

高雄榮民總醫院

口咽癌診療原則

2018年05月23日 第二版

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：2018/01/03

本共識與上一版的差異

上一版	新版
<ol style="list-style-type: none">1. 未獨立P16 Positive治療指引2. 未標示與期別相關之主要檢查	<ol style="list-style-type: none">1. 將P16 Positive獨立一個新的指引項目2. 新增*標示，註明與期別相關之主要檢查(MRI* or CT of H&N*、Chest X-ray*、Bone scan*、Abd. Sono*)。

Oropharyngeal (P16 negative) cancer Clinical staging AJCC 8th

Oropharyngeal (p16 negative) cancer TNM clinical staging AJCC UICC 2017

Primary tumor (T)	
Oropharynx (p16-)	
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.
* NOTE: 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) - Oropharynx (p16-) and hypopharynx	
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(-); or metastases in multiple ipsilateral lymph nodes, none larger than 6 cm in greatest dimension and ENE(-); or 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	Metastasis in multiple ipsilateral nodes, none larger than 6 cm in greatest dimension and ENE(-)
N2c	Metastasis 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(-); or 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)			
Oropharynx (p16-) and hypopharynx			
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, 1	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.

Oropharyngeal (P16 negative) cancer Pathological staging AJCC 8th

Oropharyngeal (p16 negative) cancer TNM pathological staging AJCC UICC 2017

Primary tumor (T)	
Oropharynx (p16-)	
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.
* NOTE: 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) - Oropharynx (p16-) and hypopharynx	
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(+); or larger than 3 cm but not larger than 6 cm in greatest dimension and ENE(-); or metastases in multiple ipsilateral lymph nodes, none larger than 6 cm in greatest dimension and ENE(-); or 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(+); or a single ipsilateral node larger than 3 cm but not larger than 6 cm in greatest dimension and ENE(-)
N2b	Metastasis in multiple ipsilateral nodes, none larger than 6 cm in greatest dimension and ENE(-)
N2c	Metastasis 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(-); or in a single ipsilateral node larger than 3 cm in greatest dimension and ENE(+); or multiple ipsilateral, contralateral or bilateral nodes, any with ENE(+); or a single contralateral node 3 cm or smaller 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(+); or multiple ipsilateral, contralateral or bilateral nodes, any with ENE(+); or a single contralateral node 3 cm or smaller 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)			
Oropharynx (p16-) and hypopharynx			
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, 1	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.

Oropharyngeal (P16 Positive) cancer

Pathological staging AJCC 8th

HPV related oropharyngeal carcinoma TNM clinical staging AJCC UICC 2017

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.*		
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.

* 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.

HPV related oropharyngeal carcinoma TNM pathologic staging AJCC UICC 2017

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.*		
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.

* 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.

