

高雄榮民總醫院

肺癌診療原則

(非小細胞癌)

2018年09月05日第一版

肺癌醫療團隊擬訂

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。

修訂指引

- 本共識依下列參考資料修改版本
 - NCCN Clinical Practice Guideline in Oncology™ ,NSCLC, **V.4.2018**

會議討論

上次會議：2017/05/10

本共識與上一版的差異

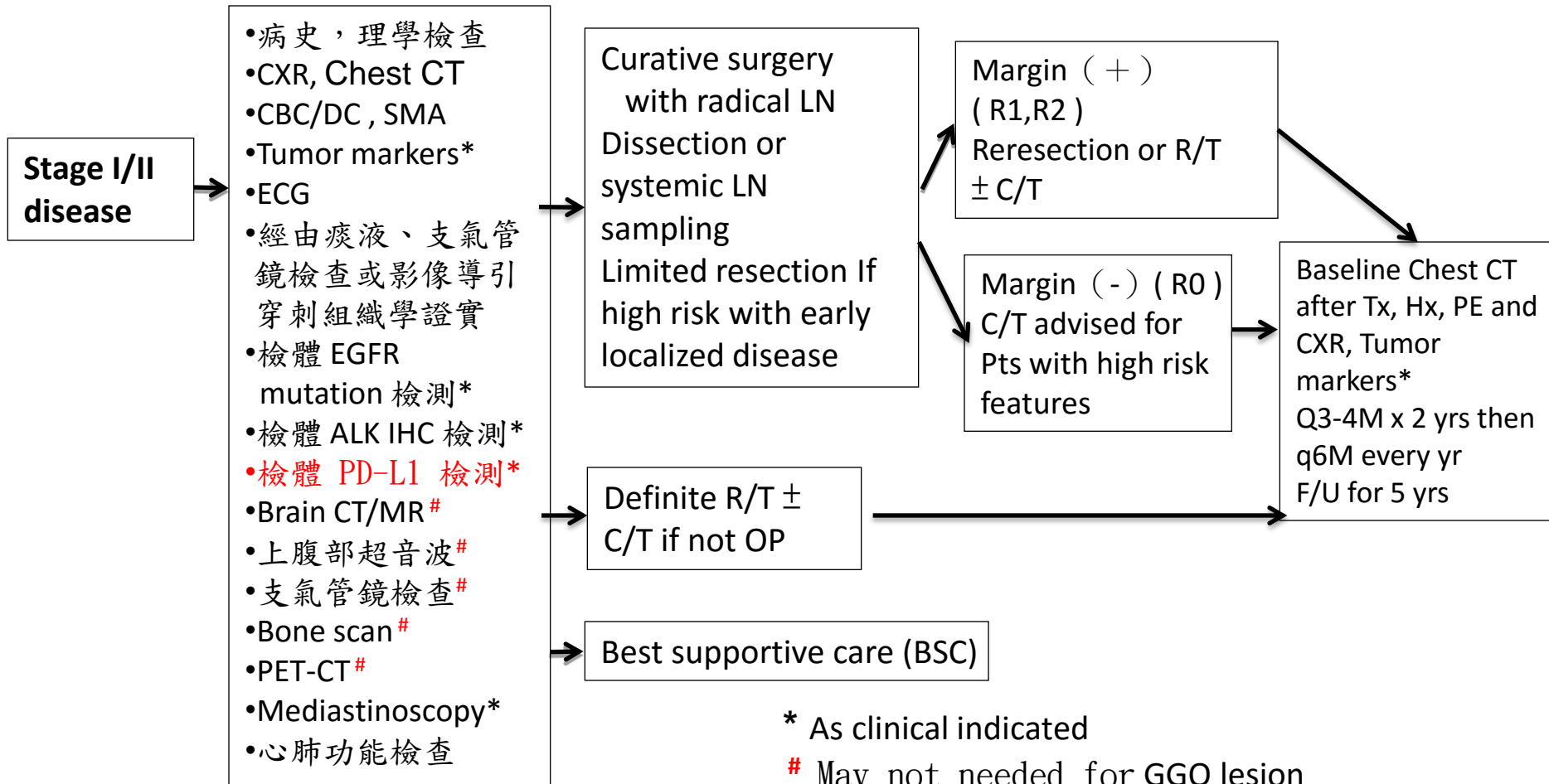
上一版	新版
<ol style="list-style-type: none">1. 只有EGFR mutation、ALK IHC 檢測(p. 4-8)。2. Stage IIB-III A, Definite CCRT療程後進入手術、追蹤階段(p. 5)3. Stage IIIA(T1-2, N2)、Stage IIB(T3, N2) CCRT治療，若No apparent PD，則手術，若PD，則進行R/T ± C/T (p. 6)。4. T3, N2 原為III A分期(p. 6)5. 只有Stage IIB分期 (p. 7)6. 第四期M1a、M1b分期，只有做local的 resectable (Brain、Lung lesion)治療 (p. 8)7. 對於Stage IVA-B, M1a、M1b、M1c 的病人有做 SENSITIZING DRIVER ONCOGE的病人，未有第一、二線治療(p. 10)8. Stage IVA-B的病人PD-L1有50%的表現，無免疫治療方式(p. 11)9. 無一線治療PD後，可以使用的免疫治療用藥(p. 12)10. 只有腎功能不佳用藥注意事項。11. 無一線的化學治療處方之免疫用藥(p. 14)12. 體能狀況不佳之一線的化學治療處方維持原用藥(p. 15)13. 維持治療處方之化療用藥無異動(p. 16)。14. Ceritinib 原劑量為750 mg(p. 17)15. 無二線及二線之後的免疫治療處方(p. 18)16. 原同步化學治療放射線治療處方及劑量(p. 21)	<ol style="list-style-type: none">1. 新增PD-L1 的檢測(p. 4-8)2. Stage IIB-III A, Definite CCRT療程後，新增免疫治療 (p. 5)。3. Stage IIIA(T1-2, N2)、Stage IIB(T3, N2) CCRT治療後，新增Durvalumab 免疫的治療 (p. 6)4. T3, N2 新分期為IIB (p. 6)5. 新增IIIC (T4N2, T1-4N3)分類(p. 7)。6. 採AJCC第8版分期，第四期新增M1c，新增腦部治療及免疫治療(p. 8)7. 新增Stage IVA-B, M1a、M1b、M1c 的病人有做 SENSITIZING DRIVER ONCOGE，的第一、二線的治療 (p. 10)。8. 新增Stage IVA-B病人沒有 DRIVER ONCOGE，沒有 mutation，但PD-L1有50%的表現，新增免疫治療(p. 11)9. 一線治療PD了，體能還很好，可以使用的免疫治療用藥 (p. 12)10. 新增化學及標靶用藥注意事項(p. 13)11. 新增一線的化學治療處方之免疫用藥(p. 14)12. 新增對於年紀大，體能狀況不佳之一線的化學治療處方 (p. 15)13. 新增維持治療處方之化療用藥(p. 16)14. 更改Ceritinib 劑量為450 mg劑量(p. 17)15. 新增二線及二線之後的免疫治療處方(p. 18)16. 新增同步化學治療放射線治療處方及劑量(p. 21)

