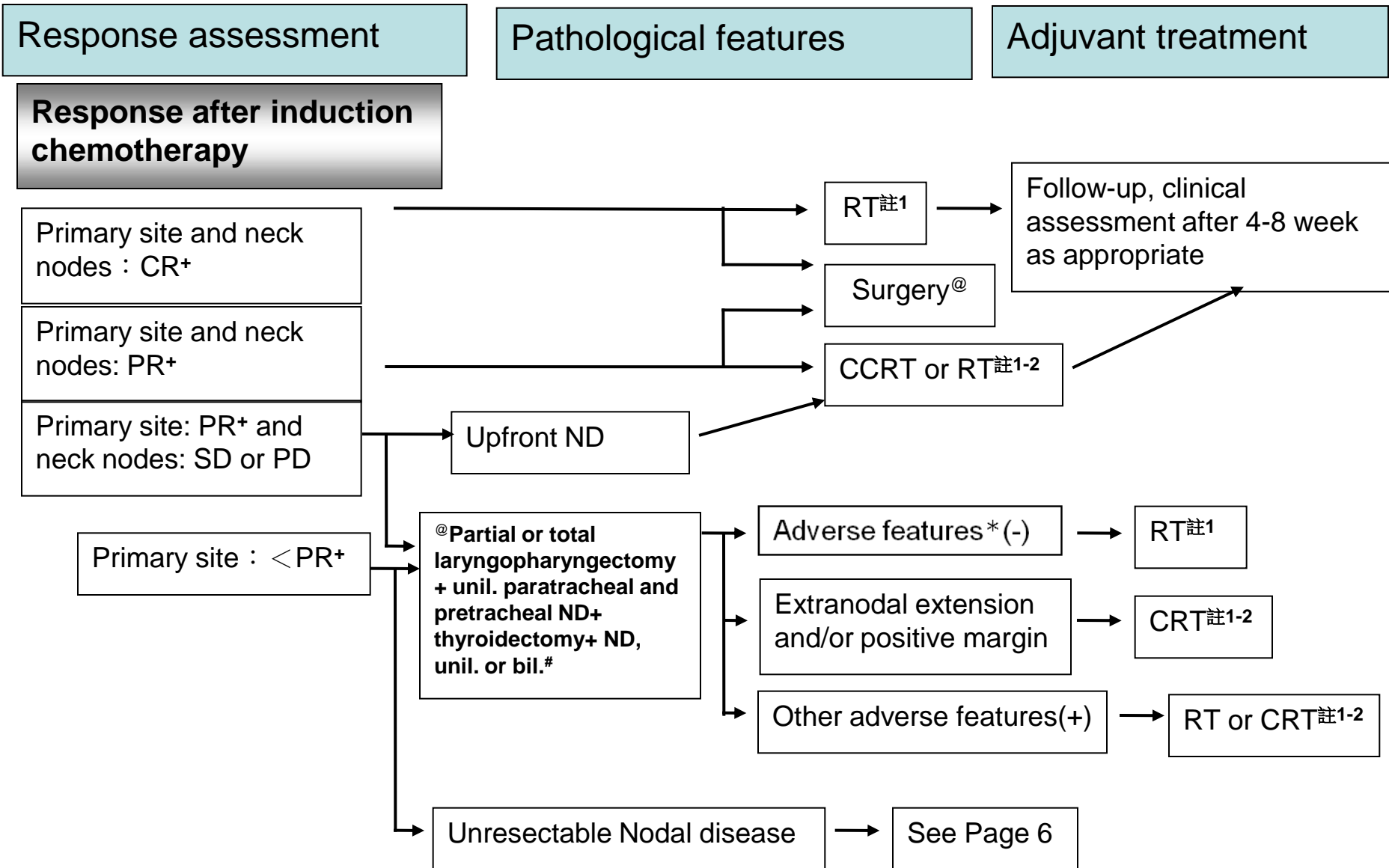


<sup>#</sup> Bil ND was recommended in post-cricoid and posterior pharyngeal wall; however, bilateral ND was still suggested in patients with pyriform sinus tumor

