

高雄榮民總醫院

肺癌診療原則

(非小細胞癌)

2021年02月24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.2.2021**

會議討論(一)

上次會議：2020/02/12

本共識與上一版的差異

上一版	新版
<p>1. Stage I/II之診斷及初步治療、輔助治療原為相同，追蹤原為Q3-4M (p. 5)。</p> <p>2. 無。</p> <p>3. Stage IIB-III A (T3 invasion, N0-1 & Resectable T4 extension, N0-1)及Stage III A(T4, N0-1), Unresectable 之診療指引原合併。(p. 7)</p> <p>4. 無。</p> <p>5. Stage III A(T1-2, N2)、Stage IIIB(T3, N2)開刀後 adjuvant C/T。(p. 9)</p> <p>6. Stage IIIB-IIIC IIIB-IIIC (T4N2, T1-4N3)原「重新評估」之治療為TKI ± RT or CCRT(p. 10)。</p> <p>7. stage IVA/IVB 之Lung及Brain OP後的治療原為「± WBRT or SRS」，CXR 的追蹤原為 Q3-6w (p. 11)。</p>	<p>1. 將Stage IA與stage IB及II之診斷及初步治療及輔助治療細分並部分做修改，Stage IA 追蹤改為 Q3-6M，原本的 definite R/T if not OP 修正為 definite R/T, preferably SABR, if not OP (p. 5)。</p> <p>2. 新增Stage IB/II disease 的診療，原本的 definite R/T if not OP 修正為 definite R/T, preferably SABR, if not OP。(p. 6)</p> <p>3. 將Stage IIB (T3 invasion, N0), Stage III A (T4 extension, N0-1; T3, N1; T4, N0-1)及Stage III A(T4, N0-1), Unresectable細分並做部分修改。(p. 7)</p> <p>4. 在 stage III A unresectable 多加了 TKI (with driver oncogene) 做為 neoadjuvant therapy，若 resectable，OP (p. 8)。</p> <p>5. Stage III A(T1-2, N2)、Stage IIIB(T3, N2) 新增在開刀後除了 adjuvant C/T，多加了 ± R/T，在 definite CCRT 後多加了 PR or SD 可以 durvalumab consolidation、TKI (with driver oncogene) in poor PS Pt (p. 9)。</p> <p>6. Stage IIIB-IIIC (T4N2, T1-4N3)將「重新評估」之CCRT移至首要治療(p. 10)。</p> <p>7. 在 stage IVA/IVB with EGFR mutation，多加了 Dacomitinib、ALK rearrangement positive，多加了 Lorlatinib、CXR 的追蹤 3 改為 Q3-8w(p. 11)。</p>

會議討論(二)

上次會議：2020/02/12

本共識與上一版的差異

上一版	新版
8. 在stage IVA/IVB，sensitizing EGFR mutation positive、ALK rearrangement positive、ROS1 的處方。(p. 13)	8. 第13頁，在 stage IVA/IVB，sensitizing EGFR mutation positive、ALK rearrangement positive、ROS1 的 subsequent therapy，多加一些用藥。(p. 13)
9. 在stage IVA/IVB，只有PD-L1 0-100%、PD-L1 \geq 50%及 ROS1 negative的建議治療及用藥。(p.14)	9. 在stage IVA/IVB，PD-L1 0-100%改 1-100%、治療多加了免疫及化療用藥，多加了 PD-L1 <1%、PD-L1 \geq 50%及 ROS1 negative的治療用藥。(p.14)
10. 標題為「一線化學治療處方」。(p.16-17)	10. 「一線化學治療處方」改為「一線抗腫瘤治療處方」。多加了 Dacomitinib 45 mg po qd (EGFR mutant)，Till PD or unacceptable toxicity。(p.16-17)
11. 未註明若年齡大，器官功能及體能狀況不佳之後續治療。(p. 17)	11. 多加了註解：若年齡大，器官功能及體能狀況不佳，可以單獨治療，不需合併治療。(p. 17)
12. 原標題為「二線及二線之後的化學治療處方」(p. 19-20)。	12. 二線及二線之後的化學治療處方，改為後續的抗腫瘤治療處方。(p. 19-20)。
13. 原處方無 squamous histology 2L therapy用藥。(p. 20)	13. 後續的抗腫瘤處方多加了Afatinib 40 mg po qd for squamous histology 2L therapy。(p. 20)
14. neoadjuvant chemotherapy 無cisplatin/etoposide 用藥。(p. 21)	14. neoadjuvant chemotherapy 多加了 cisplatin/etoposide。(p. 21)
15. adjuvant chemotherapy 無cisplatin/etoposide。(p. 22)	15. adjuvant chemotherapy 多加了 cisplatin/etoposide。(p. 22)