非小細胞肺癌

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診斷	評估	初步治療	輔助治療	追蹤
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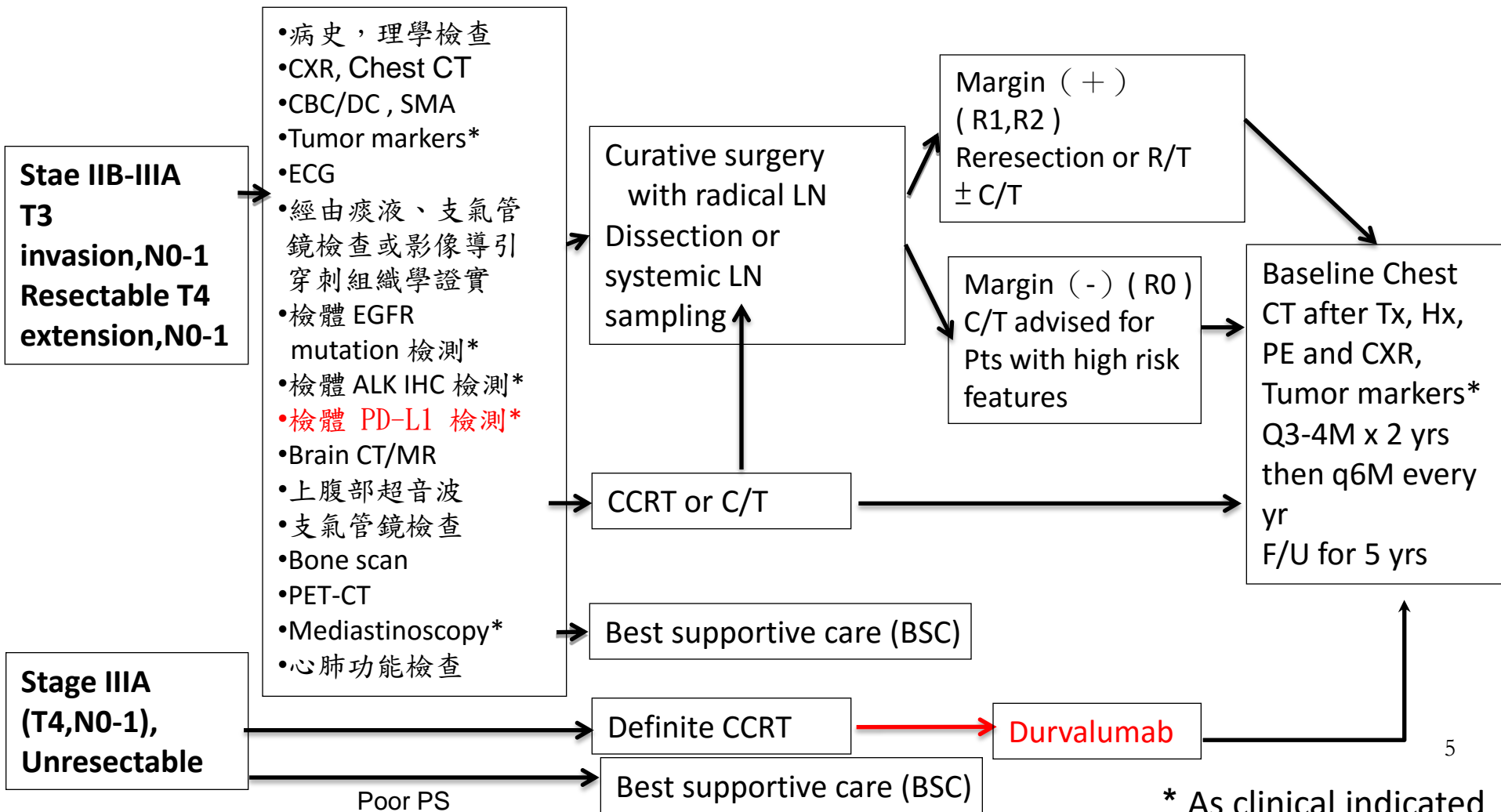