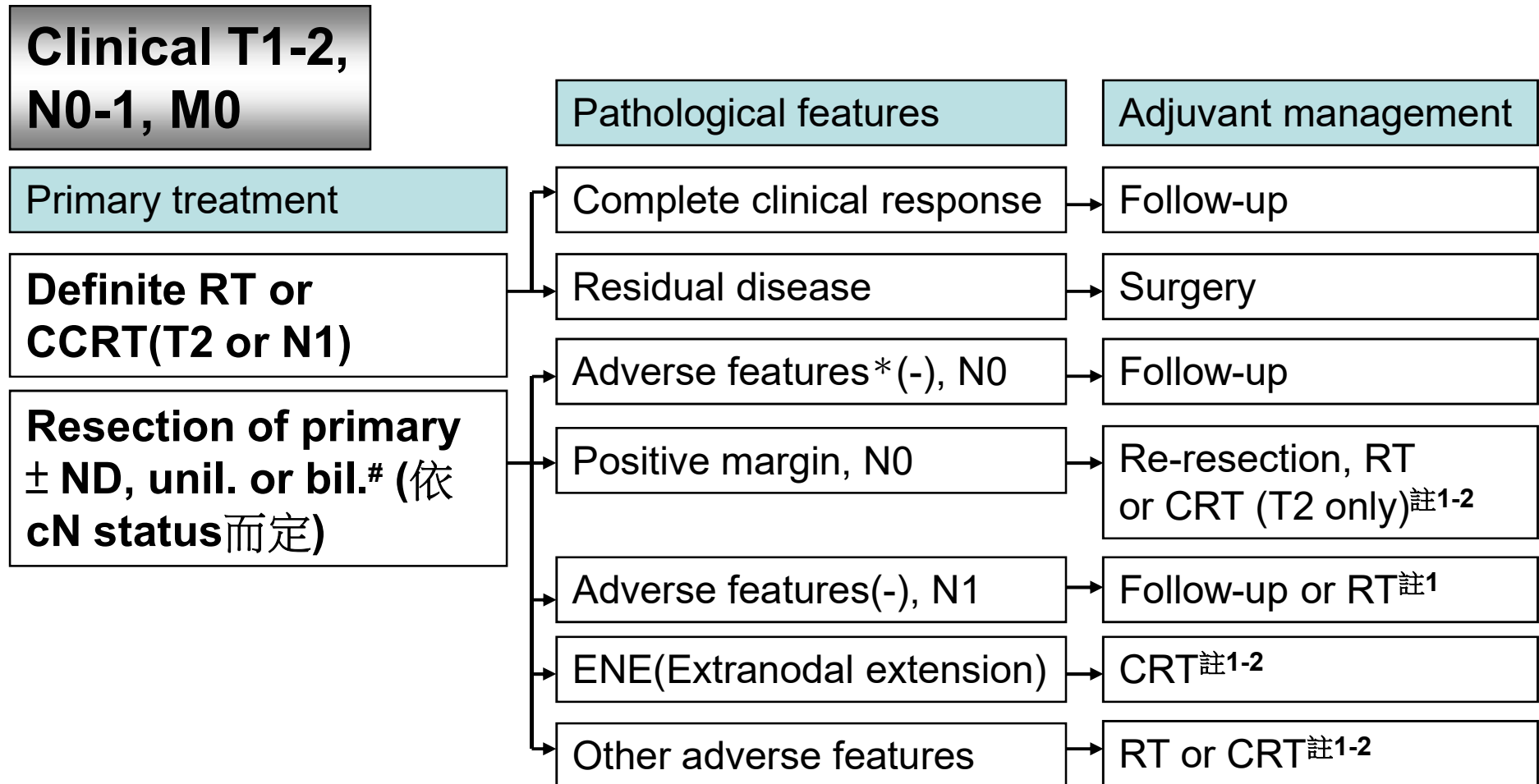
Carcinoma of Oropharynx

高雄榮民總醫院 臨床診療指引 Ver.1 修訂於 2018.05.23 Page 1 (Ref. 1,2)

WORK-UP	STAGING & TREATMENT	FOLLOW-UP
<ul style="list-style-type: none">• <u>History & PE</u>• <u>Biopsy & Pathology</u>• <u>Image</u><ul style="list-style-type: none">→ MRI* or CT of H&N* or PET→ Chest X-ray*→ Bone scan*→ Abd. Sono*→ ± Neck Sono→ ± PET scan• <u>Dental evaluation</u><ul style="list-style-type: none">→ Panorex→ ± teeth extraction• UGI series exam• <u>Multidisciplinary consultation</u>± Swallowing evaluation• p16 status <p>(*與癌症期別相關之主要檢查)</p>	<ul style="list-style-type: none">• <u>[T1-2, N0-1, M0]</u> 詳見 <i>Page 2</i>• <u>[T3-4a, N0-1, M0]</u> 詳見 <i>Page 3</i>• <u>[Any T, N2-3, M0]</u> 詳見 <i>Page 4</i>• <u>Very advanced stage</u> 詳見 <i>Page 5</i>	<ul style="list-style-type: none">• <u>[Post-Tx within 6 months]</u><ul style="list-style-type: none">→ Every 1-2 months: PE→ Baseline MRI or CT• <u>[0.5-3 years after Tx]</u><ul style="list-style-type: none">→ Every 2-3 months: PE→ Every 1 year: H & N MRI or CT, CxR, Bone scan & Abd. Sono ± Neck Sono as clinically indicated• <u>[3-5 years after Tx]</u><ul style="list-style-type: none">→ Every 4-6 months: PE• <u>[5 years later after Tx]</u><ul style="list-style-type: none">→ Every 6-12 months: PE

Carcinoma of Oropharynx(P16-)

