

# 高雄榮民總醫院

## 口咽癌診療原則

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：2023/03/22

本共識與上一版的差異

上一版	NCCN 新版
<ol style="list-style-type: none"><li>1. Multidisciplinary team adjunctive service增加pain management。Supportive service增加Physical therapy (lymphedema management)。</li><li>2. HPV(+)分期將原先T1-2,N0，新增為T0-2,N0。</li><li>3. 新增:HPV(-): cT1-2, N0-1術後，pN0 無 adverse features→ Follow up，pN1 無 adverse features→ consider RT。Footnote新增:若T1-T2 primary tumor接近中線但有 adequate margin且無adverse features，可執行staged contralateral ND以避免RT。側性明顯的tumor且pN0-1 無 adverse features，可observation。</li><li>4. 針對HPV(-),T1-4aN2-3移除N2a-b,N3以及N2c當作是否做雙側ND的治療流程劃分，而是以primary site為建議是否做雙側ND。</li><li>5. 針對HPV(+), T0-2,N0，手術治療建議從±同側或雙側ND，改成合併同側ND或者雙側ND。</li><li>6. 針對HPV(+), T0-2,N1 (single node &gt;3 cm, or 2 or more ipsilateral nodes ≤6 cm), or T0-2,N2 or T3,N0-2 移除以單側N0-3以及雙側N2-3當作是否做雙側ND的治療流程劃分，而是以primary site為建議是否做雙側ND。</li><li>7. 針對Initial M1且PS3，新增single-agent systemic therapy。</li><li>8. 針對Recurrent or persistent disease with M1，建議NGS。</li><li>9. CCRT/RT後有response，且8-12wks後Imaging positive，可做PET(≥12wk)，或者ND(if confirmed residual/persistent/progression)。</li></ol>	<p><b>Global Changes</b></p> <ol style="list-style-type: none"><li>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</li><li>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.</li><li>3.Oral UFUR(2#BID or 1#TID)可作為取代iv-formed 5-FU之替代藥物</li><li>4.Nutrition support應優先考慮腸道營養(NG, PEG)</li></ol> <p><b>ORPHPV-3</b></p> <ol style="list-style-type: none"><li>1.在IC followed by RT or CRT 修改註腳:新增對於疾病對IC沒有反應的病人，手術可以是一個治療選項</li></ol> <p><b>ORPH-A(2-1)</b></p> <ol style="list-style-type: none"><li>1.修改註腳:刪除altered fractionation會增加CRT治療副作用的論述</li></ol> <p><b>ORPH-A(2-2)</b></p> <ol style="list-style-type: none"><li>1.在PTV, low to intermediate risk處修改:新增針對p16 (HPV)-positive口咽癌的病人最多不超過4個positive LNs,或是切除後的T1-T2 margin為negative或是close margins (&lt;3 mm),或是非雙邊的N1-N2有≤1 mm 的ENE，可以考慮將RT劑量降階至50Gy</li></ol>

# 會議討論

上次會議：2023/03/22

本共識與上一版的差異

上一版	NCCN 新版
無。	<p data-bbox="799 358 919 394"><b>ORPH-B</b></p> <p data-bbox="799 425 989 461">1. 修改內文</p> <ol data-bbox="898 491 1846 1319" style="list-style-type: none"><li data-bbox="898 491 1846 662">1) P16的表現與HPV狀態相關，特別是在HPV是高比例癌症病因的地理區域。建議進行確認性HPV直接測試。在醫學中心建議確定P16和直接HPV測試的一致率，因為這可能因地區而異</li><li data-bbox="898 691 1846 819">2) 透過HPV腫瘤狀態來進一步區分P16陽性患者可以提供預後信息，P16陽性且HPV亦為陽性的腫瘤患者，其預後會比P16陽性且HPV為陰性的腫瘤患者來的好</li><li data-bbox="898 848 1846 933">3) HPV直接測試包含了聚合酶鏈反應（PCR）和原位雜交（ISH）的RNA測試</li><li data-bbox="898 962 1846 1005">4) PCR可提供額外的敏感度；ISH可增加特異度</li><li data-bbox="898 1033 1846 1076">5) 可透過細針穿刺(FNA)獲得足夠的病理樣本進行HPV測試</li><li data-bbox="898 1105 1846 1219">6) 非口咽部位(如鼻竇、口腔、喉)的腫瘤中有一小部分和HPV有關，然而鑑於缺乏一致的證據來支持預後的重要性，不建議對非口咽癌進行常規的HPV測試或p16測試</li><li data-bbox="898 1248 1846 1319">7) 在使用P16測試時，以70%的細胞核與細胞質有中度或強烈的染色視為分界點</li></ol>

# 會議討論

上次會議：2023/03/22

本共識與上一版的差異

上一版	NCCN 新版
無。	<p><b>ORPHPV-1, ORPHPV-2, ORPHPV-3, ORPHPV-4, and ORPH-A 2-2修改註腳</b></p> <p>1. 在Adverse pathologic features處將close margins 修改為close margins (&lt;3 mm)</p> <p><b>ORPHPV-2, ORPHPV-3修改註腳</b></p> <p>1. 針對p16 (HPV)-positive口咽癌的病人最多不超過4個positive LNs,或是切除後的T1-T2 margin為negative或是close margins (&lt;3 mm),或是非雙邊的N1-N2有≤1 mm 的ENE，可以考慮將RT劑量降階至50Gy</p>