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診斷	評估	初步治療	輔助治療	追蹤
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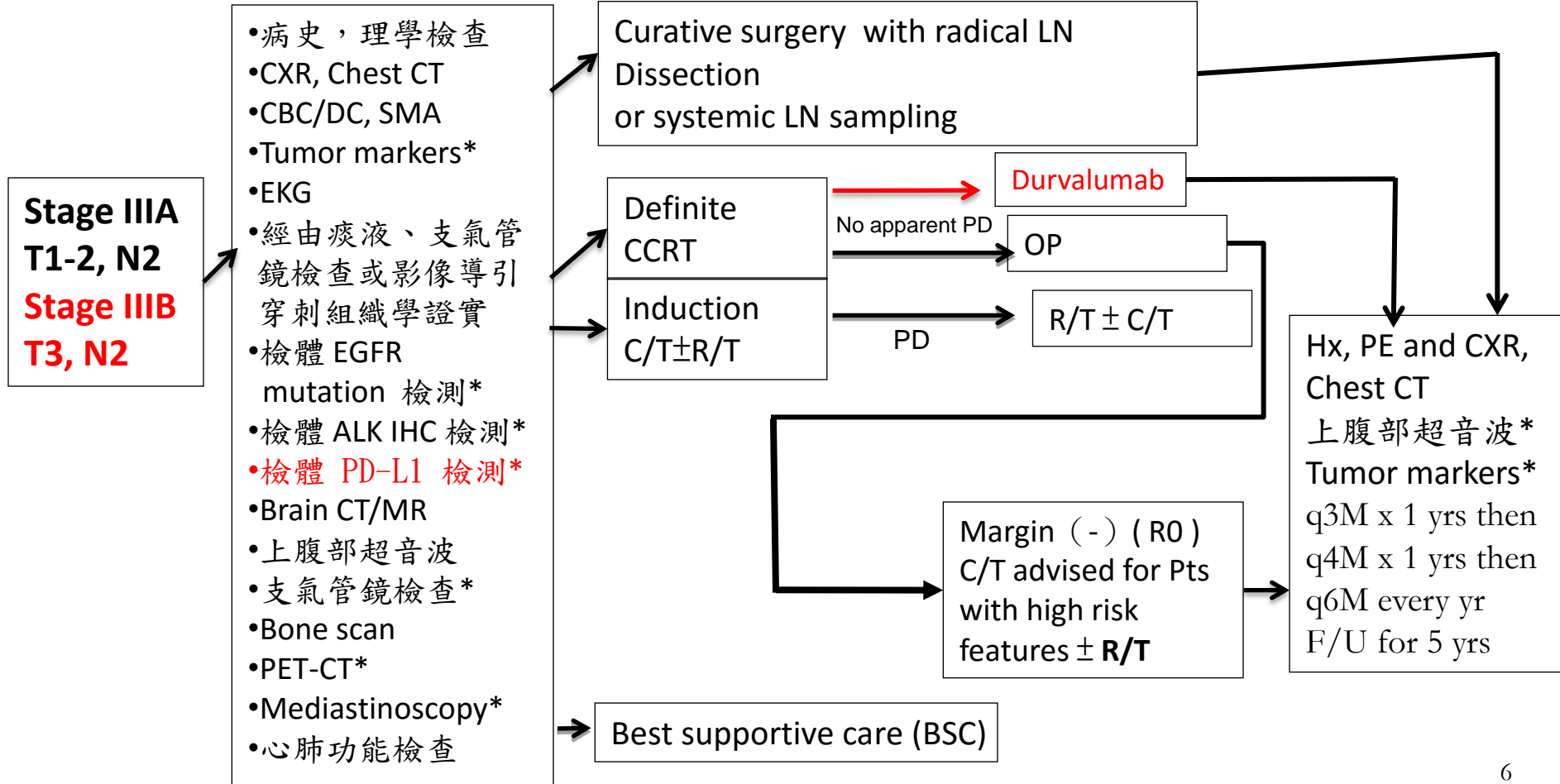


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診斷	評估	初步治療	輔助治療	追蹤
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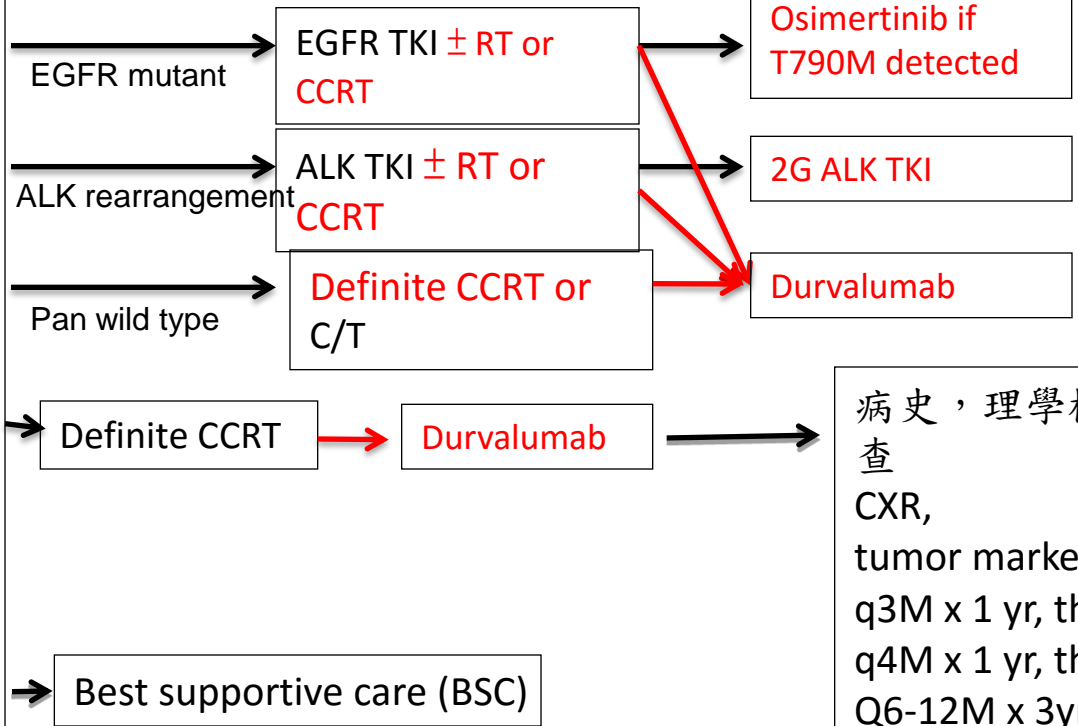
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診斷	評估	初步治療	重新評估	進一步治療	追蹤
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**Stage IIIB-IIIc
(T4N2,T1-4N3)**

