

高雄榮民總醫院

肺癌診療原則

(非小細胞癌)

2020年02月12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.2.2020**

會議討論(一)

上次會議：2019/03/06

本共識與上一版的差異

| 上一版 | 新版 |
|--|--|
| <ol style="list-style-type: none">1. Stage I/II之診療指引評估原為Mediastinoscopy且無ROS1 IHC及次世代定序癌症基因檢測(p. 5)。2. Stae IIB-III A(T3 invasion,N0-1 & Resectable T4 extension,N0-1)之診療指引評估原為Mediastinoscopy且無ROS1 IHC及次世代定序癌症基因檢測(p. 6)。3. Stage IIIA (T1-2, N2)Stage IIIB (T3, N2)之診療指引評估原為Mediastinoscopy且無ROS1 IHC及次世代定序癌症基因檢測(p. 7)4. Stage IIIB-IIIC (T4N2,T1-4N3)之診療指引評估原為Mediastinoscopy且無ROS1 IHC及次世代定序癌症基因檢測。5. EGFR TKI ± RT 列於CCRT前面(p. 8)。6. Stage IIIB-IIIC (T4N2, T1-4N3) 之診療指引 Definite CCRT 後直接可以接受durvalumab 治療，無Regimen建議(p. 8)。 | <ol style="list-style-type: none">1. Stage I/II之診療指引評估新增了檢體 ROS1 IHC 及次世代定序癌症基因檢測(p. 5)。2. Stae IIB-III A (T3 invasion,N0-1 & Resectable T4 extension,N0-1) 之診療指引評估Mediastinoscopy* 改為 Pathologic mediastinal LN evaluation* ，且新增了檢體 ROS1 IHC 檢測及次世代定序癌症基因檢測，及poor PS Pt with driver oncogene 的TKI 治療 (p. 6)。3. Stage IIIA (T1-2, N2) Stage IIIB (T3, N2) 之診療指引評估新增了檢體 ROS1 IHC 檢測及次世代定序癌症基因檢測。 Mediastinoscopy* 改為 Pathologic mediastinal LN evaluation* 。新增了 driver oncogene Pt 的 neoadjuvant TKI 治療(p. 7)。4. Stage IIIB-IIIC (T4N2,T1-4N3) 之診療指引評估，新增了檢體 ROS1 IHC 檢測及次世代定序癌症基因檢測。 Mediastinoscopy* 改為 Pathologic mediastinal LN evaluation* 。Definite CCRT 後新增了 PR 或 SD，可以接受 consolidation durvalumab 治療。5. 將CCRT列於前面， EGFR TKI ± RT 列於後面(p. 8)。6. Stage IIIB-IIIC (T4N2, T1-4N3) Definite CCRT 後新增了 PR 或 SD，可以接受 consolidation durvalumab 治療，並將 Durvalumab 劑量標註10 mg/kg IV q2w x 12 m or Durvalumab 1,500 mg IV q2w x 12m (p. 8)。 |

會議討論(二)

上一版

7. Stage IV A (M1a、M1b)、Stage IV B(M1c)之診療指引，ALK positive，一線治療為Crizotinib、Ceritinib、Alectinib，二線為Ceritinib, Alectinib, Brigatinib (p.9)。
8. Stage IV A (M1a、M1b)、Stage IV B(M1c)之診療指引，poor performance status 治療原為best supportive care or single agent C/T (p.9)。
9. 復發診療指引治療，且無ROS1 IHC及次世代定序癌症基因檢測(p. 10)。
10. Stage IV A (M1a、M1b)、Stage IV B(M1c)之診療指引，EGFR sensitizing mutation positive，原治療為Osimertinib、Gefitinib、Afatinib (p.11)。
11. Stage IV A (M1a、M1b)、Stage IV B(M1c)之診療指引，ALK rearrangement positive 治療原為Crizotinib、Ceritinib、Alectinib (p.11)。
12. Stage IV A (M1a、M1b)、Stage IV B(M1c) Disseminated Metastasis之診療指引評估原無ROS1 IHC及次世代定序癌症基因檢測(p. 12)。
13. 一線治療處方無osimertinib，brigatinib (p.14)。
14. 維持治療處方無 atezolizumab 1,200 mg IV(p.17)。
15. 二線及二線後化療處方 crizotinib 及 ceritinib 未使用在 ROS1 rearrangement 的治療 (p. 18)。
16. 二線及二線後化療處方無 brigatinib 做為 ALK rearrangement 的治療 (p. 18)。
17. 二線及二線後化療處方，無 TS-1 治療 (p. 19)。
18. 術前新輔助化療頻次為3-4次 (p. 20)。