非小細胞肺癌

高雄榮民總醫院
臨床診療指引

2021年第一版

診斷	評估	初步治療	輔助治療	追蹤
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**Stage IA disease
(peripheral
T1abc,N0)**

- 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組織學證實
- 檢體 EGFR mutation 檢測*
- 檢體 ALK IHC 檢測*
- 檢體 ROS1 IHC 檢測*
- 檢體 PD-L1 檢測*
- 次世代定序癌症基因檢測*
- Brain CT/MR#
- 上腹部超音波#
- 支氣管鏡檢查#
- Bone scan#
- PET-CT#
- Pathologic mediastinal LN evaluation*
- 肺功能檢查

Curative surgery with radical LN dissection or systemic LN sampling

**Margin (+) (R1,R2)
Reresection or R/T**

Margin (-) (R0)

Definite R/T, preferably SABR if not OP

Baseline Chest CT after Tx, Hx, PE and CXR, Tumor markers* Q3-6M x 2 yrs then q6M every yr F/U for 5 yrs

• As clinical indicated

• # May not needed for GGO lesion

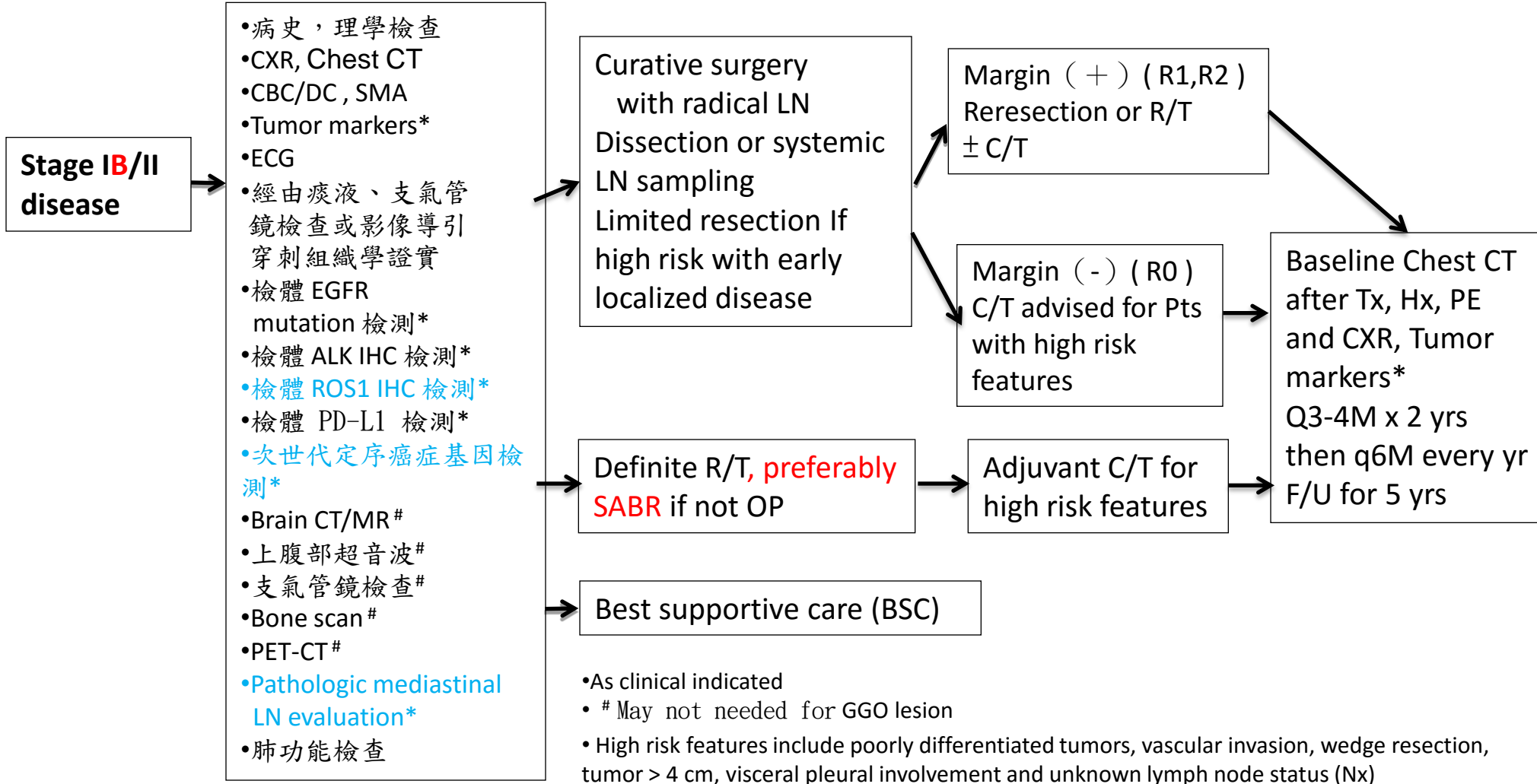
• High risk features include poorly differentiated tumors, vascular invasion, wedge resection, tumor > 4 cm, visceral pleural involvement and unknown lymph node status (Nx)