- 病史，理學檢查
- CXR, Chest CT
- CBC/DC, SMA
- Tumor markers*
- ECG
- 經由痰液、支氣管鏡檢查或影像導引穿刺或表淺淋巴結抽吸組織學證實
- 檢體 EGFR mutation 檢測*
- 檢體 ALK IHC 檢測*
- 檢體 PD-L1 檢測*
- Mediastinoscopy* for N2/N3 disease
- Brain CT/MR
- 上腹部超音波
- 支氣管鏡檢查*
- Bone scan, PET-CT*
- 心肺功能檢查



病史，理學檢查
CXR,
tumor markers*
q3M x 1 yr, then
q4M x 1 yr, then
Q6-12M x 3yrs

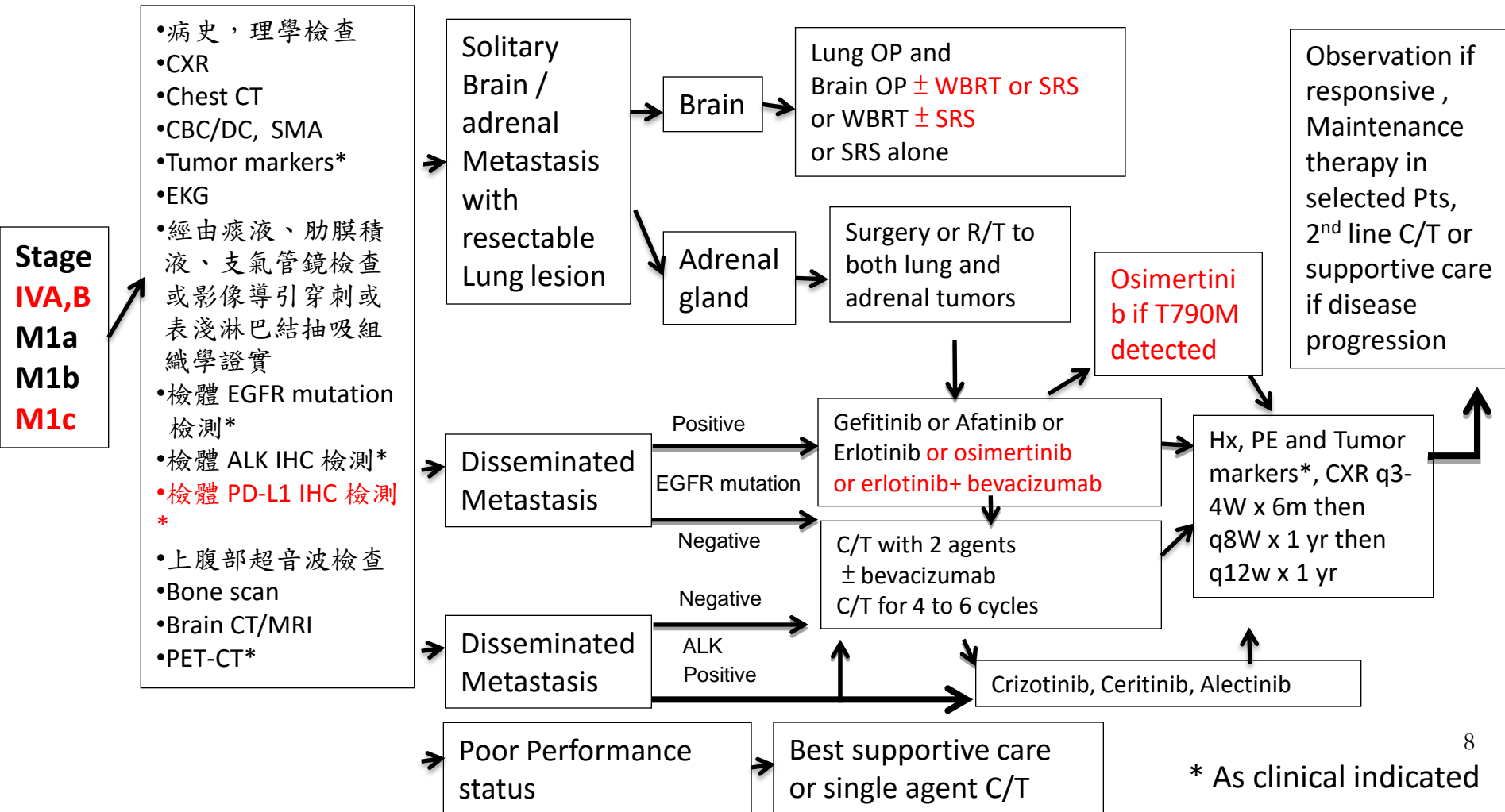
* As clinical indicated