新版

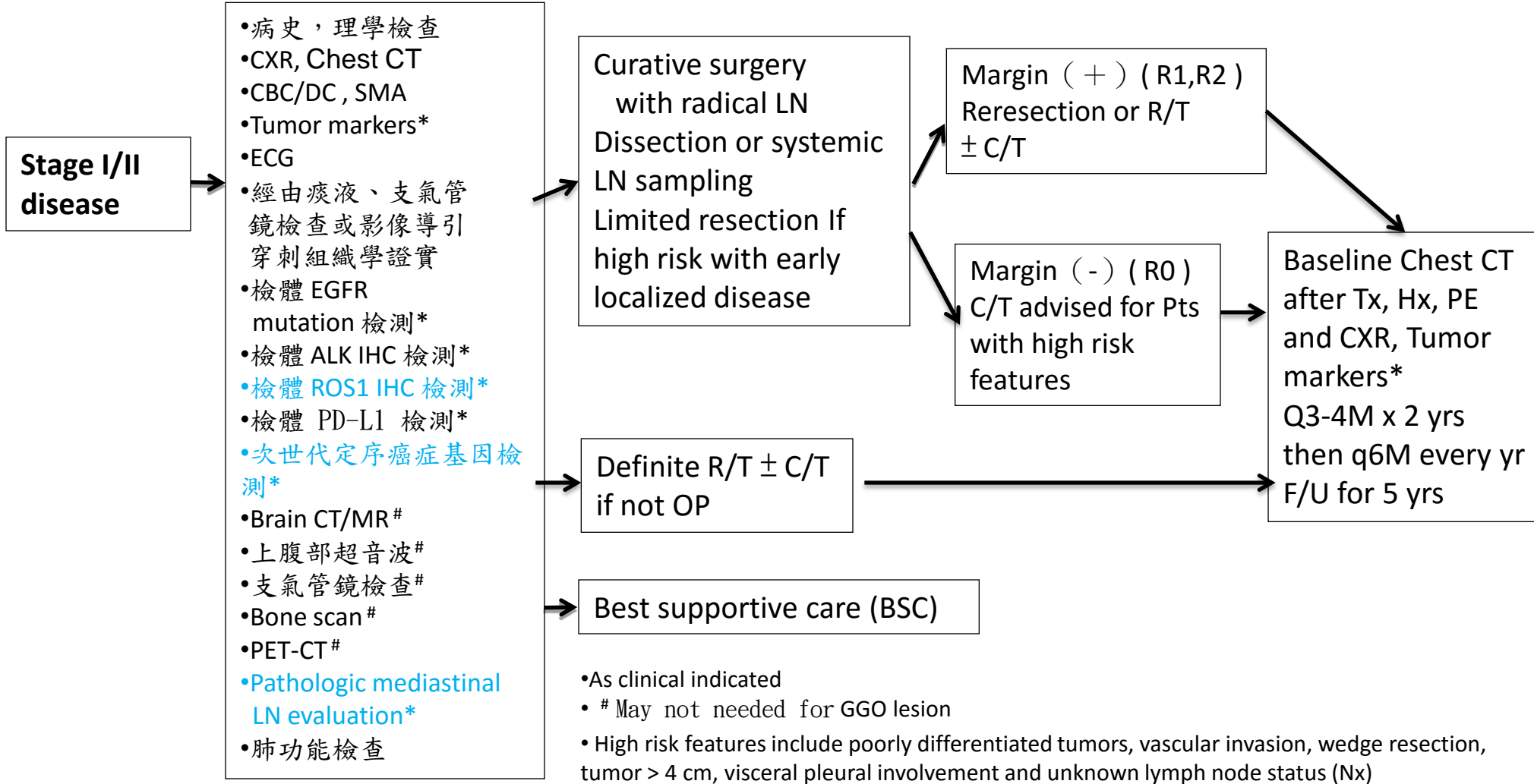
7. Stage IV A (M1a、M1b)、Stage IV B(M1c)之診療指引，ALK positive，一線新增 brigatinib 治療，二線新增 lorlatinib 治療(p. 9)。
8. Stage IV A (M1a、M1b)、Stage IV B(M1c)之診療指引，poor performance status，best supportive care 改為 integrate palliative care(p.9)。
9. 復發診療指引治療新增檢體 ROS1 IHC 檢測及次世代定序癌症基因檢測(p. 10)。
10. Stage IV A (M1a、M1b)、Stage IV B(M1c)之診療指引，EGFR sensitizing mutation positive，新增 erlotinib + ramucirumab 治療。
11. Stage IV A (M1a、M1b)、Stage IV B(M1c)之診療指引，ALK rearrangement positive，一線新增 brigatinib 治療，二線治療新增 lorlatinib 治療 (p. 11)。
12. Stage IV A (M1a、M1b)、Stage IV B(M1c) Disseminated Metastasis之診療指引評估，新增了檢體 ROS1 IHC 檢測及次世代定序癌症基因檢測(p. 12)。
13. 一線治療處方新增 osimertinib 在 EGFR mutant 一線，crizotinib 在 ROS1 一線，ceritinib 在 ROS1 一線，brigatinib 在 ALK positive 一線。
14. 維持治療處方新增 atezolizumab 1,200 mg IV (p.17)。
15. 二線及二線後化療處方新增 crizotinib 及 ceritinib 在 ROS1 rearrangement 治療。
16. 二線及二線後化療處方，新增 brigatinib 做為 ALK rearrangement 的一線治療(p. 18)。
17. 二線及二線後化療處方，新增 TS-1 40 mg/m² po bid D1-28, Q42D 在晚期轉移非小細胞肺癌接受過含鉑之化學藥物治療失敗病患(p. 19)。
18. 術前新輔助化療頻次調整為2-4次 (p. 20)。

