高 雄 榮 民 總 醫 院
鼻咽癌診療原則

2021年04月28日 第一版

鼻咽癌醫療團隊擬訂

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：2020/07/15

本共識與上一版的差異

<table>
<tr><th>上一版</th><th>新版</th></tr>
<tr><td>1. Work-up增加± Neck FNA, ± Chest CT
2. 獨立出T1N0M0治療頁面，合併M1到Any T, any N, M1(於2017年分開)
3. 在M1治療中新增treatment to oligometastatic site
4. Follow up新增3-6月追蹤TSH(if neck irridiated)
5. Definite RT 劑量上調至2.2Gy/Fr.
6. 按照NCCN guideline調整induction/ adjuvant , recurrent/metastasis chemotherapy regimen順序
7. 新增induction C/T regimen: GP
8. 刪除 Recurrent/Met MEP, PEB regimen
9. 新增metastatic regimen : immunotherapy
10. Adjuvant CT@ P5
@ N3, T3-4N1-2, or stage IV

11. Induction CT + CCRT or RT 註1-3 P5
(視病情需求, 如: EBV titer> 1000, bulky T3, advanced N2$)
$ Diffuse LAP near the cricoid cartilage, big LAP ≧ 5 cm (2020/07/08 團隊會議增訂)</td><td>1. Workup中的Multidisciplinary consultation加上會診項目Fertility/reproductive, smoking cessation, ophthalmologic and endocrine evaluation if indicated
2. Clinical staging增加T0 (EBV+)
3. [Clinical T0(EBV+)- T1, N1-3 or T2-4, any N, M0]的部分，經過治療後如果CR，刪除adjuvant C/T
4. [Clinical T0(EBV+)- T1, N1-3 or T2-4, any N, M0] Primary treatment的部分，將induction CT + CCRT or RT 的優先順序移至CCRT ± Adjuvant CT 之前。</td></tr>
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Carcinoma of Nasopharynx

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WORK-UP

- History & PE & NPscopy
- NP biopsy ± Neck FNA
- Image

→ MRI* or CT* of H&N or PET/CT

→ Chest X-ray * (if PET/CT not done)

→ Bone scan * (if PET/CT not done)

→ Abd. Sono *

→ ± PET scan ± Chest CT

- EBV status: viral load, ± EB-EA/NA, ± EB-VCA IgG/IgA
- Dental evaluation*

→ Panorex ± teeth extraction

- Hearing evaluation

→ PTA, tympanogram

- Multidisciplinary consultation

(± Fertility/reproductive, smoking cessation, ophthalmologic and endocrine evaluation if indicated)

(* 期別之相關之主要檢查)

STAGING & TREATMENT

- [T1, N0, M0]

  詳見 *Page 2*

- [T0(EBV+)-T1, N1-3, M0] or

  [T2-4, any N, M0]

  詳見 *Page 3*

- [M1]

  詳見 *Page 4*

FOLLOW-UP

- [Post-Tx within 6 months]

→ Post-Tx baseline MRI and/or CT, EBV viral load,

→ Every 2-3 months: PE, NPscopy± Neck Sono

- [0.5-3 years]

→ Every 3-4 months: PE, NPscopy+/- EBV viral load,

→ Every 1 yr: ± EB-EA/NA ± EB-VCA IgG/IgA, MRI and/or CT, CxR, WBBS & Abd. Sono as indicated, ±TSH, free T4*

- [3-5 years] → Every 4-6 months: PE, NPscopy
- [5 years later]

→ Every 6-12 months: PE, NPscopy

(*if RT, 6-12 months)