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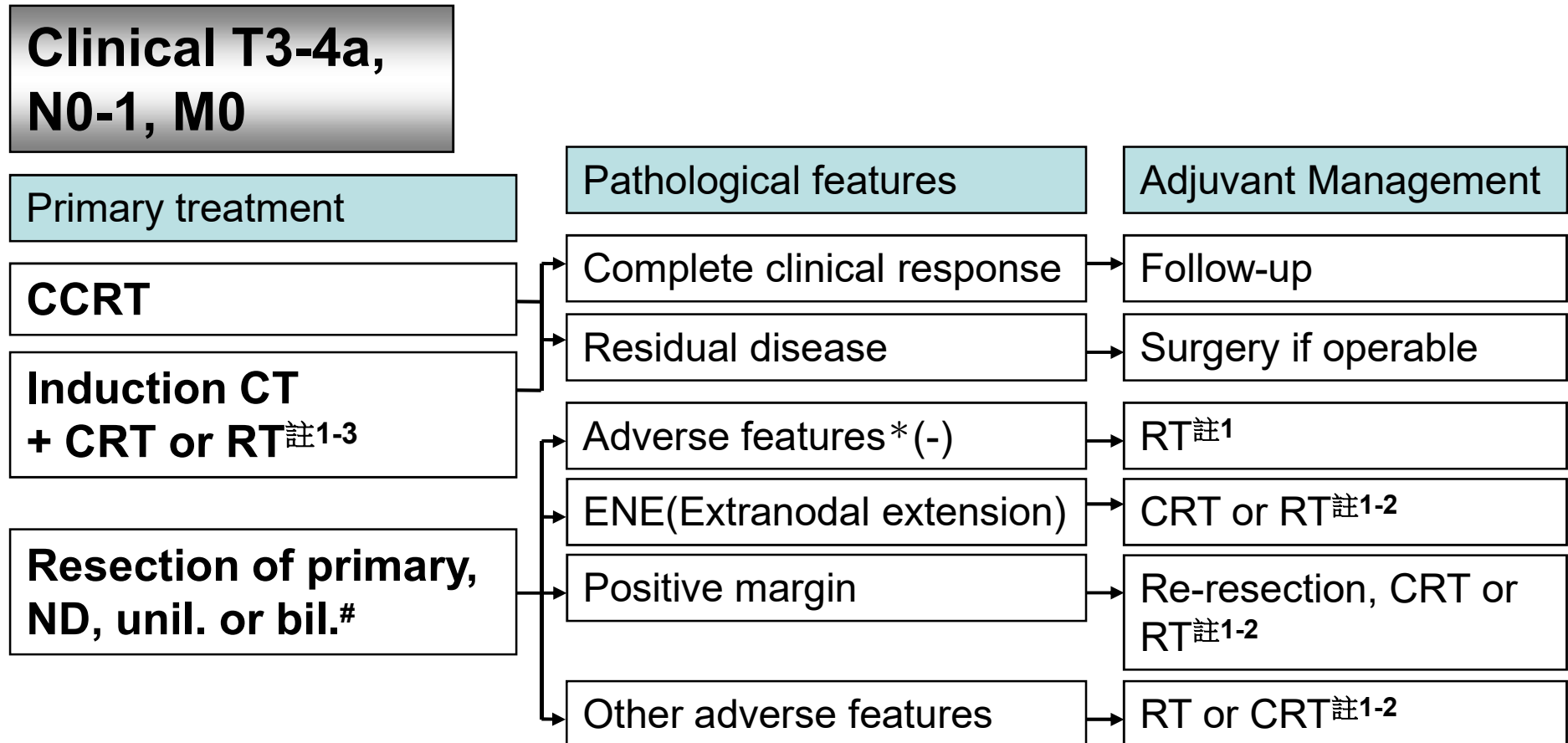


#可考慮Elective neck dissection或close follow-up

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

Carcinoma of Oropharynx(P16-)

高雄榮民總醫院 臨床診療指引 Ver.1 修訂於 2018.05.23 Page 3 (Ref. 1,2)