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診斷	評估	初步治療	輔助治療	追蹤
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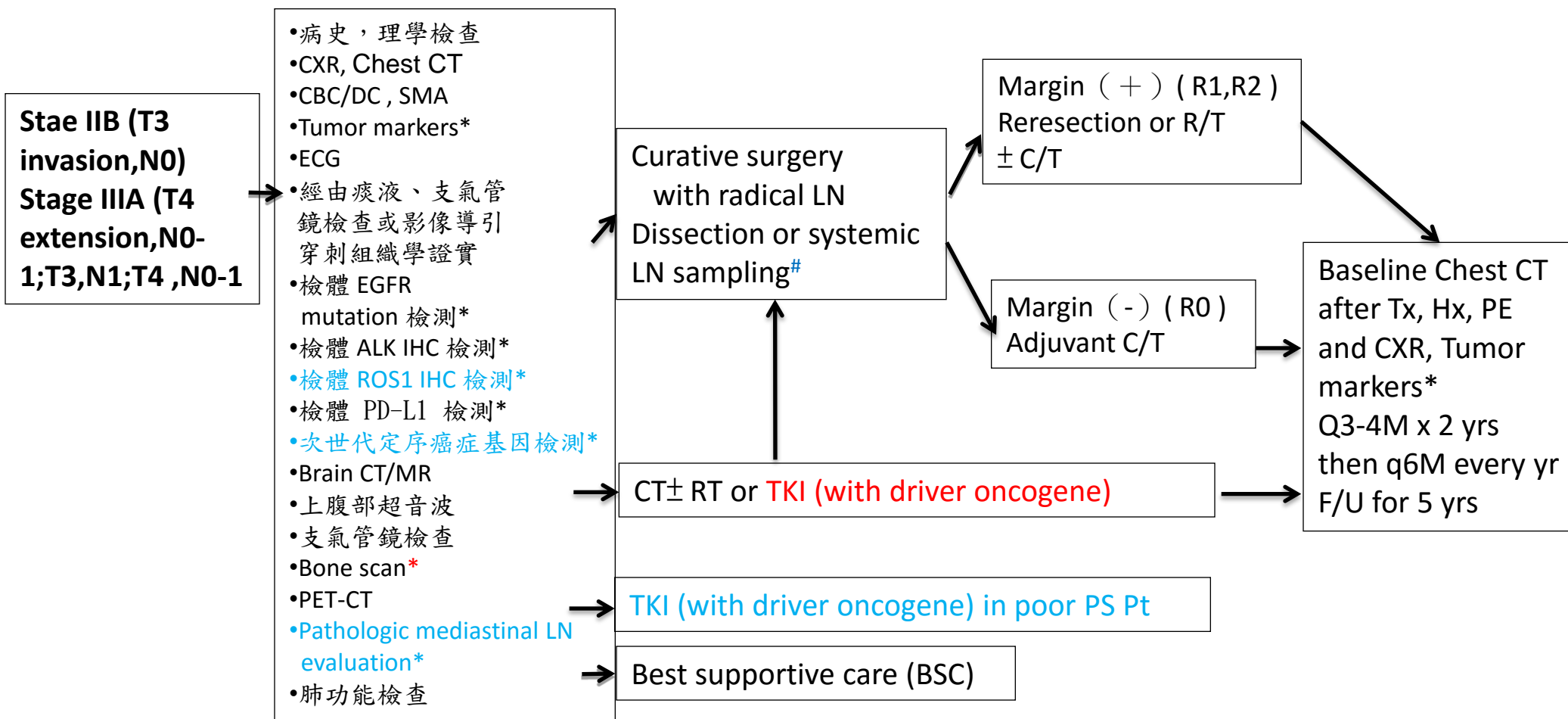