Carcinoma of Nasopharynx

Clinical T1N0M0

Primary treatment

Definitive RT to nasopharynx

And elective RT to neck

→ Follow-up

Carcinoma of Nasopharynx

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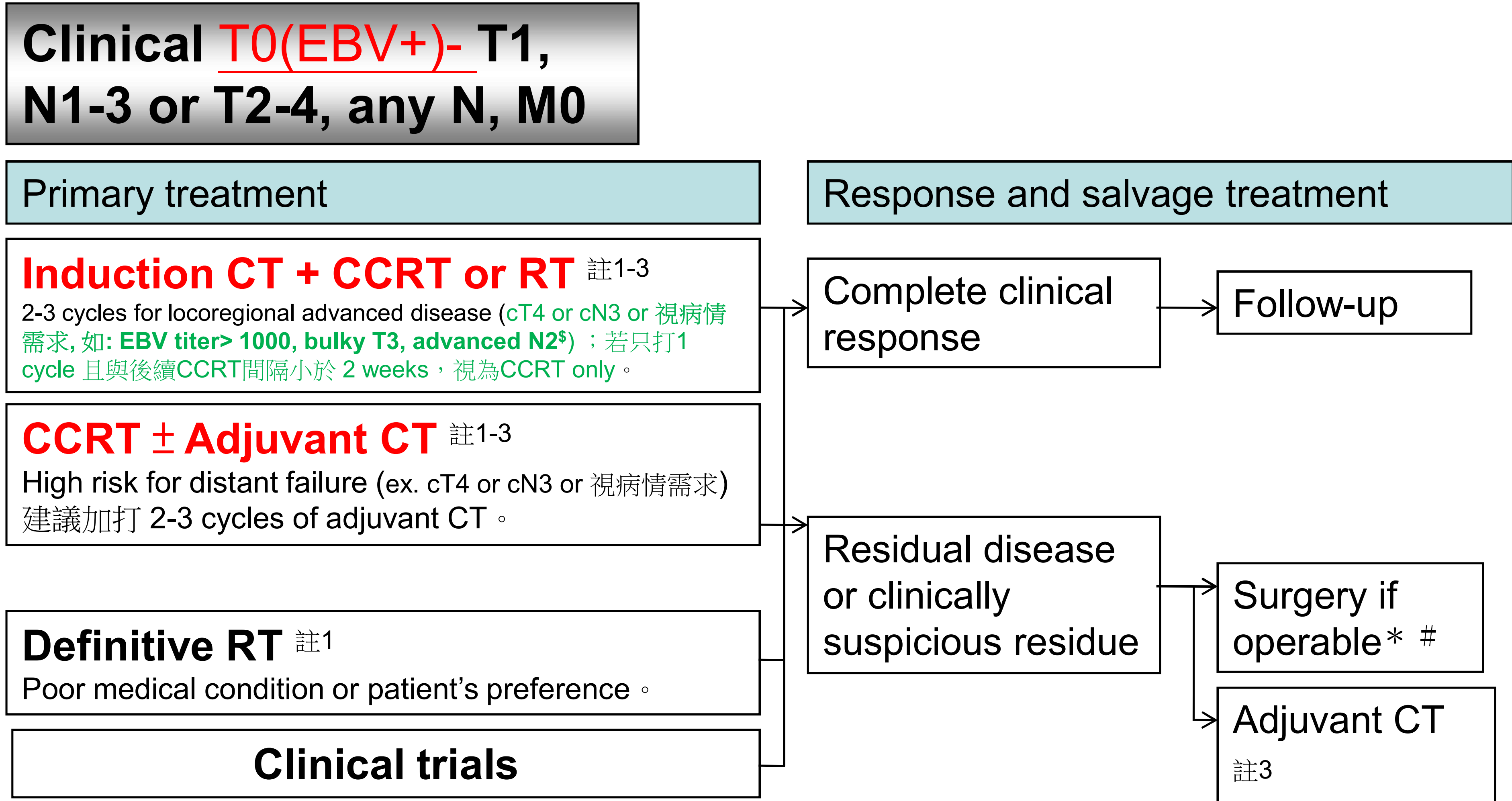

#Salvage neck dissection is indicated if residual neck disease.