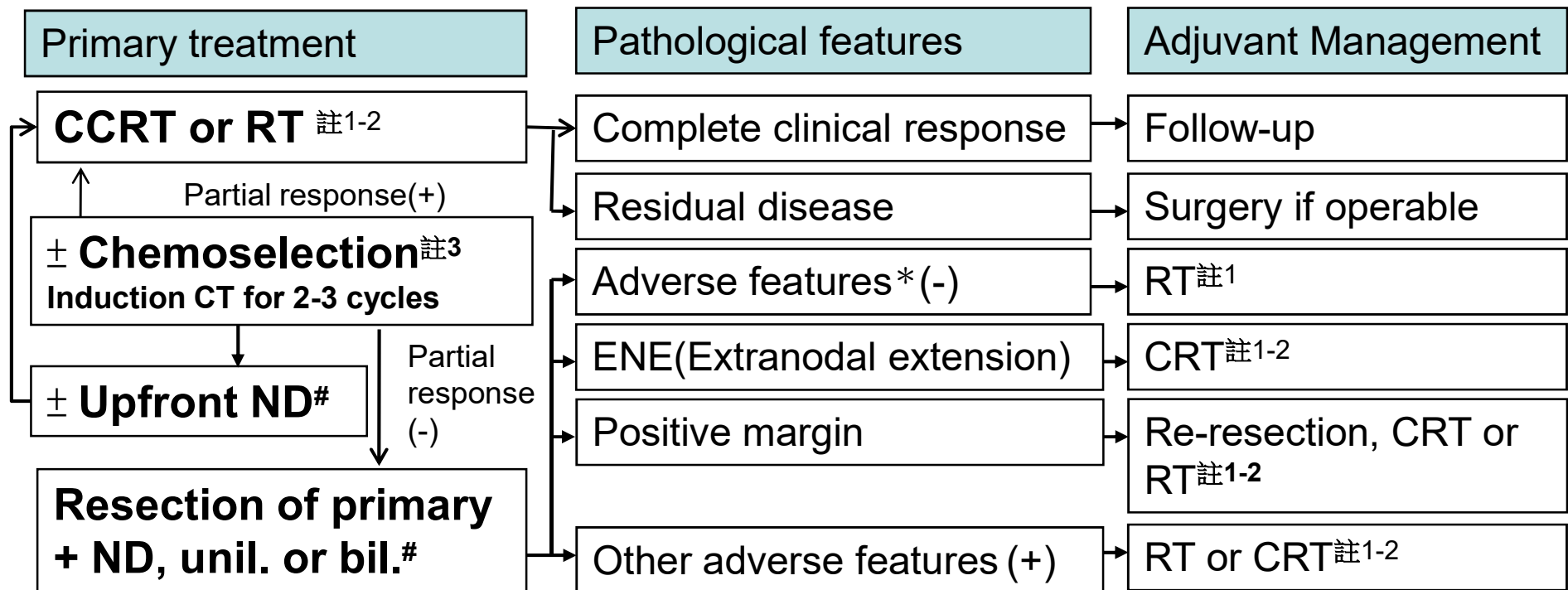
#Neck dissection level 依cN status而定。

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

Carcinoma of Oropharynx(P16-)

高雄榮民總醫院 臨床診療指引 Ver.1 修訂於 2018.05.23 Page 4 (Ref. 1,2)

Clinical any T, N2-3, M0

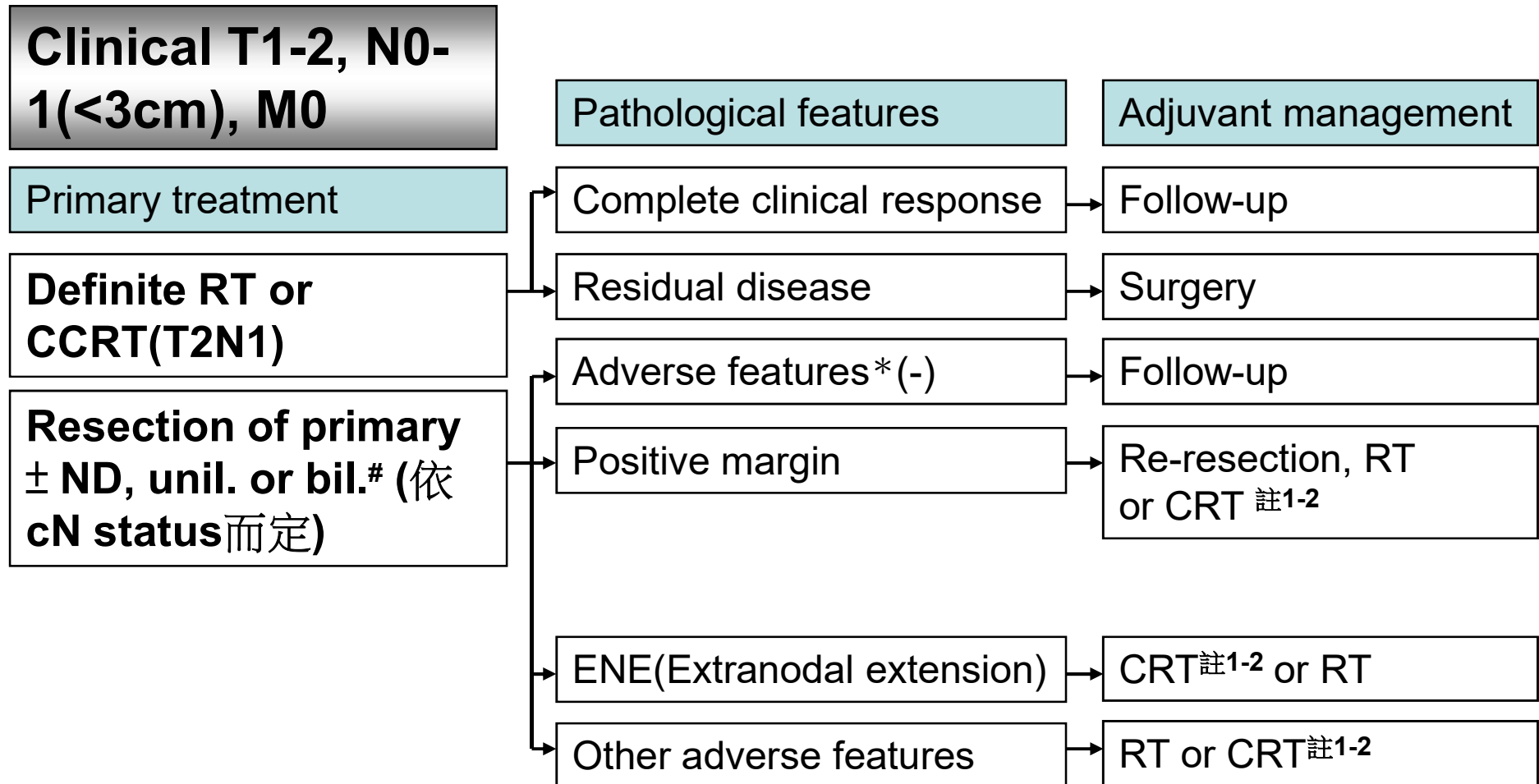


Neck dissection level 依primary部位及cN status而定。

* Adverse features : Extranodal extension, positive margins, pT3-4, N2-3 nodal disease, nodal disease in levels IV or V, perineural invasion, lymphovascular invasion.