非小細胞肺癌

高雄榮民總醫院
臨床診療指引

2020年第一版

| 診斷 | 評估 | 初步治療 | 輔助治療 | 追蹤 |
|----|----|------|------|----|
|----|----|------|------|----|



非小細胞肺癌

高雄榮民總醫院
臨床診療指引

2020年第一版

| 診斷 | 評估 | 初步治療 | 輔助治療 | 追蹤 |
|----|----|------|------|----|
|----|----|------|------|----|

- 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

Stage IIB-III A
T3 invasion, N0-1
Resectable T4
extension, N0-1

Stage III A
(T4, N0-1),
Unresectable

Curative surgery
with radical LN
Dissection or systemic
LN sampling#

CT+RT or C/T
or TKI (with driver oncogene) in poor PS Pt

Best supportive care (BSC)

CT± RT

Best supportive care (BSC)

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

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

Baseline Chest CT
after Tx, Hx, PE
and CXR, Tumor
markers*
Q3-4M x 2 yrs
then q6M every yr
F/U for 5 yrs

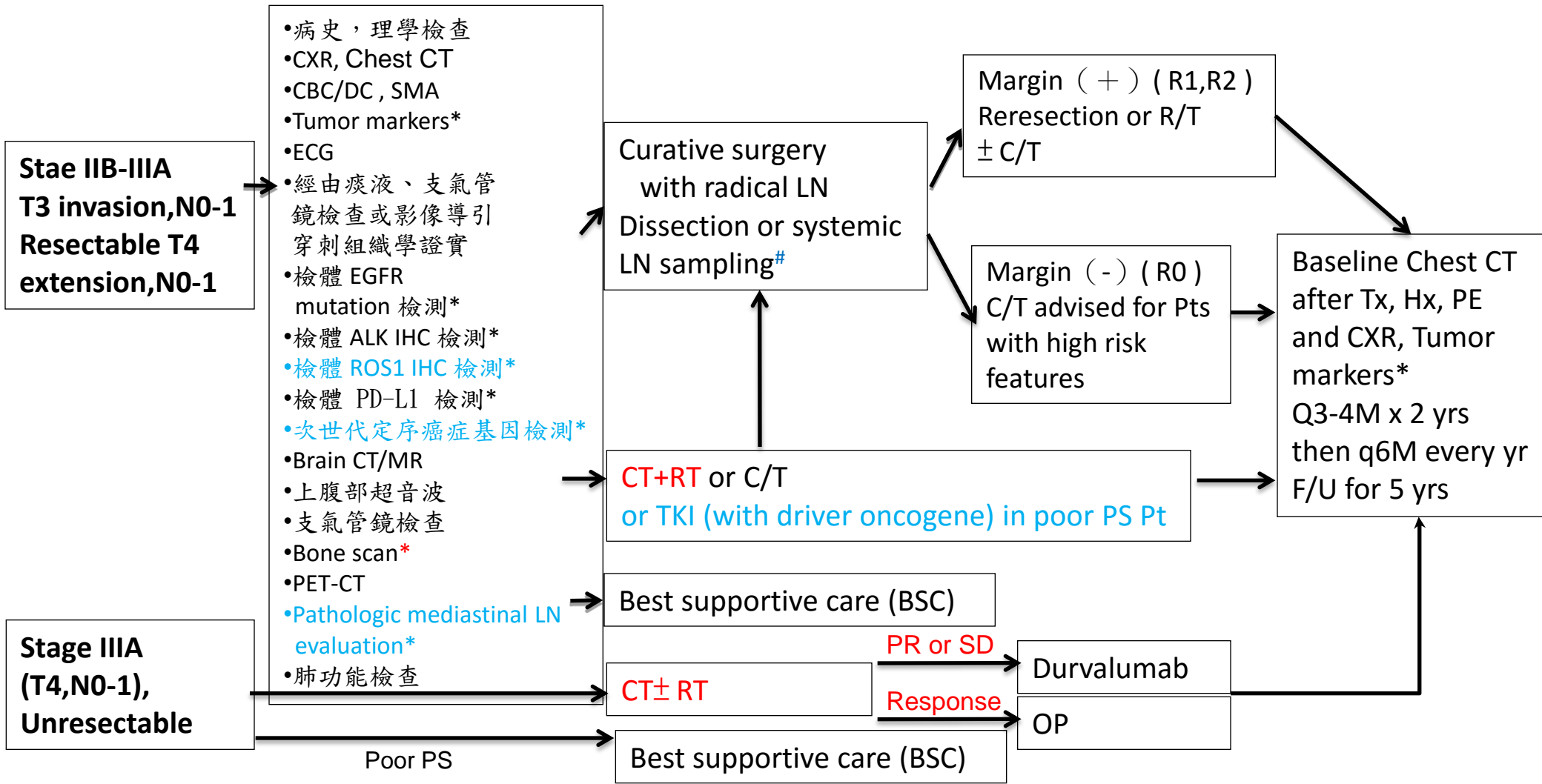
Durvalumab

OP

Poor PS

PR or SD

Response



非小細胞肺癌

高雄榮民總醫院
臨床診療指引

2020年第一版

| 診斷 | 評估 | 初步治療 | 輔助治療 | 追蹤 |
|----|----|------|------|----|
|----|----|------|------|----|