# Oropharyngeal (P16 negative) cancer

## Clinical staging AJCC 8th

### Oropharyngeal (p16 negative) cancer TNM clinical staging AJCC UICC 8th edition

Primary tumor (T)	
T category	T criteria
TX	Primary tumor cannot be assessed
Tis	Carcinoma <i>in situ</i>
T1	Tumor 2 cm or smaller in greatest dimension
T2	Tumor larger than 2 cm but not larger than 4 cm in greatest dimension
T3	Tumor larger than 4 cm in greatest dimension or extension to lingual surface of epiglottis
T4	Moderately advanced or very advanced local disease
T4a	Moderately advanced local disease. Tumor invades the larynx, extrinsic muscle of tongue, medial pterygoid, hard palate, or mandible.*
T4b	Very advanced local disease. Tumor invades lateral pterygoid muscle, pterygoid plates, lateral nasopharynx, or skull base or encases carotid artery.
* Mucosal extension to lingual surface of epiglottis from primary tumors of the base of the tongue and vallecula does not constitute invasion of the larynx.	
Regional lymph nodes (N)	
Clinical N (cN)	
N category	N criteria
NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis in a single ipsilateral lymph node, 3 cm or smaller in greatest dimension and ENE(-)
N2	Metastasis in a single ipsilateral node larger than 3 cm but not larger than 6 cm in greatest dimension and ENE(-); <b>or</b> Metastases in multiple ipsilateral lymph nodes, none larger than 6 cm in greatest dimension and ENE(-); <b>or</b> In bilateral or contralateral lymph nodes, none larger than 6 cm in greatest dimension and ENE(-)
N2a	Metastasis in a single ipsilateral node larger than 3 cm but not larger than 6 cm in greatest dimension and ENE(-)
N2b	Metastases in multiple ipsilateral nodes, none larger than 6 cm in greatest dimension and ENE(-)
N2c	Metastases in bilateral or contralateral lymph nodes, none larger than 6 cm in greatest dimension and ENE(-)
N3	Metastasis in a lymph node larger than 6 cm in greatest dimension and ENE(-); <b>or</b> Metastasis in any node(s) and clinically overt ENE(+)
N3a	Metastasis in a lymph node larger than 6 cm in greatest dimension and ENE(-)
N3b	Metastasis in any node(s) and clinically overt ENE(+)
NOTE: A designation of "U" or "L" may be used for any N category to indicate metastasis above the lower border of the cricoid (U) or below the lower border of the cricoid (L). Similarly, clinical and pathological ENE should be recorded as ENE(-) or ENE(+).	

Distant metastasis (M)			
M category	M criteria		
M0	No distant metastasis		
M1	Distant metastasis		
Prognostic stage groups			
When T is...	And N is...	And M is...	Then the stage group is...
Tis	N0	M0	0
T1	N0	M0	I
T2	N0	M0	II
T3	N0	M0	III
T1, T2, T3	N1	M0	III
T4a	N0, N1	M0	IVA
T1, T2, T3, T4a	N2	M0	IVA
Any T	N3	M0	IVB
T4b	Any N	M0	IVB
Any T	Any N	M1	IVC

TNM: tumor, node, metastasis; AJCC: American Joint Committee on Cancer; UICC: Union for International Cancer Control; ENE: extranodal extension.

Used with permission of the American College of Surgeons, Chicago, Illinois. The original source for this information is the AJCC Cancer Staging Manual, Eighth Edition (2017) published by Springer International Publishing. Corrected at 4th printing, 2018.

# Oropharyngeal (P16 negative) cancer

## Pathological staging AJCC 8th

### Oropharyngeal (p16 negative) cancer TNM pathologic staging AJCC UICC 8th edition

Primary tumor (T)	
T category	T criteria
TX	Primary tumor cannot be assessed
Tis	Carcinoma <i>in situ</i>
T1	Tumor 2 cm or smaller in greatest dimension
T2	Tumor larger than 2 cm but not larger than 4 cm in greatest dimension
T3	Tumor larger than 4 cm in greatest dimension or extension to lingual surface of epiglottis
T4	Moderately advanced or very advanced local disease
T4a	Moderately advanced local disease. Tumor invades the larynx, extrinsic muscle of tongue, medial pterygoid, hard palate, or mandible.*
T4b	Very advanced local disease. Tumor invades lateral pterygoid muscle, pterygoid plates, lateral nasopharynx, or skull base or encases carotid artery.
* Mucosal extension to lingual surface of epiglottis from primary tumors of the base of the tongue and vallecula does not constitute invasion of the larynx.	
Regional lymph nodes (N)	
Pathological N (pN)	
N category	N criteria
NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis in a single ipsilateral lymph node, 3 cm or smaller in greatest dimension and ENE(-)
N2	Metastasis in a single ipsilateral lymph node, 3 cm or smaller in greatest dimension and ENE(+); <b>or</b> Larger than 3 cm but not larger than 6 cm in greatest dimension and ENE(-); <b>or</b> Metastases in multiple ipsilateral lymph nodes, none larger than 6 cm in greatest dimension and ENE(-); <b>or</b> In bilateral or contralateral lymph node(s), none larger than 6 cm in greatest dimension and ENE(-)
N2a	Metastasis in single ipsilateral node 3 cm or smaller in greatest dimension and ENE(+); <b>or</b> A single ipsilateral node larger than 3 cm but not larger than 6 cm in greatest dimension and ENE(-)
N2b	Metastases in multiple ipsilateral nodes, none larger than 6 cm in greatest dimension and ENE(-)
N2c	Metastases in bilateral or contralateral lymph node(s), none larger than 6 cm in greatest dimension and ENE(-)
N3	Metastasis in a lymph node larger than 6 cm in greatest dimension and ENE(-); <b>or</b> In a single ipsilateral node larger than 3 cm in greatest dimension and ENE(+); <b>or</b> Multiple ipsilateral, contralateral, or bilateral nodes, any with ENE(+); <b>or</b> A single contralateral node of any size and ENE(+)
N3a	Metastasis in a lymph node larger than 6 cm in greatest dimension and ENE(-)
N3b	Metastasis in a single ipsilateral node larger than 3 cm in greatest dimension and ENE(+); <b>or</b> Multiple ipsilateral, contralateral or bilateral nodes, any with ENE(+); <b>or</b> A single contralateral node of any size and ENE(+)
NOTE: A designation of "U" or "L" may be used for any N category to indicate metastasis above the lower border of the cricoid (U) or below the lower border of the cricoid (L). Similarly, clinical and pathological ENE should be recorded as ENE(-) or ENE(+).	