Carcinoma of Oropharynx (P16+)

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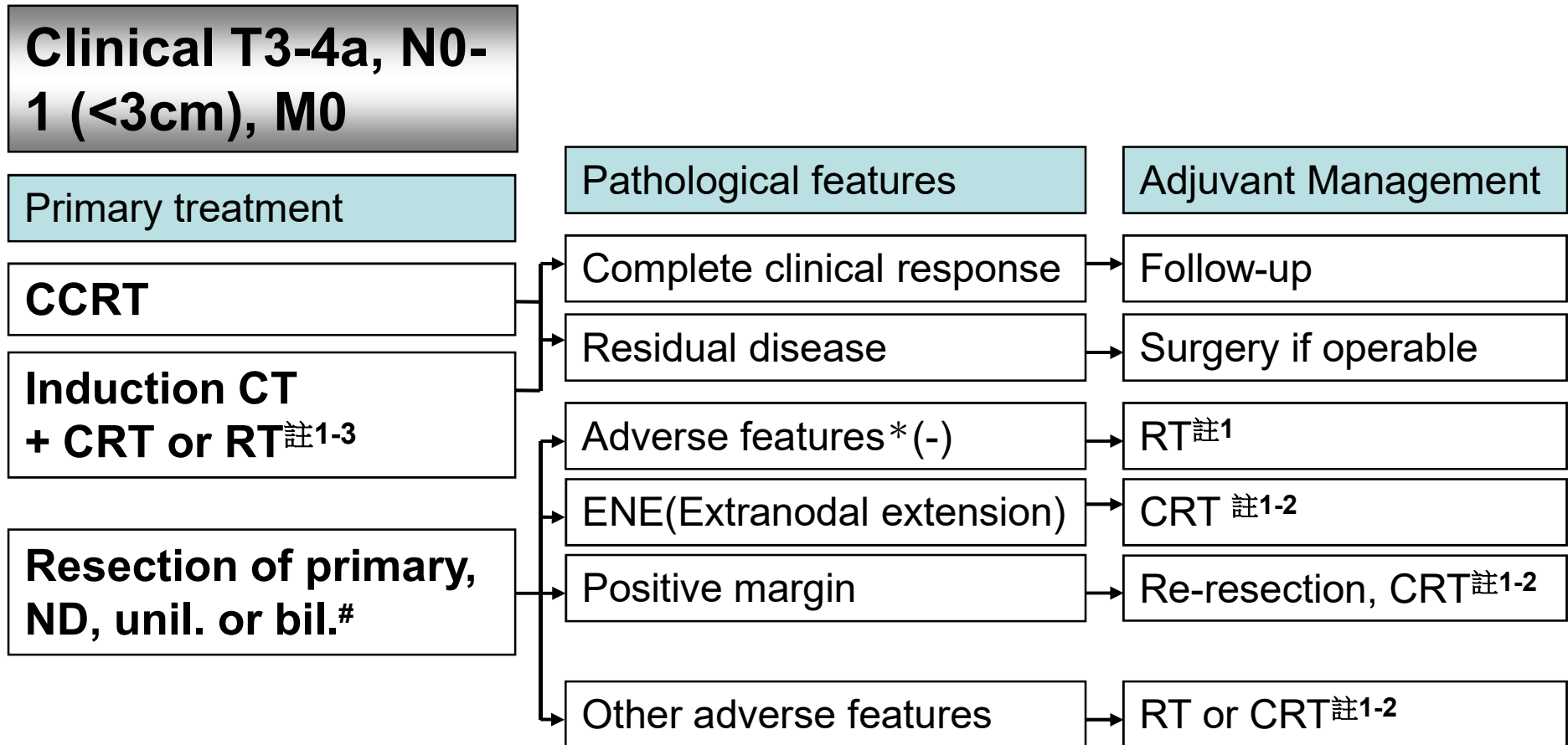


#可考慮Elective neck dissection或close follow-up

*Adverse features: Extranodal extension, positive margins, nodal disease in levels IV or V, perineural invasion, lymphatic invasion, vascular embolism

Carcinoma of Oropharynx (P16+)

高雄榮民總醫院 臨床診療指引 Ver.1 修訂於 2018.05.23 Page 3 (Ref. 1,2)