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診斷	評估	治療	重新評估	治療
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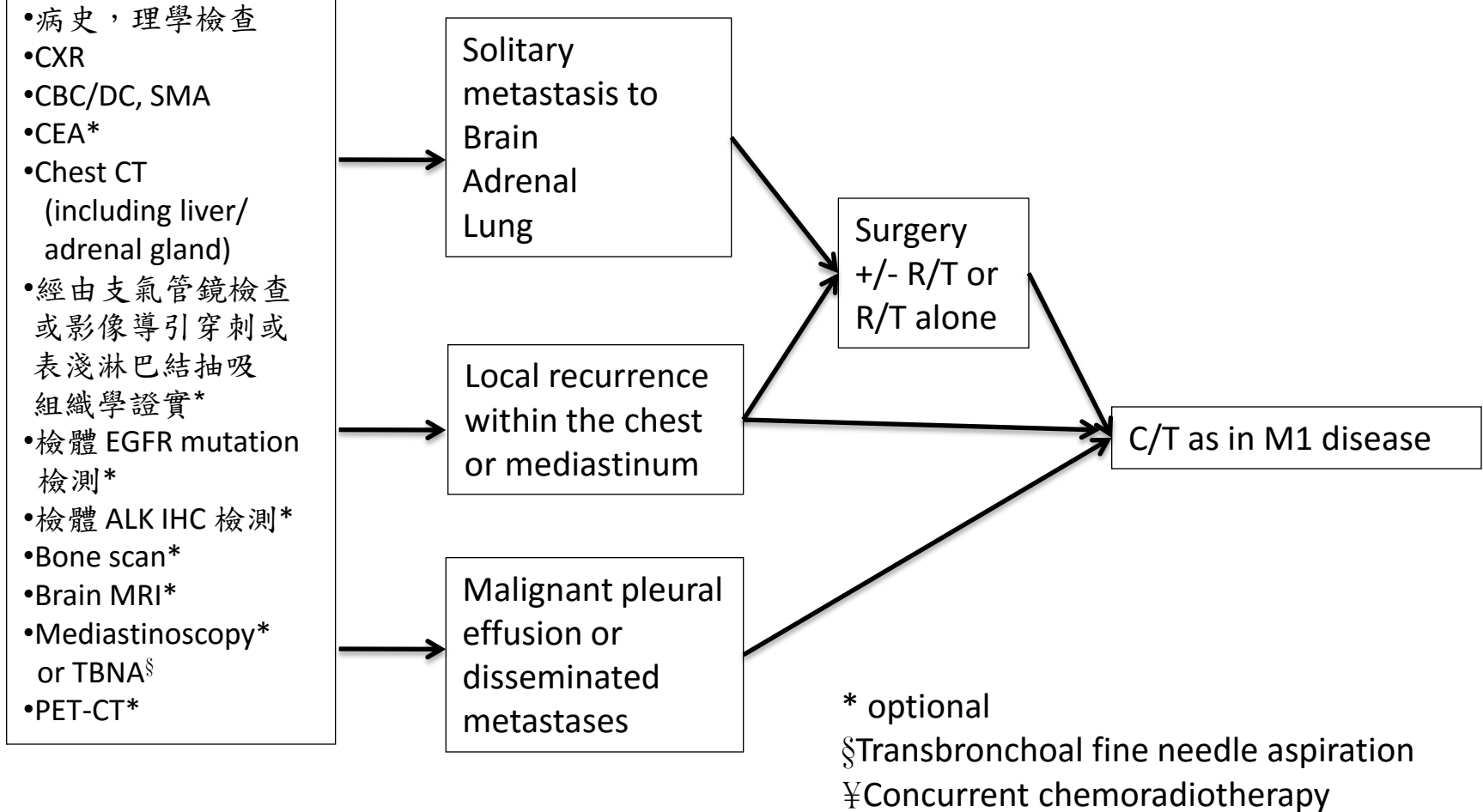


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復發



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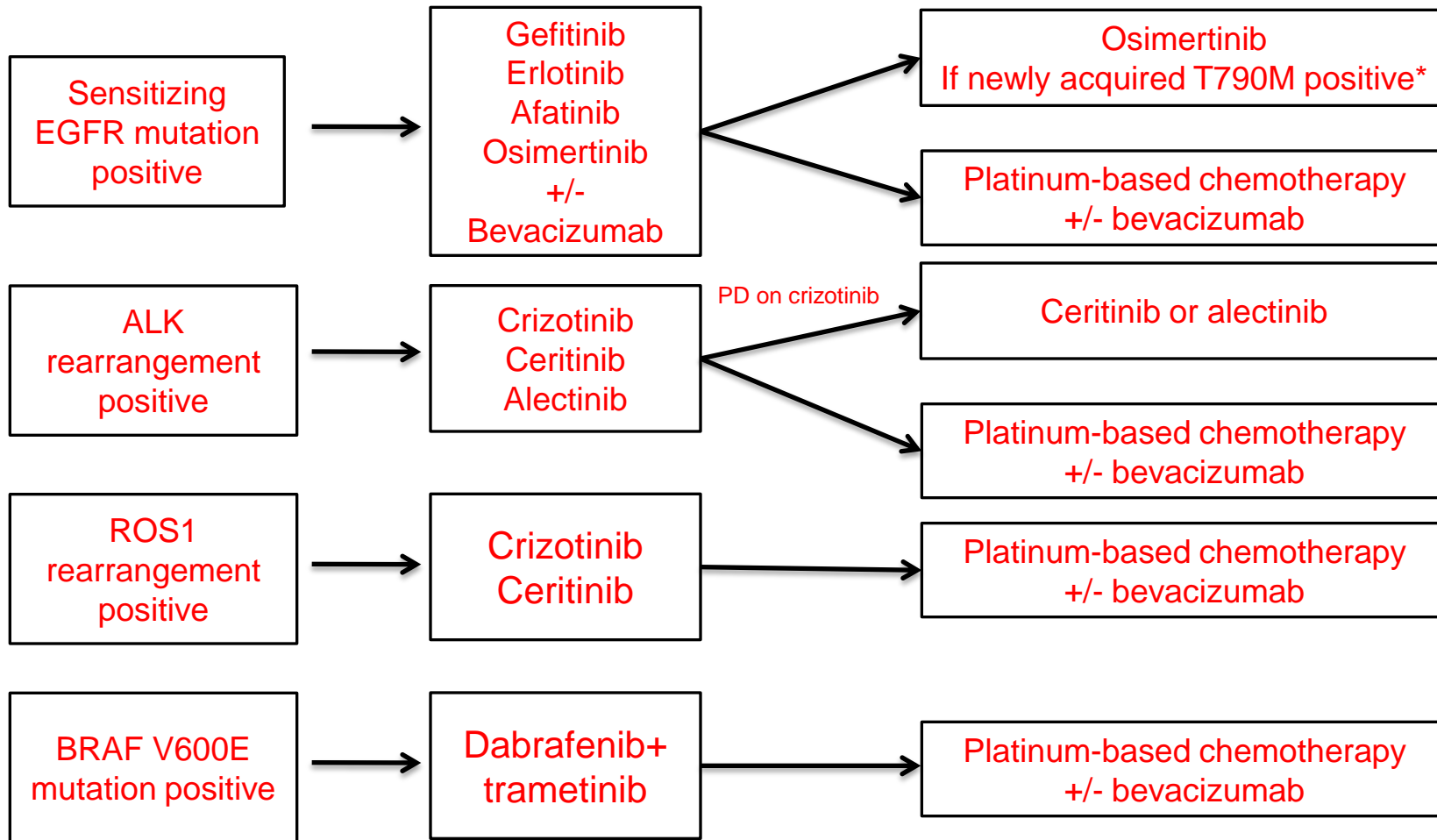
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SENSITIZING DRIVER ONCOGEN