＊Salvage nasopharyngectomy is indicated for operable residual primary tumor.

$ Diffuse LAP near the cricoid cartilage, big LAP ≧ 5 cm (2020/07/08 團隊會議增訂)

@ N3, T3-4N1-2, or stage IV (2020/07/08 團隊會議增訂)

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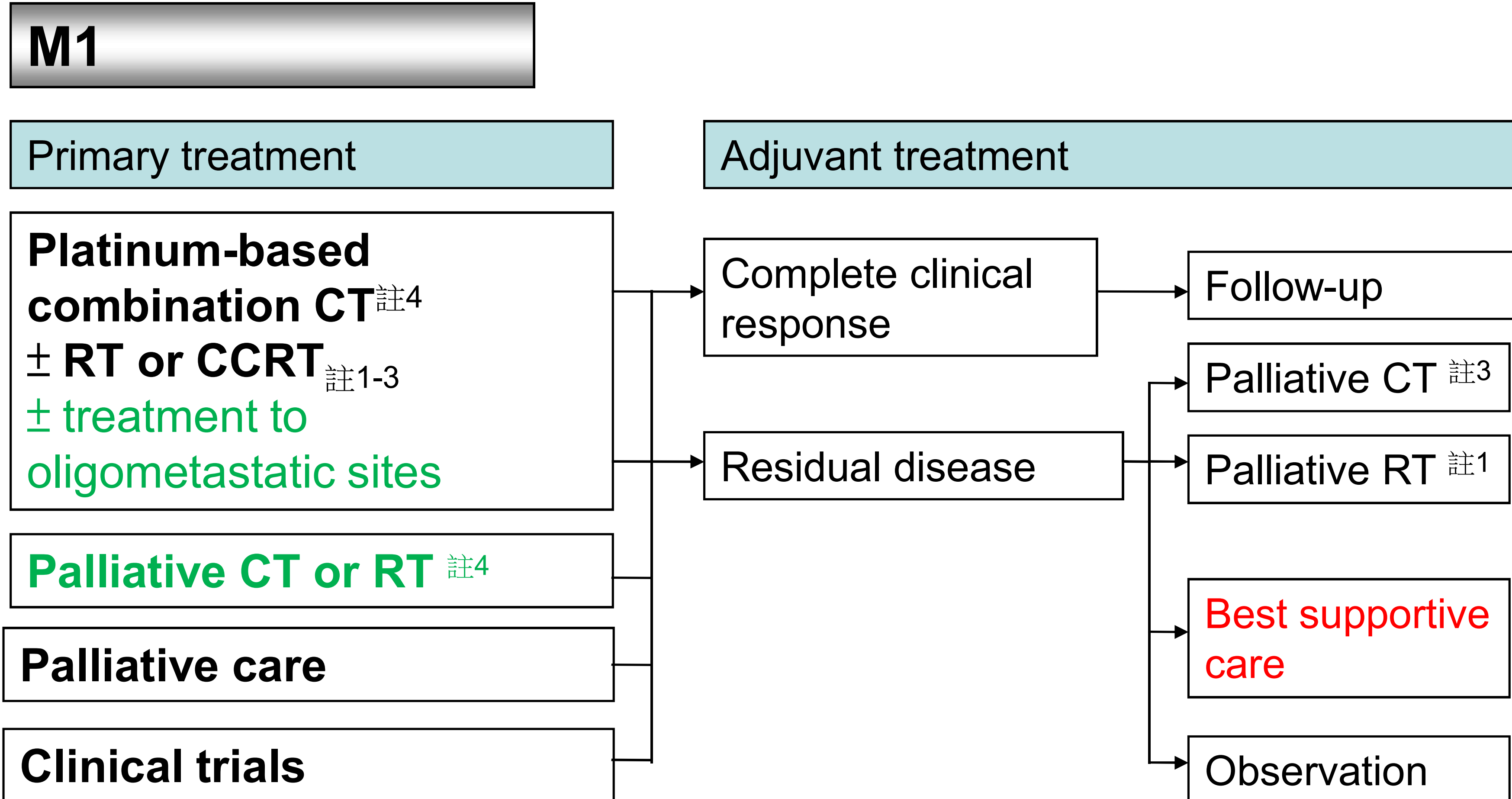