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

# Carcinoma of Hypopharynx

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+ Primary site evaluated by CT or MRI(with contrast) of primary head and neck

\* Adverse features : extranodal extension, positive margins, close margins, pT4 primary, pN2 or pN3 nodal disease, perineural invasion, vascular invasion, lymphatic invasion

# Carcinoma of Hypopharynx

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## Clinical T4a, any N

### Primary treatment

Total laryngopharyngectomy+  
hemi- or total thyroidectomy,  
**ND, unil. or bil.#** + paratracheal  
ND, unil. or bil.

### Pathological features

Extranodal extension and/or  
positive margin

Other adverse features

### Adjuvant Management

CRT or RT<sup>註1-2</sup>

RT or CRT<sup>註1-2</sup>

## Select T4a patients (high PS, multiple comorbidity or decline surgery)

**Induction CT<sup>註3</sup>** for 1-4  
cycles

CT or MRI (with contrast) of  
primary and neck

See Response  
Assessment (Page 4)

**CCRT or RT<sup>註1-2</sup>**

Complete clinical response

Follow-up

Residual disease

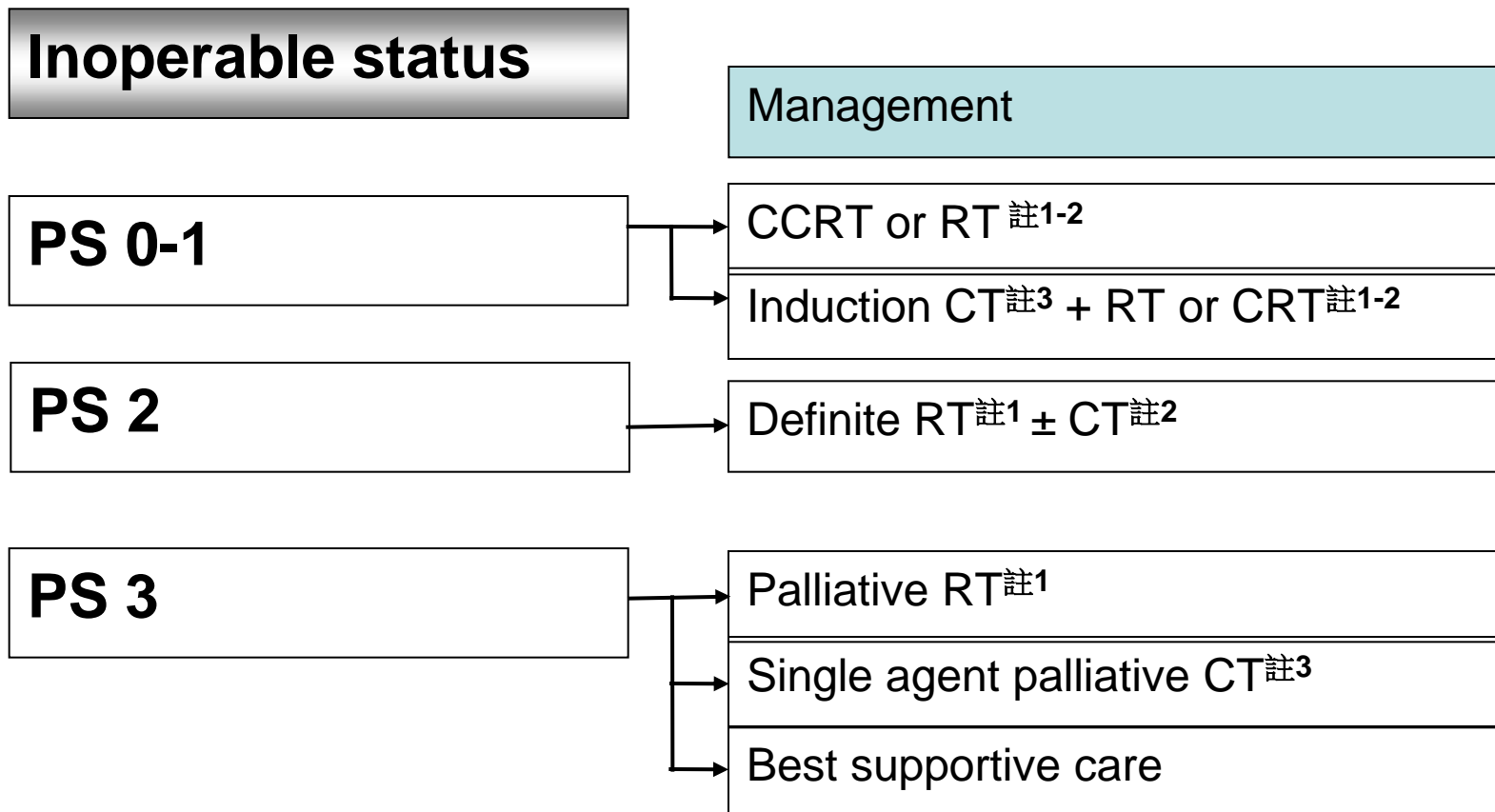
Surgery if operable

# **Neck dissection level** 依primary部位及cN status而定。

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

# Carcinoma of Hypopharynx

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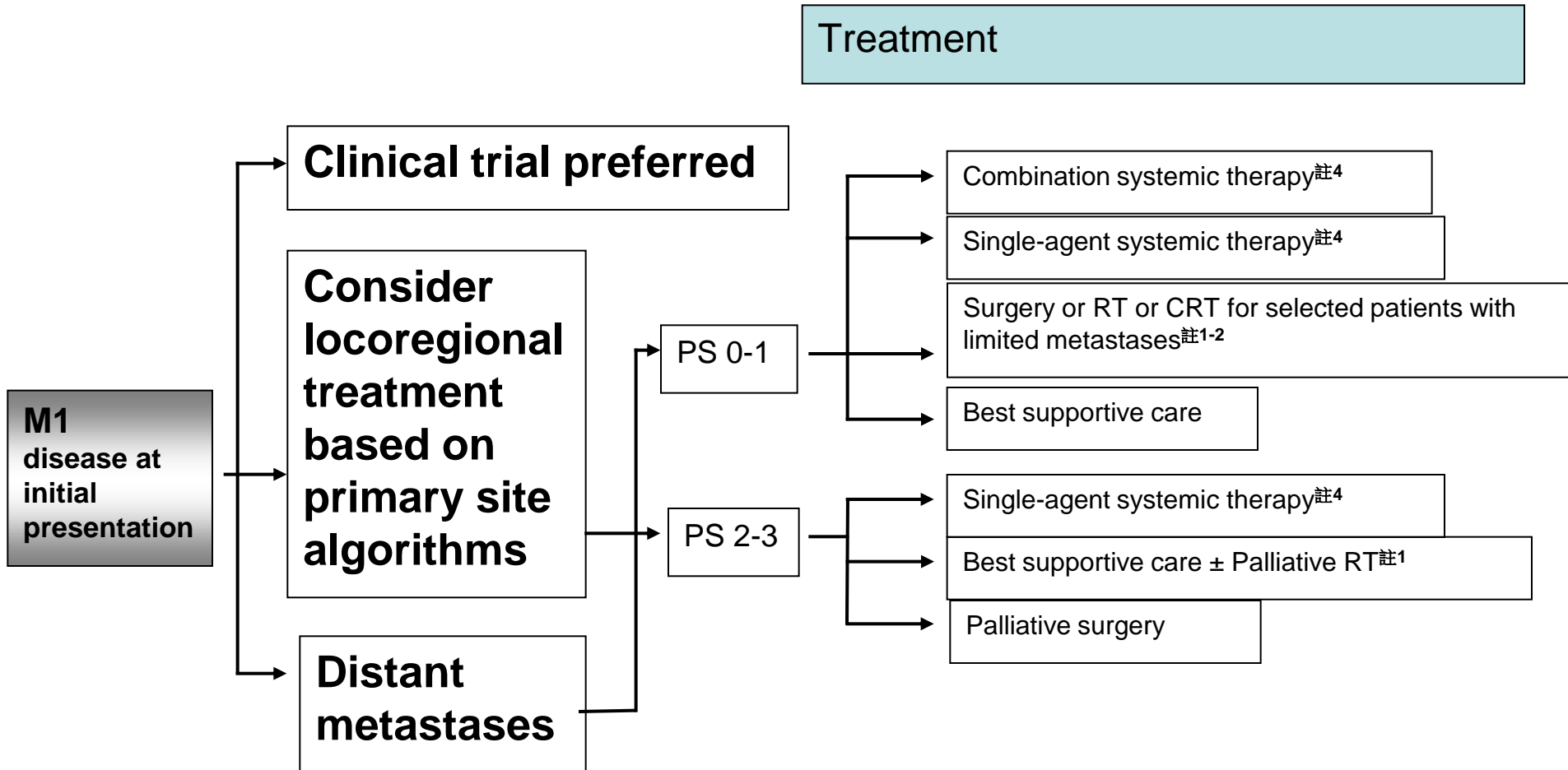
ECOG Performance Status 0-1 註6