First line therapy

Second line therapy



* First line did not received osimertinib

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診斷

評估

治療

重新評估

治療

- 病史，理學檢查
- CXR
- Chest CT
- CBC/DC, SMA
- Tumor markers*
- EKG
- 經由痰液、肋膜積液、支氣管鏡檢查或影像導引穿刺或表淺淋巴結抽吸組織學證實
- 檢體 EGFR mutation 檢測*
- 檢體 ALK IHC 檢測*
- 檢體 PD-L1 IHC 檢測*
- 上腹部超音波檢查
- Bone scan*
- Brain CT/MRI*
- PET-CT*

Stage
IVA,B
M1a
M1b
M1c

Disseminated
Metastasis

PD-L1 \geq 50%

Pembrolizumab

EGFR(-)

ALK(-)

PD-L1 0~100%

Carbo/Pemetrexed/Pembrolizumab
Carbo/Paclitaxel/Pembrolizumab
Carbo/Paclitaxel/Bevacizumab/Atezolizumab

非小細胞肺癌

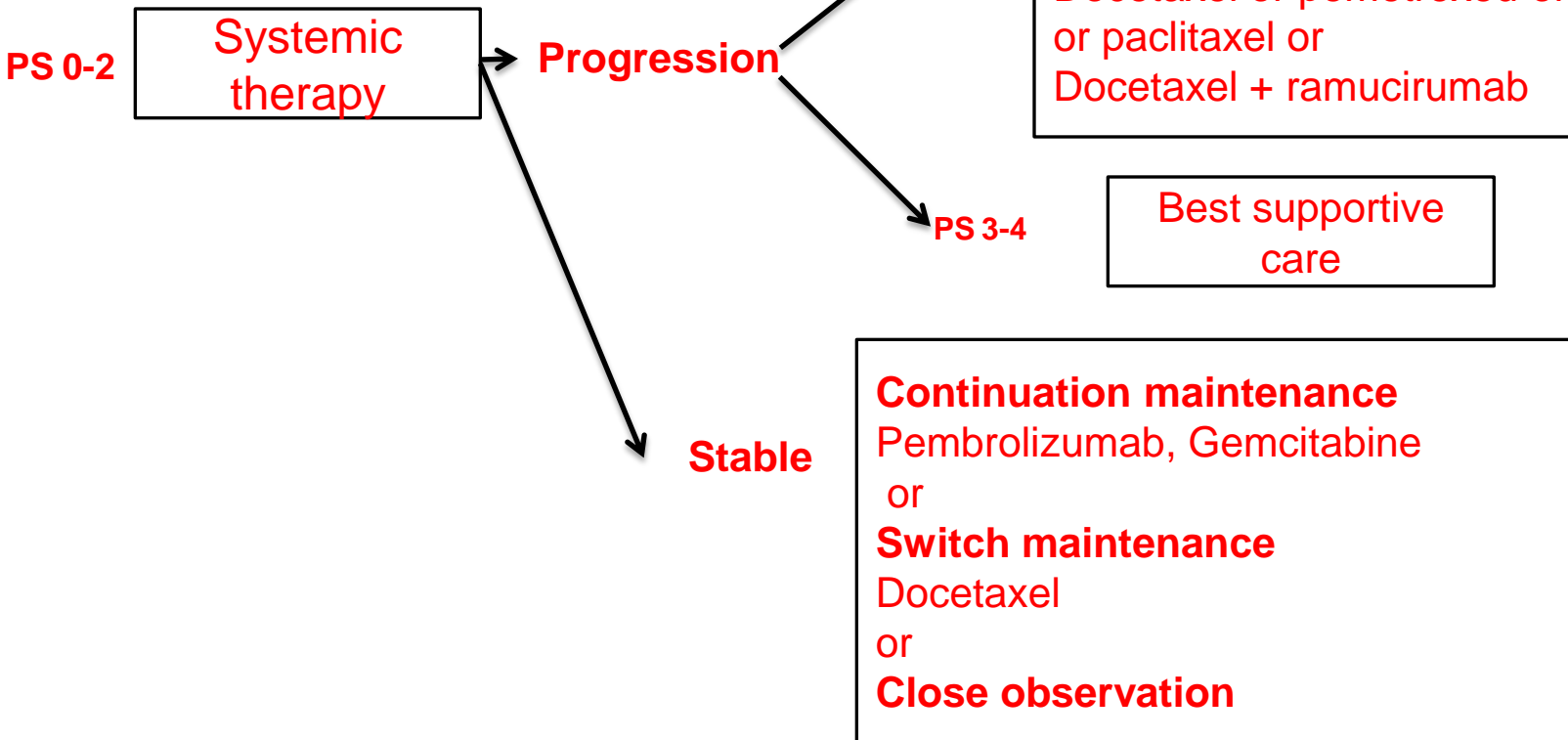
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ADENOCARCINOMA, SQUAMOUS, LARGE CELL,
NSCLC NOS
INITIAL CYTOTOXIC THERAPY