Carcinoma of Nasopharynx

Principles of Radiotherapy

Definitive Radiotherapy

•Primary and gross adenopathy：66 - 74 Gy (2.0-2.2 Gy/fraction)
•Neck uninvolved nodal stations：44 - 58 Gy (1.6-2.0 Gy/fractions)
•Suspicious Neck lymph nodes：59.4 Gy (2.2 Gy/fractions) (optional)
•Adaptive radiotherapy：direct CCRT, BW change more than 3-5 kg, high initial stage etc (optional)

CCRT or RT

•RT alone if ：Old age, Impaired renal function, Poor condition

Palliative RT

•Indicated in：Relieve local symptoms, Prevent debilitation such as spinal cord compression and pathological fracture, Achieve durable locoregional control.

Carcinoma of Nasopharynx

Principles of Chemotherapy ***Concurrent with RT***

Regimen 1: q3w CDDP ± Cetuximab + RT 註5

•Cisplatin (80-100mg/ m^2) q3w during R/T

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

Regimen 2: Weekly CDDP ± Cetuximab + RT 註5

•Cisplatin (30-40mg/ m^2) weekly during R/T

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

Regimen 3: q3w Carboplatin ± Cetuximab + RT 註5

•Carboplatin (AUC x 5mg) q3w during R/T

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

Regimen 4: Weekly Cetuximab + RT 註5

•Cetuximab(400mg/ m^2) loading dose first week, then Cetuximab(250mg/ m^2) maintain dose during RT

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Regimens of Chemotherapy

Induction or adjuvant, 建議2-3cycles

Regimen 1 : q3w G[註5] P
- Gemcitabine (1000mg/ m^2) D1, 8
- Cisplatin (80mg/ m^2) D1

Regimen 2 : q3w G[註5] Carboplatin
- Gemcitabine (1000mg/ m^2) D1, 8
- Carboplatin (AUC x 5mg) D1

Regimen 3 : q3-4 weeks T + P ± **F** ± weekly Cetuximab[註5]
- Taxotere(60 mg/ m^2) D1 [註5]
- Cisplatin(60-75 mg/ m^2) D1
- Fluorouracil (5-FU)(600-750mg/ m^2) D2-D5
- Cetuximab (400mg/ m^2) loading dose first week, then Cetuximab (250mg/ m^2) maintain dose

Regimen 4 : q3-4 weeks T + Carboplatin ± **F** ± weekly Cetuximab[註5]
- Taxotere(60 mg/ m^2) D1 [註5]
- Carboplatin (AUC x 5mg) D1
- Fluorouracil (5-FU)(600-750mg/ m^2) D2-D5
- Cetuximab (400mg/ m^2) loading dose first week, then Cetuximab (250mg/ m^2) maintain dose

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Regimens of Chemotherapy

Induction or adjuvant, *建議2-3cycles*

Regimen 5: q3-4 weeks CDDP ± F ± weekly Cetuximab 註5

•Cisplatin(80-100mg/ m^2) D1 or Cisplatin (20mg/ m^2) D1-D5

•Fluorouracil (5-FU) (1000mg/ m^2) D1-D5

•Cetuximab(400mg/ m^2) loading dose first week, then weekly Cetuximab (250mg/ m^2)

Regimen 6: q3-4 weeks Carboplatin ± F ± weekly Cetuximab 註5

•Carboplatin (AUC x 5mg) D1

•Fluorouracil (5-FU) (1000mg/ m^2) D2-D5

•Cetuximab(400mg/ m^2) loading dose first wk, then weekly Cetuximab (250mg/ m^2)