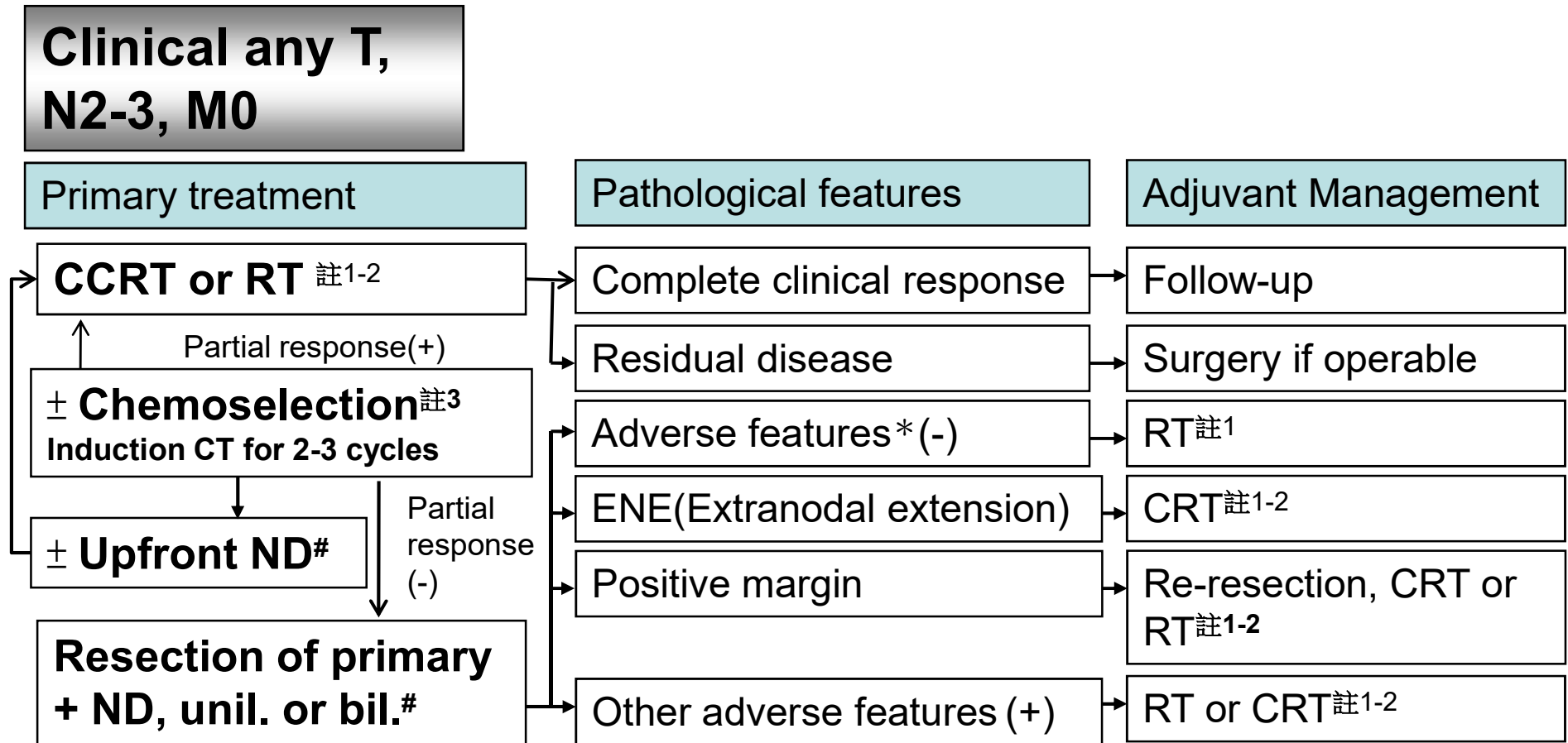


#Neck dissection level 依cN status而定。

*Adverse features: Extranodal extension, positive margins, nodal disease in levels IV or V, perineural invasion, lymphatic invasion, vascular embolism

Carcinoma of Oropharynx (P16+)

高雄榮民總醫院 臨床診療指引 Ver.1 修訂於 2018.05.23 Page 4 (Ref. 1,2)