Systemic immune checkpoint inhibitors
Nivolumab or Pembrolizumab or
atezolizumab
Other systemic therapy
Docetaxel or pemetrexed or gemcitabine
or paclitaxel or
Docetaxel + ramucirumab



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一線化學治療處方（一）

Published C/T Regimens	Schedule
Cisplatin 60-75 mg/m ² , IV, D15 + Vinorelbine 25 mg/m ² , IV, D1,8,15	Q28 d x 4-6 cycles
Cisplatin 60-75 mg/m ² , IV, D8 + Vinorelbine 60-75 mg/m ² , PO, D1,8	Q21 d x 4-6 cycles
Cisplatin 60-75 mg/m ² , IV, D15 + Docetaxel 30 mg/m ² , IV, D1,8,15	Q28 d x 4-6 cycles
Cisplatin 60-75 mg/m ² , IV, D15 + Paclitaxel 60 mg/m ² , IV, D1,8,15	Q28 d x 4-6 cycles
Cisplatin 60-75 mg/m ² , IV, D15 + Gemcitabine 900-1000 mg/m ² , IV, D1,8,15	Q28 d x 4-6 cycles
Cisplatin 60-75 mg/m ² , IV, D1 + *Pemetrexed 500 mg/m ² , IV, D1	Q21 d x 4-6 cycles
Gefitinib 250 mg po qd (EGFR mutant)	Till PD or unacceptable toxicity
Erlotinib 150 mg po qd (EGFR mutant)	Till PD or unacceptable toxicity
Afatinib 40 mg po qd (EGFR mutant)	Till PD or unacceptable toxicity
Crizotinib 250 mg po bid (ALK rearrangement)	Till PD or unacceptable toxicity
Alectinib 600 mg po bid (ALK rearrangement)	Till PD or unacceptable toxicity
Ceritinib 450 mg po qd(with low fat meal)	Till PD or unacceptable toxicity

若腎功能不佳，CCr < 60 ml/min，cisplatin 可以 carboplatin AUC 4-6 取代

若是 nonsquamous histology，沒有 bevacizumab 的 contraindication，platinum doublet 可以併用 bevacizumab

化學治療藥物劑量與標靶藥物劑量根據毒性副作用及病人耐受性做調整

* 使用於不是 squamous cell carcinoma 組織學型態的病人

一線化學治療處方（二）

Published C/T Regimens	Schedule
Pembrolizumab # 2mg/kg IV	Q3w
Cisplatin 60-75 mg/m ² , IV, D1 + *Pemetrexed 500 mg/m ² , IV, D1+ Pembrolizumab 2 mg/kg iv	Q3w

若腎功能不佳，CCr < 60 ml/min，cisplatin 可以 carboplatin AUC 4-6 取代

若是 nonsquamous histology，沒有 bevacizumab 的 contraindication，platinum doublet 可以併用 bevacizumab
化學治療藥物劑量與標靶藥物劑量根據毒性副作用及病人耐受性做調整

* 使用於不是 squamous cell carcinoma 組織學型態的病人

使用於 PD-L1 expression \geq 50% 的病人

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一線的化學治療處方（年紀大，體能狀況不佳）

Published C/T Regimens	Schedule
Gefitinib 250 mg PO QD (EGFR mutant)	Till PD or unacceptable toxicity
Erlotinib 150 mg PO QD (EGFR mutant)	Till PD or unacceptable toxicity
Afatinib 40 mg po qd (EGFR mutant)	Till PD or unacceptable toxicity
Pemetrexed 500 mg/m ² , IV, D1	Q21 d x 4-6 cycles
Docetaxel 30 mg/m ² , IV, D1,8,15	Q28 d x 4-6 cycles
Paclitaxel 60 mg/m ² , IV, D1,8,15	Q28 d x 4-6 cycles
Gemcitabine 900-1000 mg/m ² , IV, D1,8,15	Q28 d x 4-6 cycles
Vinorelbine 25 mg/ m ² IV, D1,8,15	Q28 d x 4-6 cycles
Vinorelbine 60-75 mg/m ² , PO, D1,8	Q21 d x 4-6 cycles
Crizotinib (ALK rearrangement)	Till PD or unacceptable toxicity
Alectinib 600 mg po bid (ALK rearrangement)	Till PD or unacceptable toxicity
Ceritinib 450 mg po qd(with low fat meal)	Till PD or unacceptable toxicity

* 一線，二線及二線之後的化學治療，術後輔助化學治療，依據病人年齡、性別、組織學型態、體能狀況、器官功能狀況、副作用的考量（血液學毒性、掉髮、皮疹、色素沈著、周邊神經病變等）、曾接受過的治療、病人的喜好、及分子生物標記來選擇病人的化學治療處方，給於客製化（personalized treatment）的治療。劑量根據毒性副作用及病人耐受性做調整。

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維持治療處方

Published C/T Regimens	Schedule
*Pemetrexed 500 mg/m ² IV D1	Q21 d Till PD or unacceptable toxicity
*Erlotinib 150 mg PO QD	Till PD or unacceptable toxicity
*Docetaxel 30 mg/m ² , IV, D1,8,15	Q28 d Till PD or unacceptable toxicity
#Gemcitabine 900-1000 mg/m ² , IV, D1,8,15	Q28d Till PD or unacceptable toxicity
#Bevacizumab 7.5 mg/kg IV q3w	Q21d Till PD or unacceptable toxicity
#Pemetrexed 500 mg/m ² IV + Bevacizumab 7.5 mg/kg IV	Q21d Till PD or unacceptable toxicity
#Pembrolizumab 2mg/kg IV	Q21d Till PD or unacceptable toxicity

#Continuous maintenance therapy：在沒有疾病惡化的情況下，一線化學治療 4-6 個療程後，持續使用一線化學治療配方中的一個藥物。使用於不是 squamous cell carcinoma 組織學型態的病人。