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診斷	評估	初步治療	輔助治療	追蹤
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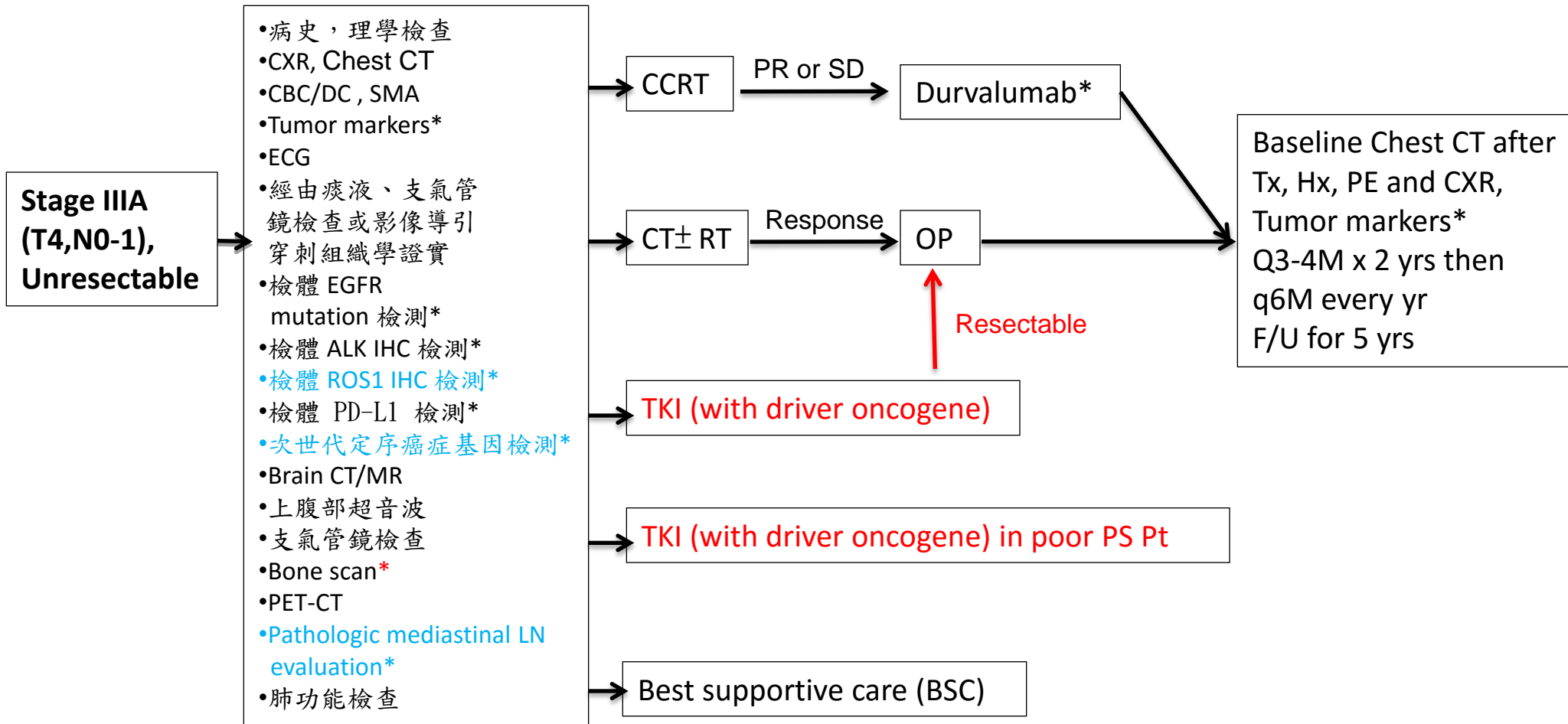


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診斷	評估	初步治療	輔助治療	追蹤
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診斷	評估	初步治療	輔助治療	追蹤
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Stage IIIA
T1-2, N2
Stage IIIB
T3, N2

- 病史，理學檢查
- CXR, Chest CT
- CBC/DC, SMA
- Tumor markers*
- EKG*
- 經由痰液、支氣管鏡檢查或影像導引穿刺組織學證實
- 檢體 EGFR mutation 檢測*
- 檢體 ALK IHC 檢測*
- 檢體 ROS1 IHC 檢測*
- 檢體 PD-L1 檢測*
- 次世代定序癌症基因檢測*
- Brain CT/MR
- 上腹部超音波
- 支氣管鏡檢查*
- Bone scan*
- PET-CT*
- Pathologic mediastinal LN evaluation*
- 肺功能檢查*

Curative surgery with radical LN Dissection or systemic LN sampling#

C/T ± R/T

Definite CCRT

PR or SD

Durvalumab*

Induction C/T or TKI ± R/T

No apparent PD

OP ± R/T (if not given)

PD

R/T ± C/T

TKI (with driver oncogene) in poor PS Pt

Margin (-) (R0)
C/T advised for Pts with high risk features ± R/T

Best supportive care (BSC)

Hx, PE and CXR, Chest CT
上腹部超音波*
Tumor markers*
q3M x 1 yrs then q4M x 1 yrs then q6M every yr
F/U for 5 yrs