Distant metastasis (M)			
M category	M criteria		
M0	No distant metastasis		
M1	Distant metastasis		
Prognostic stage groups			
When T is...	And N is...	And M is...	Then the stage group is...
Tis	N0	M0	0
T1	N0	M0	I
T2	N0	M0	II
T3	N0	M0	III
T1, T2, T3	N1	M0	III
T4a	N0, N1	M0	IVA
T1, T2, T3, T4a	N2	M0	IVA
Any T	N3	M0	IVB
T4b	Any N	M0	IVB
Any T	Any N	M1	IVC

TNM: tumor, node, metastasis; AJCC: American Joint Committee on Cancer; UICC: Union for International Cancer Control; ENE: extranodal extension.

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# Oropharyngeal (P16 positive) cancer Clinical & Pathological staging AJCC 8th

## HPV-related oropharyngeal carcinoma TNM clinical staging AJCC UICC 8th edition

Primary tumor (T)			
T category	T criteria		
T0	No primary identified		
T1	Tumor 2 cm or smaller in greatest dimension		
T2	Tumor larger than 2 cm but not larger than 4 cm in greatest dimension		
T3	Tumor larger than 4 cm in greatest dimension or extension to lingual surface of epiglottis		
T4	Moderately advanced local disease. Tumor invades the larynx, extrinsic muscle of tongue, medial pterygoid, hard palate, or mandible or beyond.*		
* Mucosal extension to lingual surface of epiglottis from primary tumors of the base of the tongue and vallecula does not constitute invasion of the larynx.			
Regional lymph nodes (N) - Clinical N (cN)			
N category	N criteria		
NX	Regional lymph nodes cannot be assessed		
N0	No regional lymph node metastasis		
N1	One or more ipsilateral lymph nodes, none larger than 6 cm		
N2	Contralateral or bilateral lymph nodes, none larger than 6 cm		
N3	Lymph node(s) larger than 6 cm		
Distant metastasis (M)			
M category	M criteria		
M0	No distant metastasis		
M1	Distant metastasis		
Prognostic stage groups - Clinical			
When T is...	And N is...	And M is...	Then the stage group is...
T0, T1, or T2	N0 or N1	M0	I
T0, T1, or T2	N2	M0	II
T3	N0, N1, or N2	M0	II
T0, T1, T2, T3, or T4	N3	M0	III
T4	N0, N1, N2, or N3	M0	III
Any T	Any N	M1	IV

HPV: human papillomavirus; TNM: tumor, node, metastasis; AJCC: American Joint Committee on Cancer; UICC: Union for International Cancer Control.

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## HPV related oropharyngeal carcinoma TNM pathologic staging AJCC UICC 8th edition

Primary tumor (T)			
T category	T criteria		
T0	No primary identified		
T1	Tumor 2 cm or smaller in greatest dimension		
T2	Tumor larger than 2 cm but not larger than 4 cm in greatest dimension		
T3	Tumor larger than 4 cm in greatest dimension or extension to lingual surface of epiglottis		
T4	Moderately advanced local disease. Tumor invades the larynx, extrinsic muscle of tongue, medial pterygoid, hard palate, or mandible or beyond.*		
* Mucosal extension to lingual surface of epiglottis from primary tumors of the base of the tongue and vallecula does not constitute invasion of the larynx.			
Regional lymph nodes (N) - Pathological N (pN)			
N category	N criteria		
NX	Regional lymph nodes cannot be assessed		
pN0	No regional lymph node metastasis		
pN1	Metastasis in four or fewer lymph nodes		
pN2	Metastasis in more than four lymph nodes		
Distant metastasis (M)			
M category	M criteria		
M0	No distant metastasis		
M1	Distant metastasis		
Prognostic stage groups - Pathological			
When T is...	And N is...	And M is...	Then the stage group is...
T0, T1, or T2	N0, N1	M0	I
T0, T1, or T2	N2	M0	II
T3 or T4	N0, N1	M0	II
T3 or T4	N2	M0	III
Any T	Any N	M1	IV

HPV: human papillomavirus; TNM: tumor, node, metastasis; AJCC: American Joint Committee on Cancer; UICC: Union for International Cancer Control.

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# Carcinoma of Oropharynx

高雄榮民總醫院 臨床診療指引 Ver.1 修訂於 2024.05.01 Page 1 (Ref. 1,2)

WORK-UP	STAGING & TREATMENT	FOLLOW-UP
<ul style="list-style-type: none"><li>• History &amp; PE</li><li>• Biopsy &amp; Pathology</li><li>• Image<ul style="list-style-type: none"><li>→ MRI w/ and w/o contrast and/or CT w/ contrast of H&amp;N* or PET</li><li>→ WBBS (if PET/CT not done)/ Abd. Sono/ CXR</li><li>→ ± Chest CT* (if PET/CT not done)</li><li>→ ± Neck sono</li><li>→ ± EUA with endoscopy/ PES</li></ul></li><li>• Dental evaluation<ul style="list-style-type: none"><li>→ Panorex ± teeth extraction</li></ul></li><li>• <u>Multidisciplinary consultation</u> (± Fertility/reproductive, ± smoking cessation)</li><li>± Swallowing evaluation</li><li>• <b>Screening for HBV/HCV</b></li><li>• <u>p16 status</u></li></ul> <p>(*與癌症期別相關之主要檢查)</p>	<ul style="list-style-type: none"><li>• (P16-)[T1-2, N0-1, M0] 詳見 Page 2</li><li>• (P16-)[T3-4a, N0-1, M0] 詳見 Page 3</li><li>• (P16-)[T1-4a, N2-3, M0] 詳見 Page 3</li><li>• (P16+)[T0-2, N0-1, M0] (single node=<math>\leq</math>3cm) 詳見 Page 4</li><li>• (P16+)[T0-2, N1-2, M0] (<b>single node<math>&gt;</math>3cm, 2 or more ipsilateral nodes<math>\leq</math>6cm</b>) or [T3, N0-2, M0] 詳見 Page 5</li><li>• (P16+)[T0-3, N3, M0] or [T4, N0-3, M0] 詳見 Page 5</li><li>• Tonsil Page 6</li><li>• Very advanced stage 詳見 Page 7, 8</li></ul>	<ul style="list-style-type: none"><li>• <u>[Post-Tx within 3-6 months]</u><ul style="list-style-type: none"><li>→ Baseline MRI or CT (PET)</li><li>→ Every 1-2 months: PE</li></ul></li><li>• <u>[2nd year after Tx]</u><ul style="list-style-type: none"><li>→ Every 2-3 months: PE</li></ul></li><li>• <u>[ 3-5 years after Tx]</u><ul style="list-style-type: none"><li>→ Every 4-8 months: PE</li></ul></li><li>• <u>[ 5 years after Tx]</u><ul style="list-style-type: none"><li>→ Every 12 months: PE</li></ul></li><li>• Every year: H &amp; N MRI or CT, CxR, Bone scan &amp; Abd. Sono, Neck Sono, PES, ± TSH、free T4(if RT, 6-12 months) as clinically indicated</li></ul> <p>(AM cortisol, GH, free T4, prolactin, IGF-2, LH, FSH, ACTH, TSH, testosterone levels if RT to the skull base)</p>