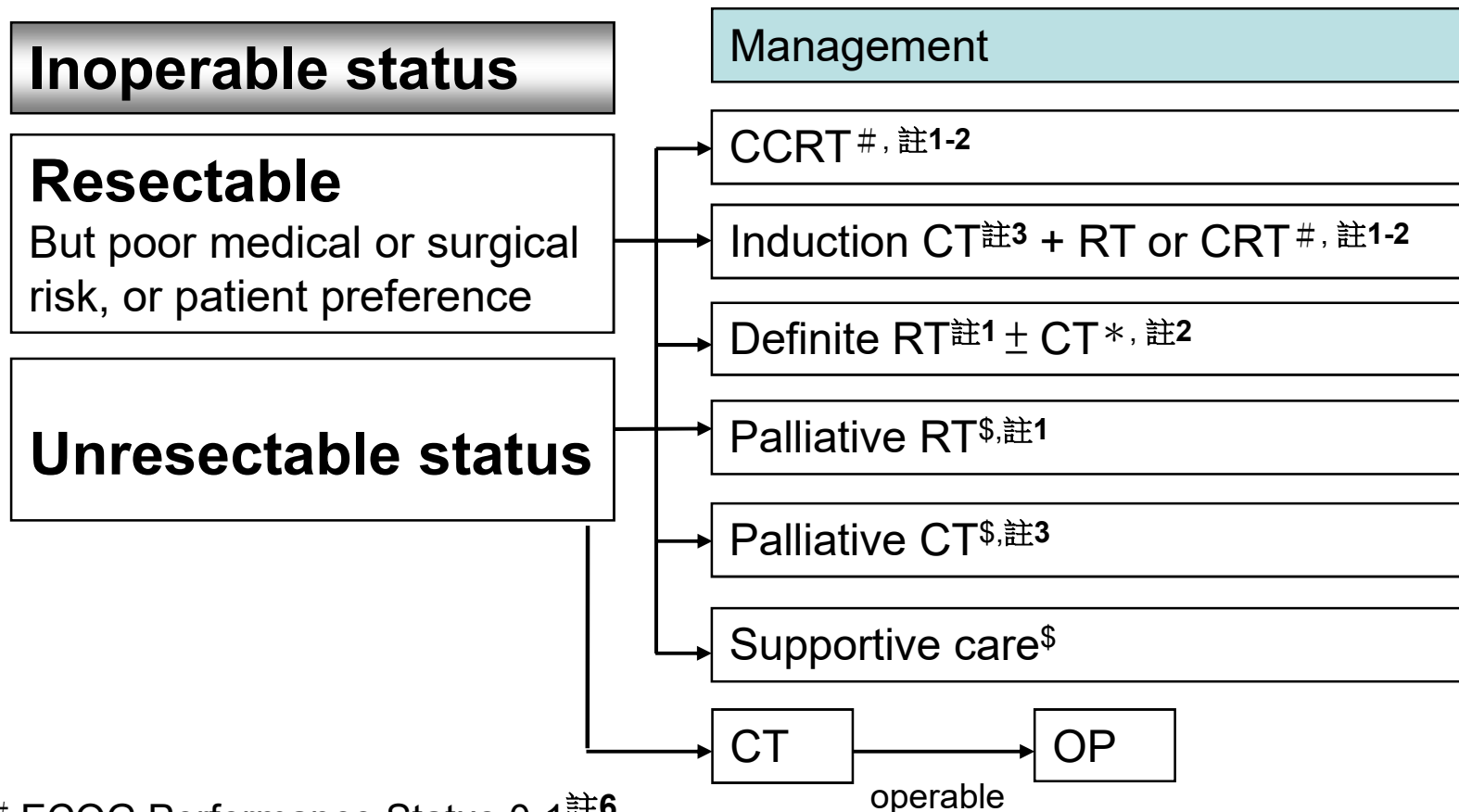


Neck dissection level 依primary部位及cN status而定。

* Adverse features: Extranodal extension, positive margins, nodal disease in levels IV or V, perineural invasion, lymphatic invasion, vascular embolism

Carcinoma of Oropharynx

高雄榮民總醫院 臨床診療指引 Ver.1 修訂於 2018.05.23 Page 6 (Ref. 1,2)