Regimen 7: oral Fluorouracil

•Ufur cap (tegafur 100mg+uracil 224mg) 2# BID-TID

(作為取代 IV form 5-FU之替代藥物)

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Regimens of Chemotherapy

Recurrent or metastatic disease

Regimen 1 (First line): q3w G[註5] ± P

- Gemcitabine (1000mg/ m^2) D1, 8
- Cisplatin (80mg/ m^2) D1

Regimen 2: q4w GGG[註5] ±P

- Gemcitabine (1000mg/ m^2) D1, 8, 15
- Cisplatin (50-60mg/ m^2) D22

Regimen 3: q3w G[註5] Carboplatin

- Gemcitabine (1000mg/ m^2) D1, 8
- Carboplatin (AUC x 5mg) D1

Regimen 4: q3-4 weeks P ± F

- Cisplatin(80-100mg/ m2) D1 or Cisplatin (20mg/ m2) D1-D5
- Fluorouracil (5-FU) (600-1000 mg/m2) D2-D5

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Regimens of Chemotherapy

Recurrent or metastatic

Regimen 5: q3-4 weeks Carboplatin ± F
- Carboplatin (AUC x 5mg) D1
- Fluorouracil (5-FU) (1000mg/ m^2) D2-D5

Regimen 6: q3-4 weeks T ± P
- Taxotere(60 mg/ m^2) D1 註5
- Cisplatin(60-75 mg/ m^2) D1

Regimen 7: q3-4 weeks T ± Carboplatin
- Taxotere(60 mg/ m^2) D1 註5
- Carboplatin (AUC x 5mg) D1

Regimen 8: q3-4 weeks Carboplatin ± weekly Cetuximab 註5
- Carboplatin (AUC x 5mg) D1
- Cetuximab(400mg/ m^2) loading dose first week, then weekly Cetuximab (250mg/ m^2)

Carcinoma of Nasopharynx

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Regimens of Chemotherapy ***Recurrent or metastatic***

Regimen 9: weekly Methotrexate
- Methotrexate (40-60mg/ m^2)

Regimen 10: weekly Cetuximab 註5
- Cetuximab (400mg/ m^2) loading dose first week, then Cetuximab (250mg/ m^2) maintain dose

Regimen 11: oral Fluorouracil
- Ufur cap (tegafur 100mg+uracil 224mg) 2# BID-TID (作為取代 IV form 5-FU之替代藥物)

Regimen 12: q3 weeks Pembrolizumab
- Pembrolizumab(200mg) D1

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Regimens of Chemotherapy ***Recurrent or metastatic***

Regimen 13: q2 weeks Nivolumab
•Nivolumab(3mg/kg) D1

Regimen 14: FL
•Leucovorin (250 mg/ m2) D1
•Fluorouracil (5-FU) (2500 mg/ m^2) D1

Regimen 15: P-FL
•Cisplatin (60mg/ m^2) week 1, 3, 5, 7
• Fluorouracil (5-FU)(2500mg/ m^2) + Leucovorin (250mg/ m^2) mixed week 2, 4, 6, 8

Carcinoma of Nasopharynx

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。

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。

- 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。需經事前審查核准後使用，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。 (106/4/1)

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 Nasopharynx

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≦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≧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≦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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特殊用藥健保給付規定

Gemcitabine

限用於：

1.晚期或無法手術切除之非小細胞肺癌及胰臟癌病患。

2.晚期膀胱癌病患。

3.Gemcitabine與paclitaxel併用，可使用於曾經使用過anthracycline之局部復發且無法手術切除或轉移性之乳癌病患。

4.用於曾經使用含鉑類藥物(platinum-based) 治療後復發且間隔至少6個月之卵巢癌，作為第二線治療。

5.無法手術切除或晚期或復發之膽道癌(含肝內膽管)病患。

備註：頭頸癌與鼻咽癌目前無健保給付

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