# Carcinoma of Oropharynx(P16-)

高雄榮民總醫院 臨床診療指引 Ver.1 修訂於 2024.05.01 Page 2 (Ref. 1,2)

**Clinical T1-2,  
N0-1, M0**

Primary treatment

Definitive RT or CCRT(T1-2 ,N1 only)

Pathological features

Adjuvant management

Complete clinical response

Follow-up

Residual disease

Surgery

pN0 and adverse features (-)

Follow-up

pN1 and adverse features (-)

Consider RT<sup>註1</sup> or  
Follow-up (if high quality ND<sup>€</sup>)

Resection of  
primary  $\pm$  ND,  
unil. or bil.<sup>#</sup>

Extranodal extension  
 $\pm$  positive margin

CRT<sup>註1-2</sup>

Adverse  
features(+)

Positive margin

Re-resection, or RT, or CRT <sup>註1-2</sup>

Other adverse features

RT or CRT<sup>註1-2</sup>

$\pm$  Induction<sup>註3</sup> CT

# 依primary site而定，若T1-T2 primary tumor接近中線但有adequate margin且無adverse features，可執行staged contralateral ND以避免RT。側性明顯的tumor且pN0-1無adverse features，可以observation。

\* 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, vascular embolism lymphatic invasion

€ lymph node yield  $\geq 18$

# Carcinoma of Oropharynx(P16-)

高雄榮民總醫院 臨床診療指引 Ver.1 修訂於 2024.05.01 Page 3 (Ref. 1,2)

Clinical T3-4a, N0-1, M0

T1-4a, N2-3, M0

Primary treatment

Pathological features

Adjuvant Management

CRT or RT<sup>註1-2</sup>

Complete clinical response

Follow-up

Residual disease

Surgery if operable

See page 7 if inoperable

± Induction<sup>註3</sup> CT

Resection of primary, ND, unil. or bil.<sup>#</sup>

Adverse features\*(-)