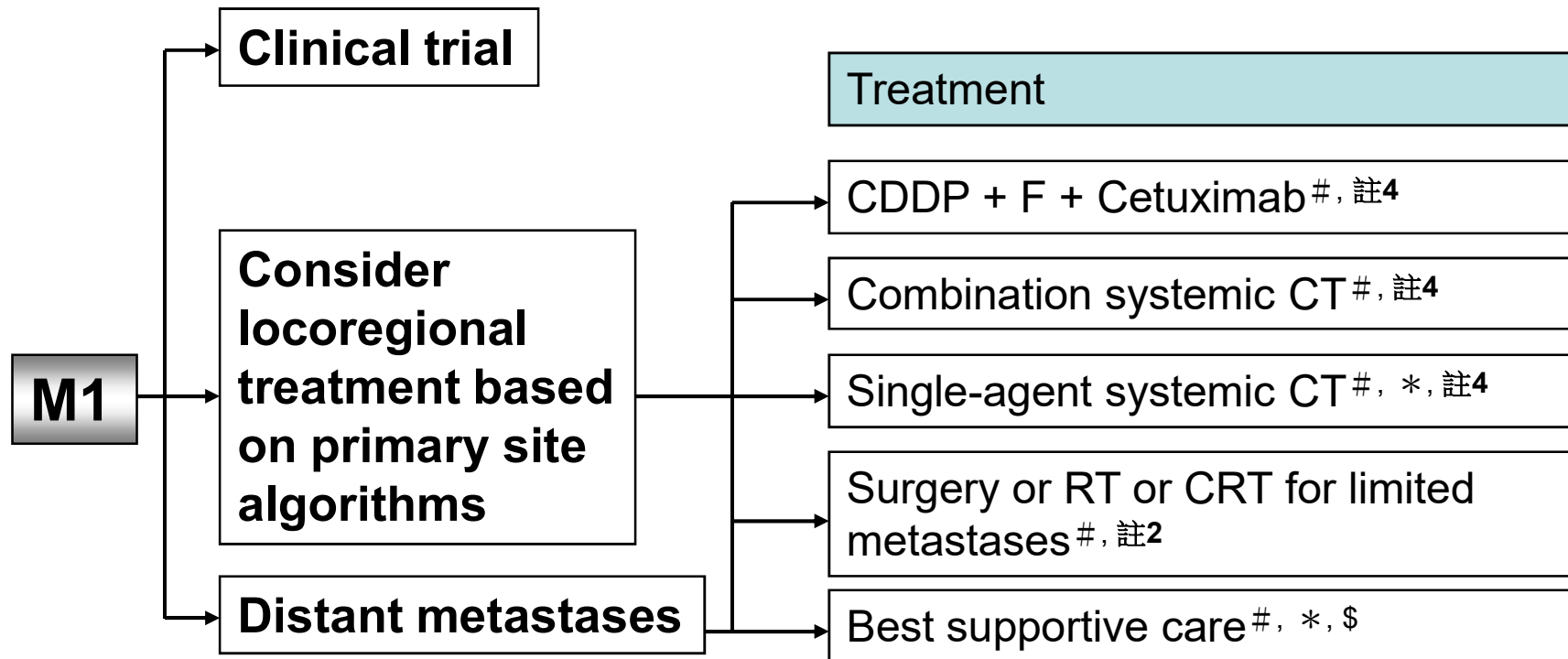
ECOG Performance Status 0-1 註6

* ECOG Performance Status 2

\$ ECOG Performance Status 3

Carcinoma of Oropharynx

高雄榮民總醫院 臨床診療指引 Ver.1 修訂於 2018.05.23 Page 7 (Ref. 1,15-17)



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 - 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)

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

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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4} ± 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

Carcinoma of Oropharynx

註3

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Regimens of Chemotherapy

Induction, adjuvant, 建議2-3cycles

Regimen 1: q3-4 weeks CDDP ± F ± weekly Cetuximab^{註5}

- Cisplatin(80-100mg/ m²) D1
- Fluorouracil (5-FU) (600-1000 mg/m²) D2-D5
- Cetuximab(400mg/ m²) loading dose first week, then weekly Cetuximab (250mg/ m²)

Regimen 2: q3-4 weeks P ± F ± weekly Cetuximab^{註5}

- Cisplatin (20mg/ m²) D1-D5
- Fluorouracil (5-FU) (600-1000 mg/ m²) D1-D5
- Cetuximab(400mg/ m²) loading dose first week, then weekly Cetuximab (250mg/ m²)

Regimen 3: q3-4 weeks Carboplatin ± F ± weekly Cetuximab^{註5}

- 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)

Carcinoma of Oropharynx

註3

高雄榮民總醫院 臨床診療指引 Ver.1 修訂於 2018.05.23 Page 11 (Ref. 11-15)

Regimens of Chemotherapy

Induction, adjuvant, 建議2-3cycles

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

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

Regimen 5: weekly Cetuximab^{註5}

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

Regimen 6: 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 7: weekly Methotrexate

- Methotrexate (40-60mg/ m²)

Carcinoma of Oropharynx

註4

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Regimens of Chemotherapy

Salvage or Metastasis

Regimen 1: q3-4 weeks CDDP ± F ± weekly Cetuximab^{註5}

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

Regimen 2: q3-4 weeks Carboplatin^{註6} ± F ± weekly Cetuximab^{註5}

- Carboplatin (AUC x 5mg) D1
- Fluorouracil (5-FU) (1000mg/ m²) D2-D5
- Cetuximab(400mg/ m²) loading dose first week, then weekly Cetuximab (250mg/ m²)

Regimen 3: q3-4 weeks T^{註5} ± P

- Taxotere(60 mg/ m²) D1
- Cisplatin(60-75 mg/ m²) D1

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

- Taxotere(60 mg/ m²) D1
- Carboplatin (AUC x 5mg) D1

Carcinoma of Oropharynx

註5

高雄榮民總醫院 臨床診療指引 Ver.1 修訂於 2018.05.23 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，且符合下列條件之一：
 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。
- 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。

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6

高雄榮民總醫院 臨床診療指引 Ver.1 修訂於 2018.05.23 Page 14

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

References

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