ECOG Performance Status 2

ECOG Performance Status 3

# Carcinoma of the Hypopharynx

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1. PS 0-1若治療無效，除 best supportive care 外可再考慮systemic therapy, clinical trial or palliative RT
2. PS 2-3 single agent systemic therapy 若治療無效，除 best supportive care 外可再考慮 alternate single agent systemic therapy or palliative RT

# ***Carcinoma of Hypopharynx***

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註1

## **Principles of Radiotherapy**

### **Definitive Radiotherapy**

- Primary and gross adenopathy : 66 - 74Gy (2.0-2.2 Gy/fraction)
- Low to intermediate risk : 44 - 64 Gy (2.0 Gy/fractions) in 3D RT, 54- 63 Gy (1.6-1.8 Gy/fractions)

### **Postoperative Radiotherapy**

- Preferred interval between operation and radiotherapy is  $\leq 6$  weeks.
- High risk(adverse feature) : 60 - 66 Gy (2.0 Gy/fraction)
- Low to intermediate risk : 44 - 64 Gy (2.0 Gy/fractions) in 3D RT, 54- 63 Gy (1.6-1.8 Gy/fractions)

### **CCRT or RT**

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

### **Palliative RT**

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

# Carcinoma of Hypopharynx

註2

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## 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 Hypopharynx

註3

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## Regimens of Chemotherapy

Induction, adjuvant, 建議1-4cycles

**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) (600-1000mg/m<sup>2</sup>) or **UFUR** D2-D5
- Cetuximab(400mg/m<sup>2</sup>) loading dose first week, then weekly Cetuximab (250mg/ m<sup>2</sup>)

# Carcinoma of Hypopharynx

註3

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## Regimens of Chemotherapy

Induction, adjuvant, 建議1-4cycles

### 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

### 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/ m<sup>2</sup>)

# Carcinoma of Hypopharynx

註4

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## 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>)

\*針對Recurrent or persistent disease with M1，建議NGS

# Carcinoma of Hypopharynx

註4

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## Regimens of Chemotherapy

**Recurrent, unresectable, metastatic** \*

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

- Taxotere (60 mg/ m<sup>2</sup>) D1
- Cisplatin (60-75 mg/ m<sup>2</sup>) D1 or 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

\* 針對 Recurrent or persistent disease with M1，建議 NGS

# Carcinoma of Hypopharynx

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.Ccr  $< 50$ 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 (CCr  $< 60$ ) 或曾作單側或以上腎切除之惡性腫瘤患者使用。

# Carcinoma of Hypopharynx

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 Hypopharynx

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 the Hypopharynx

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