RT<sup>註1</sup>

Extranodal extension ± positive margin

CRT or RT<sup>註1-2</sup>

Other adverse features

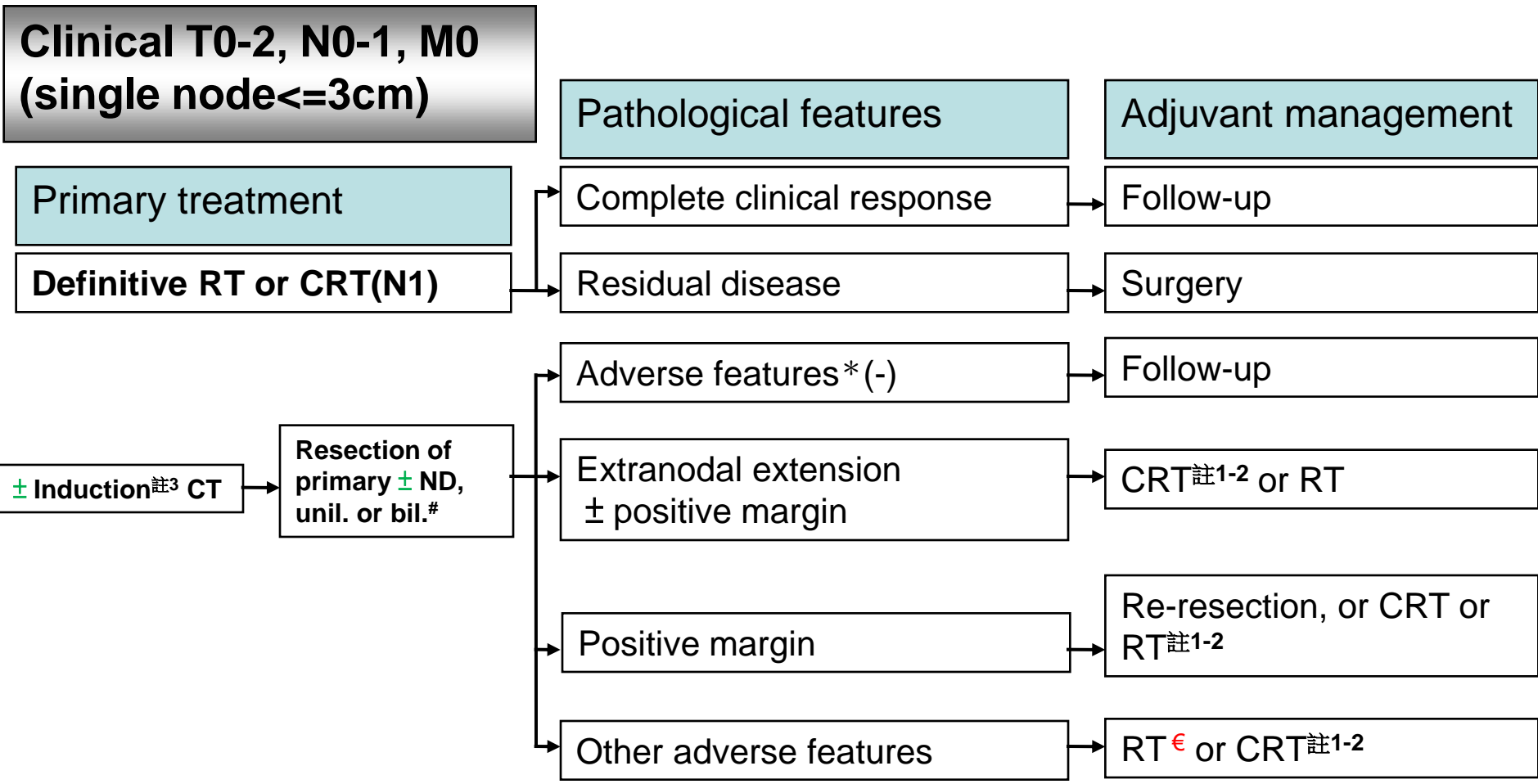
RT or CRT<sup>註1-2</sup>

# Neck dissection level 跟單雙側依cN status及primary site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, vascular embolism lymphatic invasion

# Carcinoma of Oropharynx (P16+)

高雄榮民總醫院 臨床診療指引 Ver.1 修訂於 2024.05.01 Page 4 (Ref. 1,2)



# 依primary site而定

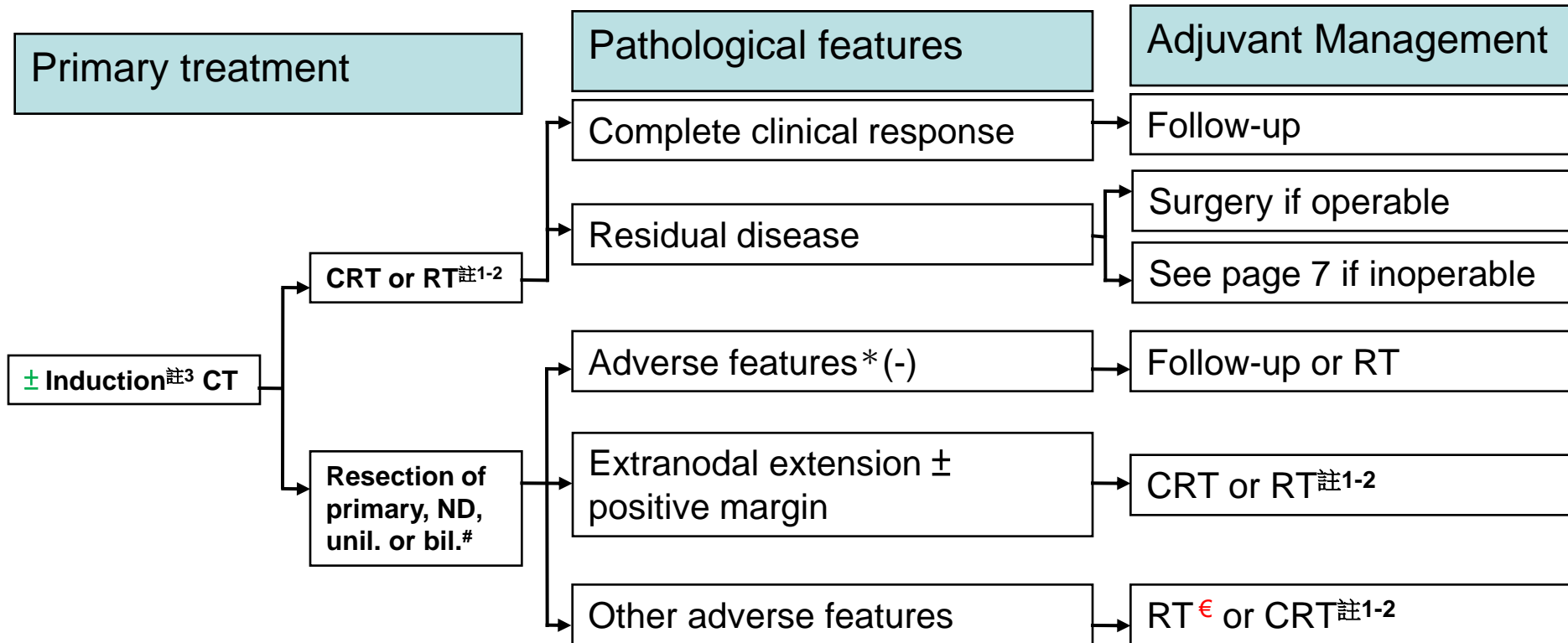
\* Adverse features : Extranodal extension, positive or close margins(<3 mm), pT3 or pT4 primary, one positive node >3 cm or multiple positive nodes, nodal disease in levels IV or V, perineural invasion, lymphovascular invasion

€最多不超過4個positive LNs,或是切除後的T1-T2 margin為negative或是close margins (<3 mm),或是非雙邊的N1-N2有≤1 mm的ENE, 可以考慮將RT劑量降階至50Gy

# Carcinoma of Oropharynx (P16+)

高雄榮民總醫院 臨床診療指引 Ver.1 修訂於 2024.05.01 Page 5 (Ref. 1,2)

Clinical T0-2, N1-2, M0 (single node >3cm, 2 or more nodes ≤6cm) or T3, N0-2, M0  
T0-3, N3, M0, or T4, N0-3, M0