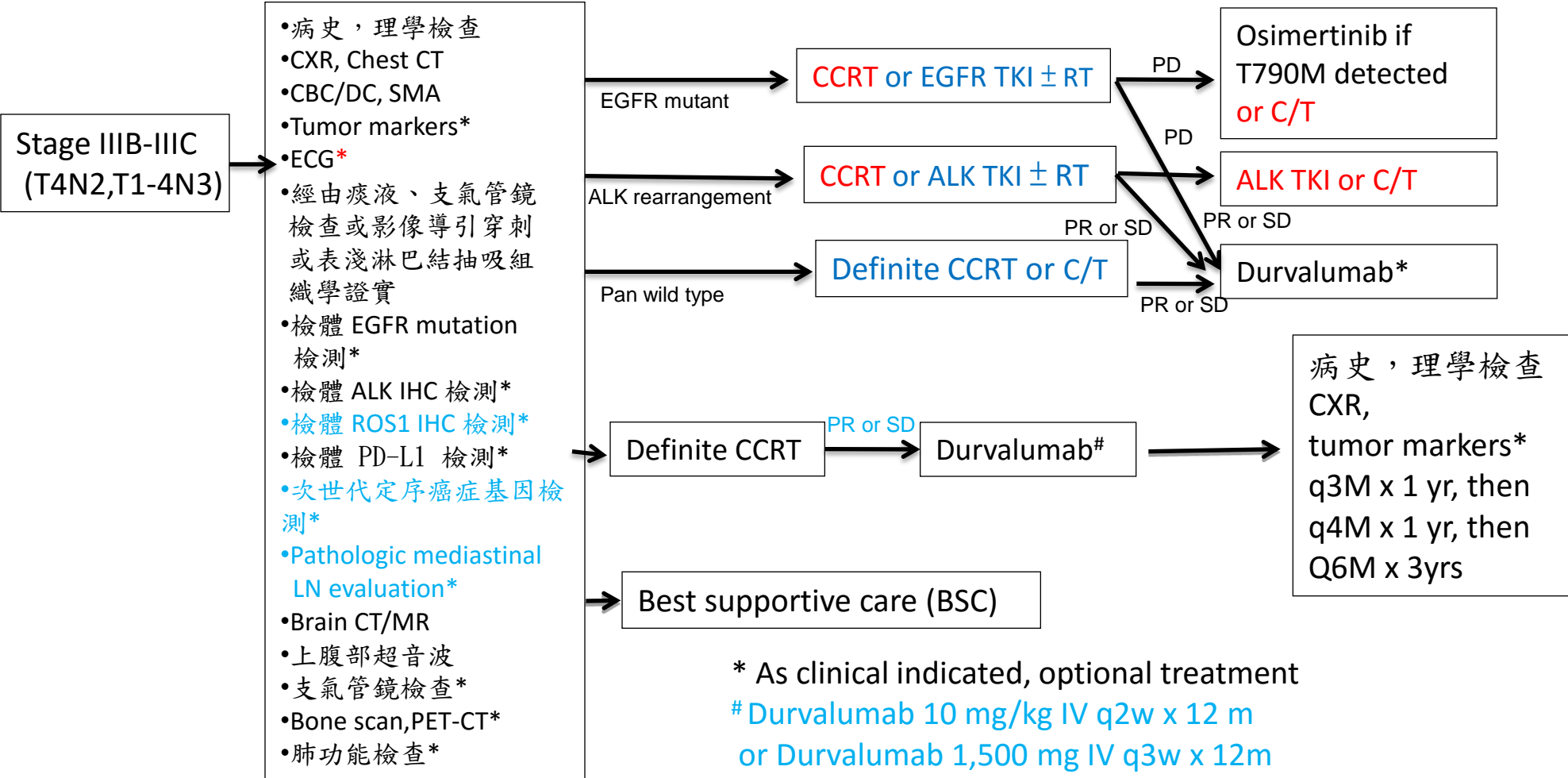
* As clinical indicated, optional treatment
Limited resection is appropriate in poor pulmonary reserve or other major comorbidity that contraindicate lobectomy

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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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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 ROS1 IHC 檢測*
- 檢體 PD-L1 檢測*
- 次世代定序癌症基因檢測*
- 上腹部超音波檢查
- Bone scan*
- Brain CT/MRI
- PET-CT*

Stage
IVA,B
M1a
M1b
M1c

Solitary Brain / adrenal Metastasis with resectable Lung lesion (NO)

Brain

Lung OP and Brain OP ± SRS or WBRT or SRS ± WBRT

Adrenal gland

Surgery or R/T to both lung and adrenal tumors

Osimertinib if T790M detected

Observation if responsive, Maintenance therapy in selected Pts, 2nd line C/T or supportive care if disease progression

Disseminated Metastasis

Positive EGFR mutation

Gefitinib or Afatinib or Erlotinib or **dacomitinib** or osimertinib or erlotinib+ bevacizumab or erlotinib + ramucirumab

Negative

C/T with 2 agents ± bevacizumab ± ICI or ICI in PD-L1 ≥ 50% C/T for 4 to 6 cycles