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#

Definite CCRT

Durvalumab

Induction C/T or TKI ± R/T

No apparent PD

OP

PD

R/T ± C/T

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

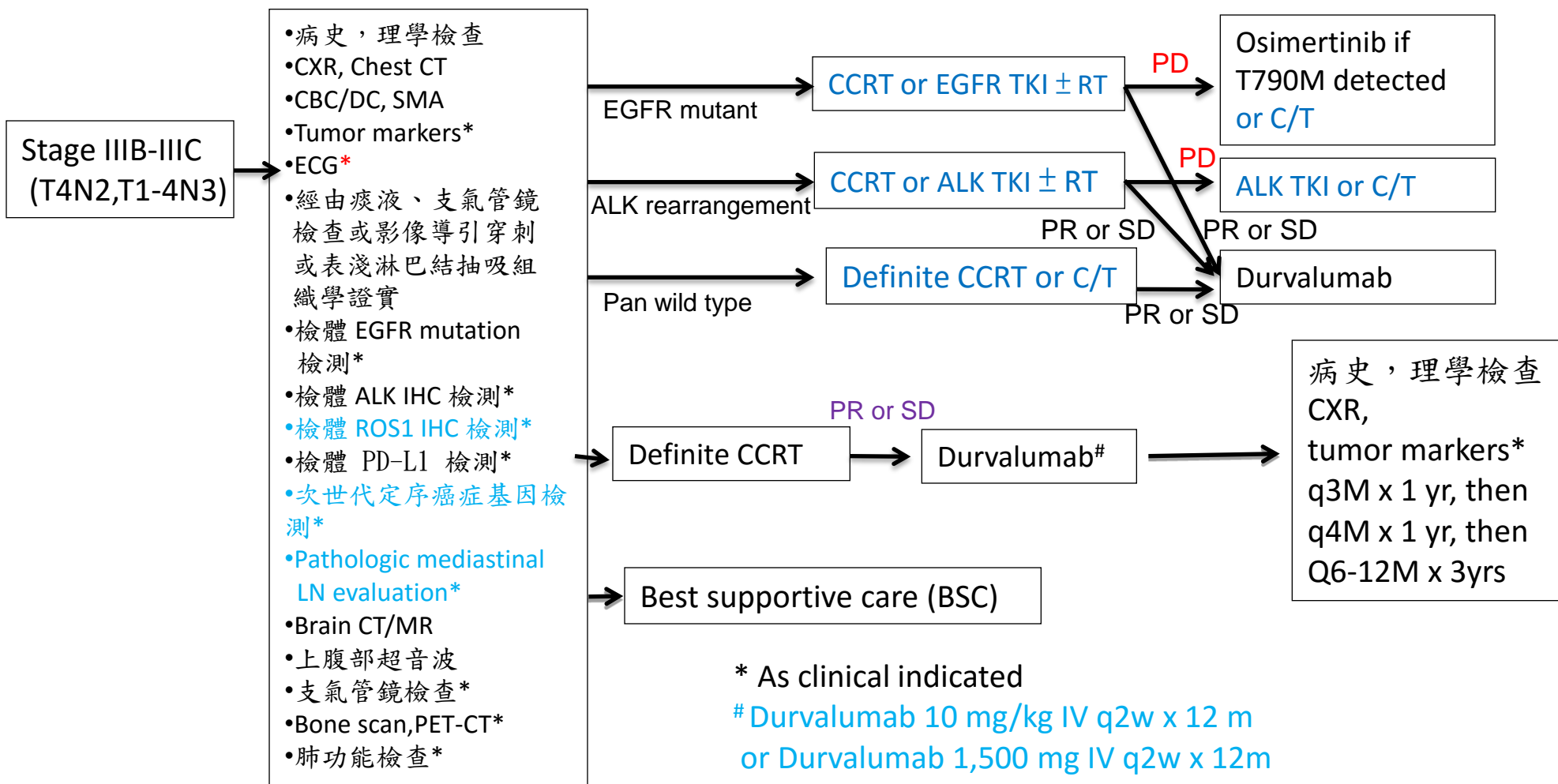
Limited resection is appropriate in poor pulmonary reserve or other major comorbidity that contraindicate lobectomy

非小細胞肺癌

高雄榮民總醫院
臨床診療指引

2020年第一版

| 診斷 | 評估 | 初步治療 | 重新評估 | 進一步治療 | 追蹤 |
|----|----|------|------|-------|----|
|----|----|------|------|-------|----|



非小細胞肺癌

高雄榮民總醫院
臨床診療指引

2020年第一版

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

Brain

Lung OP and
Brain OP ± WBRT or SRS
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 osimertinib
or erlotinib+ bevacizumab

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
q3-6W x 6m then
q8W x 1 yr then
q12w x 1 yr

Disseminated
Metastasis

Negative
ALK
Positive

Crizotinib, Ceritinib, Alectinib, Brigatinib

Poor Performance
status