# Neck dissection level 跟單雙側依cN status及primary site而定(對於疾病對IC沒有反應的病人，手術可以是一個治療選項)

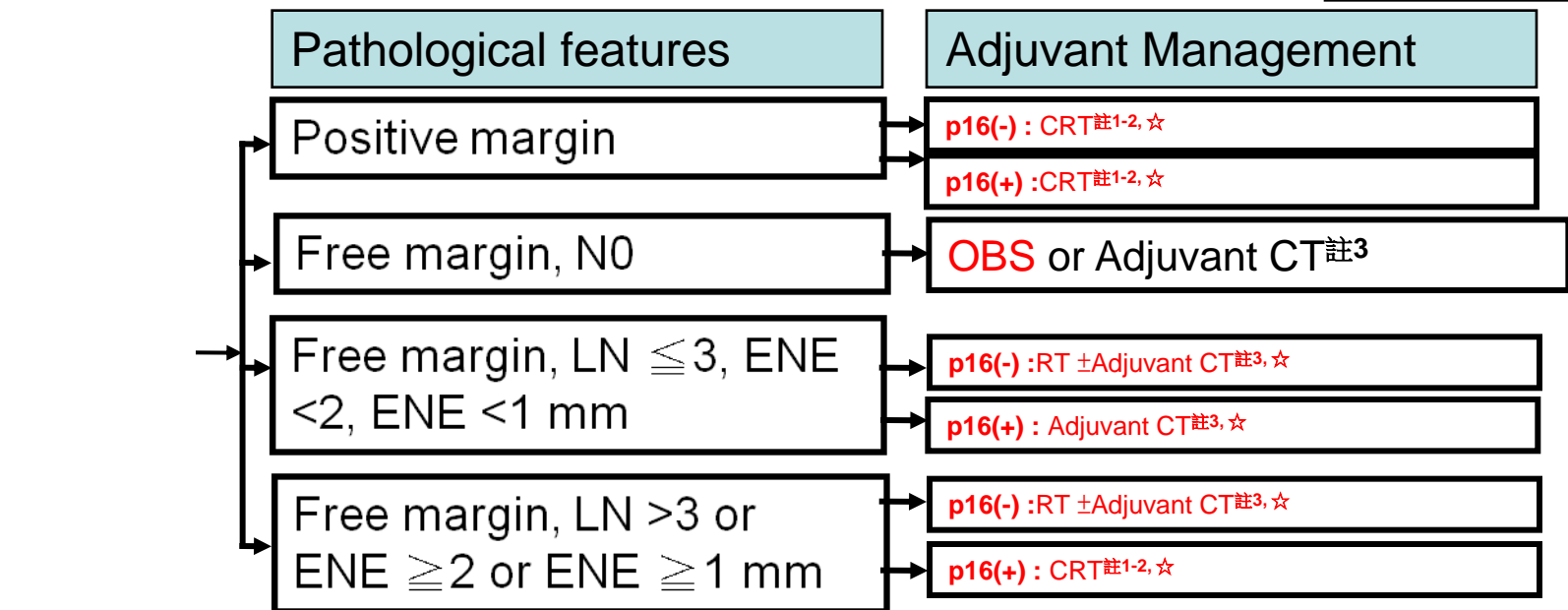
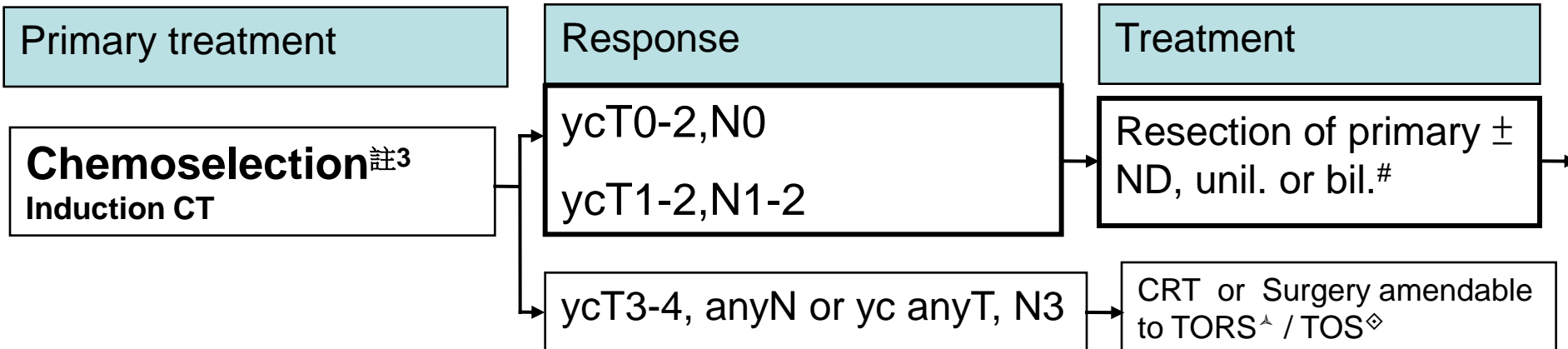
\* Adverse features : Extranodal extension, positive or close margins(<3 mm), pT3 or pT4 primary, one positive node >3 cm or multiple positive nodes, nodal disease in levels IV or V, perineural invasion, lymphovascular invasion

€最多不超過4個positive LNs,或是切除後的T1-T2 margin為negative或是close margins (<3 mm),或是非雙邊的N1-N2有≤1 mm的ENE，可以考慮將RT劑量降階至50Gy

# Carcinoma of Oropharynx (VGHKS Option)

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**Clinical any T, any N, for both p16(+) and p16(-)**



# Neck dissection level 依primary部位及cN status而定

^ Transoral Robotic Surgery

◇ Transoral Surgery

☆ 放射治療劑量參考口咽癌放射治療政策及執行情序

# Carcinoma of Oropharynx

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**P16(-), Clinical T4b, any N or unresectable primary/nodal disease or inoperable patient status**