Hx, PE and Tumor markers*, CXR q3-8W

Disseminated Metastasis

Negative ALK Positive

Alectinib, Ceritinib, Crizotinib, **Brigatinib**, **Lorlatinib**

Poor Performance status

Integrate palliative care or single agent C/T

Ceritinib, Alectinib, Brigatinib, **Lorlatinib**

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復發

- 病史，理學檢查
- CXR
- CBC/DC, SMA
- Tumor markers*
- Chest CT (including liver/adrenal gland)
- 經由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 ROS1 IHC 檢測*
- 檢體 PD-L1 檢測*
- 次世代定序癌症基因檢測*
- Bone scan*
- Brain MRI*
- Mediastinoscopy* or TBNA[§]
- PET-CT*

Solitary metastasis to Brain
Adrenal
Lung

Local recurrence within the chest or mediastinum

Malignant pleural effusion or disseminated metastases

Surgery +/- R/T or R/T alone

C/T as in M1 disease

* optional

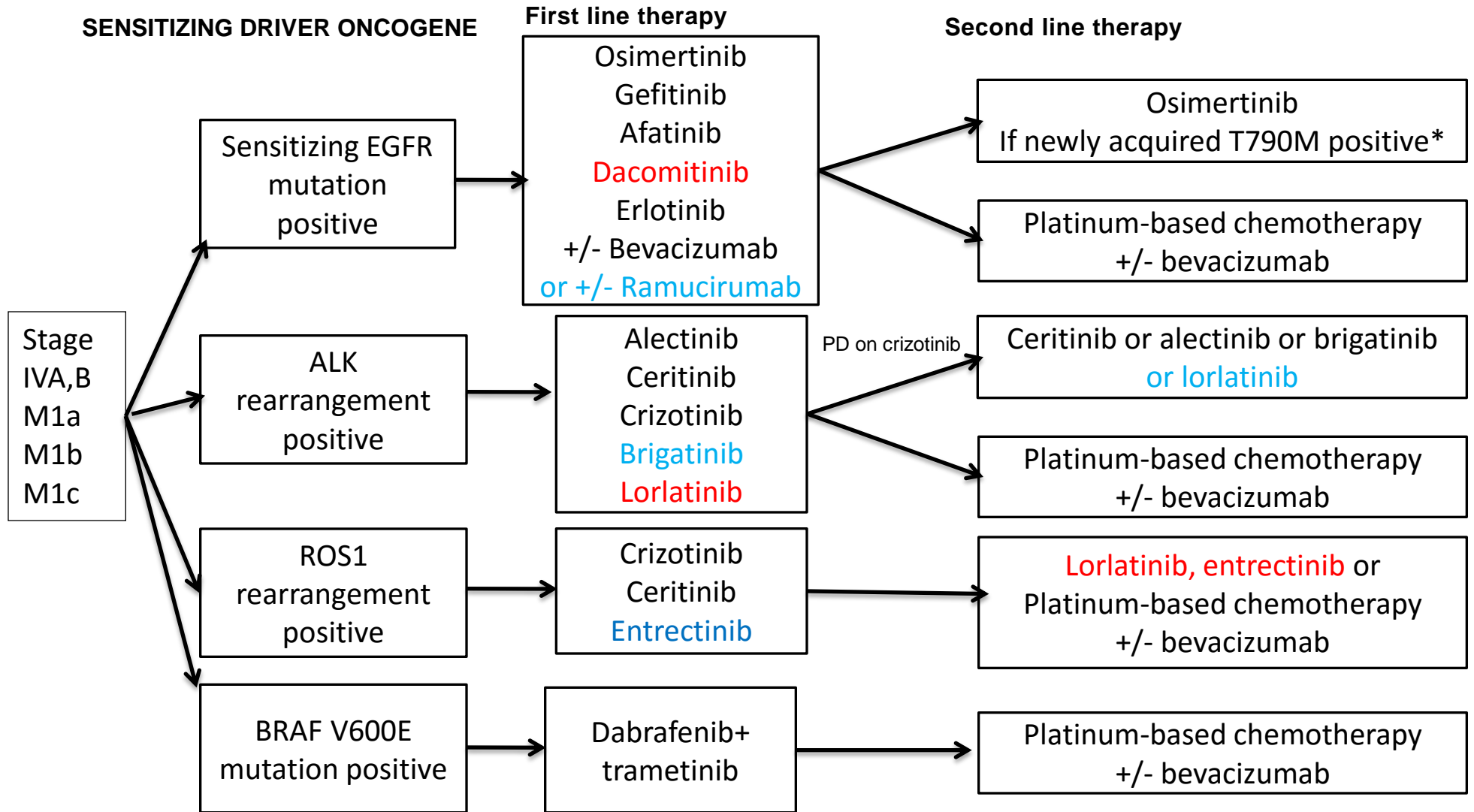
§ Transbronchoal fine needle aspiration

¥ Concurrent chemoradiotherapy