* Switch maintenance therapy：在沒有疾病惡化的情況下，一線化學治療 4-6 個療程後，使用與一線化學治療配方不同的藥物。

二線及二線之後的化學治療處方（一）

Published C/T Regimens	Schedule
Gefitinib 250 mg PO QD	Till PD or unacceptable toxicity
Erlotinib 150 mg PO QD	Till PD or unacceptable toxicity
Crizotinib 250 mg PO BID (ALK rearrangement)	Till PD or unacceptable toxicity
*Ceritinib 450 mg PO QD (ALK rearrangement)	Till PD or unacceptable toxicity
*Alectinib 600mg PO BID (ALK rearrangement)	Till PD or unacceptable toxicity
Docetaxel 30 mg/m ² , IV, D1,8,15	Q28 d x 4-6 cycles
#Pemetrexed 500 mg/m ² , IV, D1	Q21 d x 4-6 cycles
Paclitaxel 60 mg/m ² , IV, D1,8,15	Q28 d x 4-6 cycles
Gemcitabine 900-1000 mg/m ² , IV, D1,8,15	Q28 d x 4-6 cycles
Vinorelbine 25 mg/ m ² IV, D1,8,15	Q28 d x 4-6 cycles
Vinorelbine 60-75 mg/m ² , PO, D1,8	Q21 d x 4-6 cycles

* 一線 crizotinib 治療惡化或不耐受

* 一線，二線及二線之後的化學治療，術後輔助化學治療，依據分子生物標記、病人年齡、性別、組織學型態、體能狀況、器官功能狀況、副作用的考量（血液學毒性、掉髮、皮疹、色素沈著、周邊神經病變等）、曾接受過的治療、及病人的喜好來選擇病人的化學治療處方，給於客製化（personalized treatment）的治療。

使用於不是 squamous cell carcinoma 組織學型態的病人

二線及二線之後的化學治療處方（二）

Published C/T Regimens	Schedule
Nivolumab 3mg/kg IV	Q2w
*Pembrolizumab 2mg/kg IV	Q3w
Atezolizumab 1200 mg IV	Q3w

* PD-L1 expression \geq 1% 的病人

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術前新輔助化學治療處方

Published C/T Regimens	Schedule
Cisplatin 60-75 mg/m ² , IV, D15 Vinorelbine 25 mg/m ² , IV, D1,8,15	Q28 d x 3-4 cycles
Cisplatin 60-75 mg/m ² , IV, D8 Vinorelbine 60-75 mg/m ² , PO, D1,8	Q21 d x 3-4 cycles
Cisplatin 60-75 mg/m ² , IV, D15 Docetaxel 30 mg/m ² , IV, D1,8,15	Q28 d x 3-4 cycles
Cisplatin 60-75 mg/m ² , IV, D15 Paclitaxel 60 mg/m ² , IV, D1,8,15	Q28 d x 3-4 cycles
Cisplatin 60-75 mg/m ² , IV, D15. Gemcitabine 900-1000 mg/m ² , IV, D1,8,15.	Q28 d x 3-4 cycles
Cisplatin 60-75 mg/m ² , IV, D1 #Pemetrexed 500 mg/m ² , IV, D1	Q21 d x 3-4 cycles

若腎功能不佳，CCr < 60 ml/min，cisplatin 可以 carboplatin AUC 4-6 取代

使用於不是 squamous cell carcinoma 組織學型態的病人

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術後輔助化學治療處方

Published C/T Regimens	Schedule
Cisplatin 60-75 mg/m ² , IV, D15 Vinorelbine 25 mg/m ² , IV, D1,8,15	Q28 d x 4 cycles
Cisplatin 60-75 mg/m ² , IV, D15 Vinorelbine 60-75 mg/m ² , PO, D1,8	Q21 d x 4 cycles
Cisplatin 60-75 mg/m ² , IV, D15 Docetaxel 30 mg/m ² , IV, D1,8,15	Q28 d x 4 cycles
Cisplatin 60-75 mg/m ² , IV, D15 Paclitaxel 60 mg/m ² , IV, D1,8,15	Q28 d x 4 cycles
Cisplatin 60-75 mg/m ² , IV, D15. Gemcitabine 900-1000 mg/m ² , IV, D1,8,15.	Q28 d x 4 cycles
Cisplatin 60-75 mg/m ² , IV, D1 #Pemetrexed 500 mg/m ² , IV, D1	Q21 d x 4 cycles
Tagafur/Uracil 300-500 mg PO QD *	Maintenance for 2 years

若腎功能不佳，CCr < 60 ml/min，cisplatin 可以 carboplatin AUC 4-6 取代

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同步化學治療放射線治療處方

Published C/T Regimens	Schedule
Cisplatin 50 mg/m ² , IV, D15 Vinorelbine 20-25 mg/m ² , IV , D1,8,15	Q28 d x 4 cycles with concurrent thoracic RT
Cisplatin 50 mg/m ² , IV, D15 Vinorelbine 60-75 mg/m ² , PO,D1,8	Q21 d x 4 cycles with concurrent thoracic RT
Cisplatin 50 mg/m ² , IV D1,8,29,36 Etoposide 50 mg/m ² , IV, D1-5,29-33	Concurrent thoracic RT
Carboplatin AUC 2, IV, QW Paclitaxel 45-50 mg/m ² , IV, QW	Concurrent thoracic RT
Cisplatin 50-60 mg/m ² , IV, D1 #Pemetrexed 500 mg/m ² ,IV, D1	Q21 d x 3 cycles with concurrent thoracic RT
Carboplatin AUC 5, IV, D1 #Pemetrexed 500 mg/m ² ,IV, D1	Q21 d x 4 cycles with concurrent thoracic RT
Cisplatin 50-60 mg/m ² , IV, D1 Docetaxel 20-25 mg/m ² ,IV,D1,8,15	Q28 d x 2 cycles with concurrent thoracic RT

若腎功能不佳，CCr < 60 ml/min，cisplatin 可以 carboplatin AUC 4取代

使用於不是 squamous cell carcinoma 組織學型態的病人

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