Management

**PS 0-1**

CCRT or RT 註1-2

Induction CT 註3 + RT or CRT 註1-2

**PS 2**

Definite RT 註1 ± CT 註2

**PS 3**

Palliative RT 註1

Single agent palliative CT 註3

Best supportive care

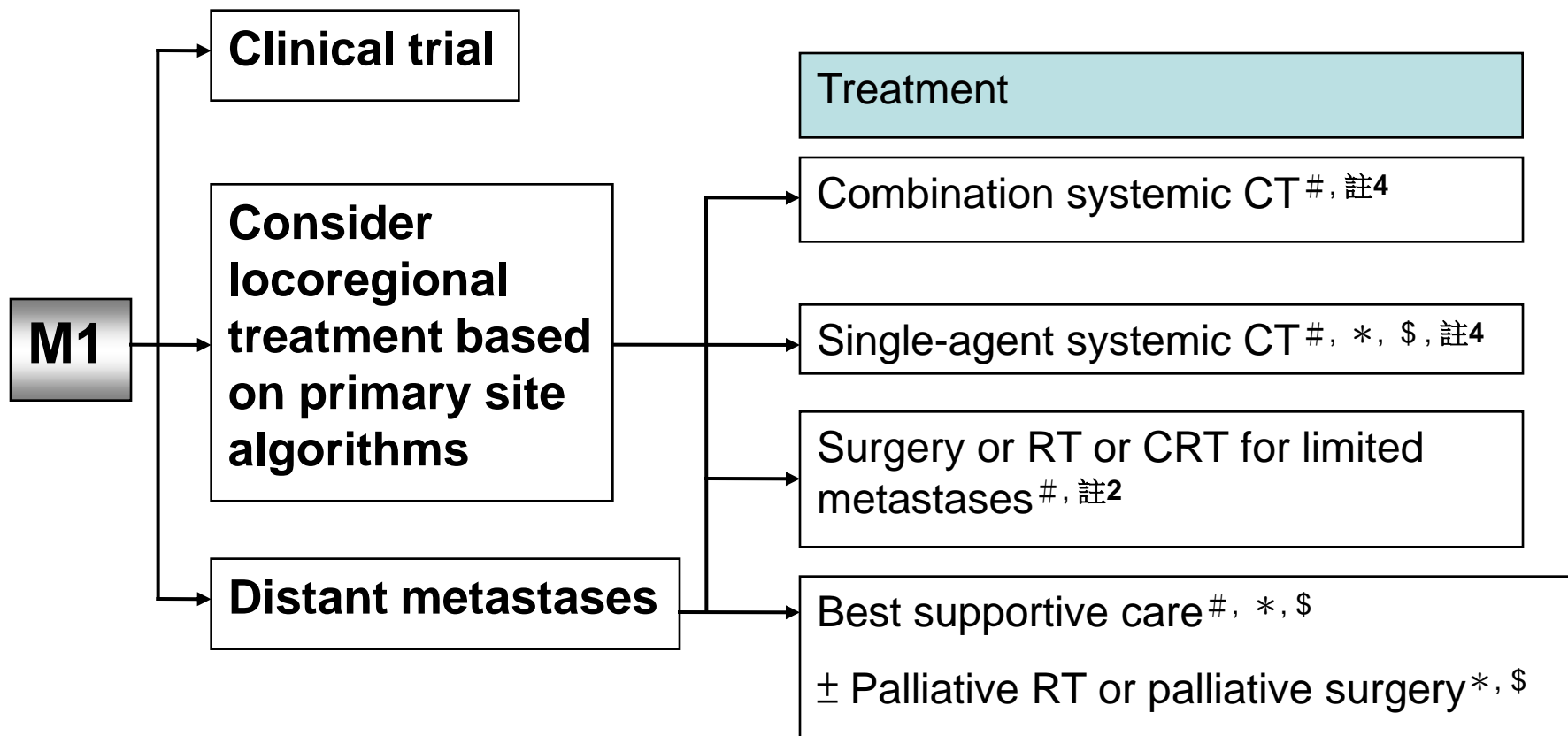
ECOG Performance Status 0-1 註6

ECOG Performance Status 2

ECOG Performance Status 3

# Carcinoma of Oropharynx

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# ECOG Performance Status 0-1 註6

\* ECOG Performance Status 2

\$ ECOG Performance Status 3

# Carcinoma of Oropharynx

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註1

## Principles of Radiotherapy

### Definitive Radiotherapy

- Primary and gross adenopathy : 66 - 72 Gy (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)
- De-escalation to 50 Gy may be considered in patients with p16 (HPV)-positive oropharynx cancer who have up to 4 positive lymph nodes, T1-T2 resected to negative or close margins (<3 mm), and/or N1–N2 disease (excluding bilateral disease based on ECOG 3311 criteria) with  $\leq 1$  mm extranodal extension

### 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 Oropharynx

註2 高雄榮民總醫院 臨床診療指引 Ver.1 修訂於 2024.05.01 Page 10 ([Ref. 8-12](#))

## 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

# Carcinoma of Oropharynx

註3 高雄榮民總醫院 臨床診療指引 Ver.1 修訂於 2024.05.01 Page 11 ([Ref. 13-17](#))

## Regimens of Chemotherapy

Induction, adjuvant, 建議2-3cycles

**Regimen 1 : q3-4 weeks T + P ± Pembrolizumab ± 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
- Pembrolizumab(200mg) D1 (if CPS ≥ 1)

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

# Carcinoma of Oropharynx

註3

高雄榮民總醫院 臨床診療指引 Ver.1 修訂於 2024.05.01 Page 12 ([Ref. 13-17](#))

## Regimens of Chemotherapy

Induction, adjuvant, 建議2-3cycles

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

# Carcinoma of Oropharynx

註4

高雄榮民總醫院 臨床診療指引 Ver.1 修訂於 2024.05.01 Page 13 (Ref. 18,19)

## Regimens of Chemotherapy

### Recurrent, unresectable, metastatic\*

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

- Pembrolizumab(200mg) D1 (if CPS  $\geq$  1)
- 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  $\geq$  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 T + P ± Pembrolizumab 註5

- Taxotere(60 mg/ m<sup>2</sup>) D1
- Cisplatin(60-75 mg/ m<sup>2</sup>) D1
- Pembrolizumab(200mg) D1 (if CPS  $\geq$  1)

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

# Carcinoma of Oropharynx

註4

高雄榮民總醫院 臨床診療指引 Ver.1 修訂於 2024.05.01 Page 14 ([Ref. 18,19](#))

## Regimens of Chemotherapy

### Recurrent, unresectable, metastatic\*

#### **Regimen 6: 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 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 Oropharynx