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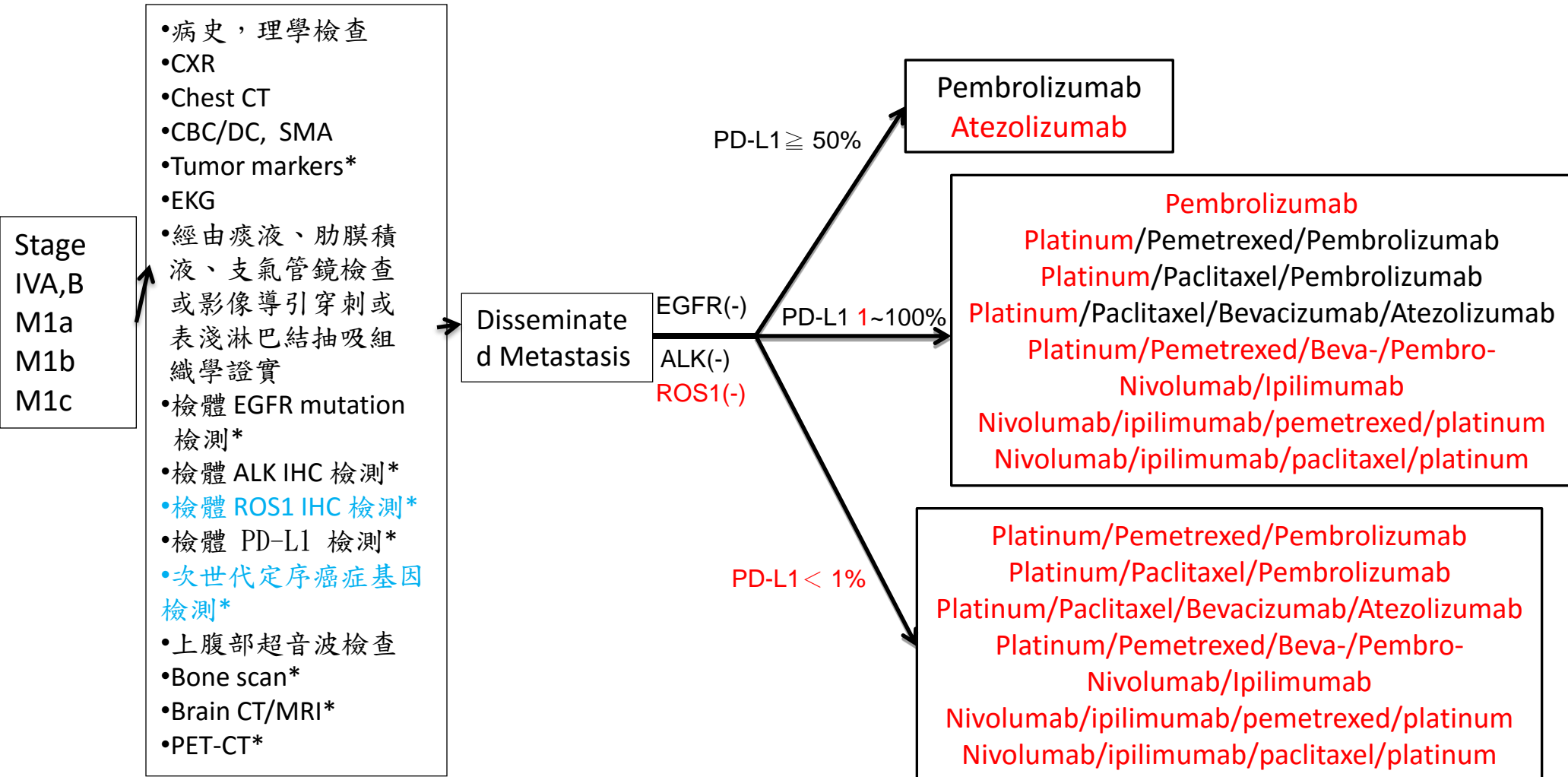
* First line did not received osimertinib

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

PS 0-2

Systemic therapy

Progression

PS 0-2

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

PS 3-4

Best supportive care

Stable

Continuation maintenance
Pembrolizumab, Gemcitabine
or
Switch maintenance
Docetaxel
or
Close observation

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一線抗腫瘤治療處方 (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
Dacomitinib 45 mg po qd (EGFR mutant)	Till PD or unacceptable toxicity
Osimertinib 80 mg po qd (EGFR mutant)	Till PD or unacceptable toxicity
Crizotinib 250 mg po bid (ALK rearrangement or ROS1 rearrangement)	Till PD or unacceptable toxicity
Alectinib 600 mg po bid (ALK rearrangement)	Till PD or unacceptable toxicity
Ceritinib 450 mg po qd (ALK rearrangement or ROS1 rearrangement)	Till PD or unacceptable toxicity