註5

高雄榮民總醫院 臨床診療指引 Ver.1 修訂於 2024.05.01 Page 15

## 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 Oropharynx

註5 高雄榮民總醫院 臨床診療指引 Ver.1 修訂於 2024.05.01 Page 16

## 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(CPS  $\geq$  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。
- 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 表現量一線: CPS  $\geq$  20; 二線: TPS  $\geq$  50%, TC  $\geq$  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  $\leq$  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 Oropharynx

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 Oropharynx

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1. NCCN Clinical Practice Guidelines in Oncology – Head and Neck Cancers Version 3. 2024
2. AJCC (American Joint Committee on Cancer) Manual for Staging of Cancer, 8th ed, Amin M, Edge S, Greene F, et al. (Eds), Springer-Verlag, New York 2017.
3. Nader Sadeghi, Ning-Wei Li, M. Reza Taheri, Samantha Easley, Robert S. Siegel. Neoadjuvant chemotherapy and transoral surgery as a definitive treatment for oropharyngeal cancer: A feasible novel approach. *Head & Neck* 2016 Dec;38(12):1837-1846
4. Esther Lee, Daniel Gorelik, Hannah R. Crowder, Christopher Badger, Jennifer Schottler et al. Swallowing Function Following Neoadjuvant Chemotherapy and Transoral Robotic Surgery for Oropharyngeal Carcinoma: A 2-Year Follow-up. *Otolaryngology–Head and Neck Surgery* 2022 Aug;167(2):298-304.
5. Peter AP, Michael EC, Greg D, et al. Up-front neck dissection followed by concurrent chemoradiation in patients with regionally advanced head and neck cancer. *Head Neck*. 2012;34:1798-1803
6. Bradley, PJ, MacLennan, K, Brakenhoff, RH, Leemans, CR. Status of primary tumour surgical margins in squamous head and neck cancer: prognostic implications. *Curr Opin Otolaryngol Head Neck Surg* 2007; 15:74.
7. Vermorken JB, Remenar E, van Herpen C, Gorlia T, Mesia R, Degardin M, Stewart JS, Jelic S, Betka J, Preiss JH, et al. Cisplatin, fluorouracil, and docetaxel in unresectable head and neck cancer. *N Engl J Med*. 2007 Oct 25; 357(17):1695-704
8. Forastiere AA, Zhang Q, Weber RS, et al. Long-term results of RTOG 91-11: a comparison of three nonsurgical treatment strategies to preserve the larynx in patients with locally advanced larynx cancer. *J Clin Oncol* 2013;31:845-852.
9. Adelstein DJ, Li Y, Adams GL, et al. An intergroup phase III comparison of standard radiation therapy and two schedules of concurrent chemoradiotherapy in patients with unresectable squamous cell head and neck cancer. *J Clin Oncol* 2003;21(1):92-98.
10. Bonner JA, Harari PM, Giralt J, et al. Radiotherapy plus cetuximab for locoregionally advanced head and neck cancer: 5-year survival data from a phase 3 randomised trial, and relation between cetuximab-induced rash and survival. *Lancet Oncol* 2010;11:21-28
11. Denis F, Garaud P, Bardet E, et al. Final results of the 94-01 French Head and Neck Oncology and Radiotherapy Group randomized trial comparing radiotherapy alone with concomitant radiochemotherapy in advanced-stage oropharynx carcinoma. *J Clin Oncol* 2004;22:69-76
12. Bourhis J, Sire C, Graff P, et al. Concomitant chemoradiotherapy versus acceleration of radiotherapy with or without concomitant chemotherapy in locally advanced head and neck carcinoma (GORTEC 99-02): an open-label phase 3 randomised trial. *Lancet Oncol* 2012;13:145-153.
13. Forastiere AA, Zhang Q, Weber RS, et al. Long-term results of RTOG 91-11: a comparison of three nonsurgical treatment strategies to preserve the larynx in patients with locally advanced larynx cancer. *J Clin Oncol* 2013;31:845-852.
14. Adelstein DJ, Li Y, Adams GL, et al. An intergroup phase III comparison of standard radiation therapy and two schedules of concurrent chemoradiotherapy in patients with unresectable squamous cell head and neck cancer. *J Clin Oncol* 2003;21(1):92-98.
15. Bonner JA, Harari PM, Giralt J, et al. Radiotherapy plus cetuximab for locoregionally advanced head and neck cancer: 5-year survival data from a phase 3 randomised trial, and relation between cetuximab-induced rash and survival. *Lancet Oncol* 2010;11:21-28. Denis F, Garaud P, Bardet E, et al. Final results of the 94-01 French Head and Neck Oncology and Radiotherapy Group randomized trial comparing radiotherapy alone with concomitant radiochemotherapy in advanced-stage oropharynx carcinoma. *J Clin Oncol* 2004;22:69-76.
16. Bourhis J, Sire C, Graff P, et al. Concomitant chemoradiotherapy versus acceleration of radiotherapy with or without concomitant chemotherapy in locally advanced head and neck carcinoma (GORTEC 99-02): an open-label phase 3 randomised trial. *Lancet Oncol* 2012;13:145-153.
17. Posner MR, Hershock DM, Blajman CR, Mickiewicz E, Winquist E, Gorbounova V, Tjulandin S, Shin DM, Cullen K, Ervin TJ, et al. Cisplatin and fluorouracil alone or with docetaxel in head and neck cancer. *N Engl J Med*. 2007 Oct 25; 357(17):1705-1
18. Vermorken JB, Mesia, R, Rivera F, Platinum-Based Chemotherapy plus Cetuximab in Head and Neck Cancer *N Engl J Med*. 2008 Sep 11; 359:1116-27
19. Guigay J, Fayette J, Dillies A-F, et al. Cetuximab, docetaxel, and cisplatin (TPEX) as first-line treatment in patients with recurrent or metastatic (R/M) squamous cell carcinoma of the head and neck (SCCHN): Final results of phase II trial GORTEC 2008-03 [abstract]. *J Clin Oncol* 2012;30(Suppl 15):Abstract 5505.