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一線抗腫瘤治療處方（二）

Published C/T Regimens	Schedule
Brigatinib 90 mg (first 7 days lead-in) -> 180 mg (ALK rearrangement)	Till PD or unacceptable toxicity
Entrectinib 600 mg po qd	Till PD or unacceptable toxicity
Pembrolizumab # 2mg/kg IV or Pembrolizumab 200 mg IV	Q3w until PD or 2yr
Atezolizumab 1200 mg IV	Q3w
Cisplatin 60-75 mg/m ² , IV, D1 + *Pemetrexed 500 mg/m ² , IV, D1+ Pembrolizumab 2 mg/kg iv or Pembrolizumab 200 mg IV x 6 cycles and then Pemetrexed 500 mg/m ² ,IV,D1 + Pembrolizumab 2mg/kg or 200 mg,IV,D1	Q3w until PD

若年齡大，器官功能及體能狀況不佳，可以單獨治療，不需合併治療。

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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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 or Pembrolizumab 200 mg IV	Q21d Till PD or unacceptable toxicity or 2yr
Atezolizumab 1200 mg 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。

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後續的抗腫瘤治療處方（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 or ROS1 rearrangement)	Till PD or unacceptable toxicity
Ceritinib 450 mg PO QD (ALK rearrangement or ROS1 rearrangement)	Till PD or unacceptable toxicity
Alectinib 600mg PO BID (ALK rearrangement)	Till PD or unacceptable toxicity
Brigatinib 90 mg (first 7 days lead in) -> 180 mg (ALK rearrangement)	Till PD or unacceptable toxicity
Lorlatinib 100 mg po qd (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

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後續的抗腫瘤治療處方（二）

Published C/T Regimens	Schedule
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
Docetaxel 30 mg/m ² , IV, D1,8,15 + Ramucirumab 10 mg/kg IV	Q28 d x 4-6 cycles
Nivolumab 3mg/kg IV	Q2w
*Pembrolizumab 2mg/kg IV or Pembrolizumab 200 mg IV	Q3w
Atezolizumab 1200 mg IV	Q3w
TS-1 40 mg/m ² po bid,D1-28	Q42d
Afatinib 40 mg po qd (2L therapy for squamous histology)	Till PD or unacceptable toxicity

* 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

* 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, D1 #Pemetrexed 500 mg/m ² , IV, D1	Q21 d x 2-4 cycles
Cisplatin 60-75 mg/m ² , IV, D15. Gemcitabine 900-1000 mg/m ² , IV, D1,8,15.	Q28 d x 2-4 cycles
Cisplatin 60-75 mg/m ² , IV, D15 Docetaxel 30 mg/m ² , IV, D1,8,15	Q28 d x 2-4 cycles
Cisplatin 60-75 mg/m ² , IV, D15 Vinorelbine 25 mg/m ² , IV, D1,8,15	Q28 d x 2-4 cycles
Cisplatin 60-75 mg/m ² , IV, D8 Vinorelbine 60-75 mg/m ² , PO, D1,8	Q21 d x 2-4 cycles
Cisplatin 60-75 mg/m ² , IV, D15 Paclitaxel 60 mg/m ² , IV, D1,8,15	Q28 d x 2-4 cycles
Cisplatin 60-75 mg/m², IV, D1 Etoposide 60-75 mg/m², IV, D1-3	Q28d x 2-4 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

非小細胞肺癌

高雄榮民總醫院
臨床診療指引

2021年第一版

術後輔助化學治療處方

Published C/T Regimens	Schedule
Cisplatin 60-75 mg/m ² , IV, D1 #Pemetrexed 500 mg/m ² , IV, D1	Q21 d x 2-4 cycles
Cisplatin 60-75 mg/m ² , IV, D15. Gemcitabine 900-1000 mg/m ² , IV, D1,8,15.	Q28 d x 2-4 cycles
Cisplatin 60-75 mg/m ² , IV, D15 Docetaxel 30 mg/m ² , IV, D1,8,15	Q28 d x 2-4 cycles
Cisplatin 60-75 mg/m ² , IV, D15 Vinorelbine 25 mg/m ² , IV, D1,8,15	Q28 d x 2-4 cycles
Cisplatin 60-75 mg/m ² , IV, D8 Vinorelbine 60-75 mg/m ² , PO, D1,8	Q21 d x 2-4 cycles
Cisplatin 60-75 mg/m ² , IV, D15 Paclitaxel 60 mg/m ² , IV, D1,8,15	Q28 d x 2-4 cycles
Cisplatin 60-75 mg/m ² , IV, D1 Etoposide 60-75 mg/m ² , IV, D1-3	Q28d x 2-4 cycles
Tagafur/Uracil 300-500 mg PO QD *	Maintenance for 2 years

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同步化學治療放射線治療處方

Published C/T Regimens	Schedule
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
Carboplatin AUC 2, IV, QW Paclitaxel 45-50 mg/m ² , IV, QW	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
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

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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