Integrate palliative care
or single agent C/T

Ceritinib, Alectinib, Brigatinib,
Lorlatinib

非小細胞肺癌

高雄榮民總醫院
臨床診療指引

2020年第一版

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

非小細胞肺癌

高雄榮民總醫院
臨床診療指引

2020年第一版

SENSITIZING DRIVER ONCOGEN

First line therapy

Second line therapy

Sensitizing EGFR
mutation
positive

Osimertinib
Gefitinib
Afatinib
Erlotinib
+/- Bevacizumab
or +/- Ramucirumab

Osimertinib
If newly acquired T790M positive*

Platinum-based chemotherapy
+/- bevacizumab

Stage
IVA,B
M1a
M1b
M1c

ALK
rearrangement
positive

Crizotinib
Ceritinib
Alectinib
Brigatinib

PD on crizotinib

Ceritinib or alectinib **or brigatinib**
or lorlatinib

Platinum-based chemotherapy
+/- bevacizumab

ROS1
rearrangement
positive

Crizotinib
Ceritinib
Entrectinib

Platinum-based chemotherapy
+/- bevacizumab

BRAF V600E
mutation positive

Dabrafenib+
trametinib

Platinum-based chemotherapy
+/- bevacizumab

* First line did not received osimertinib

非小細胞肺癌

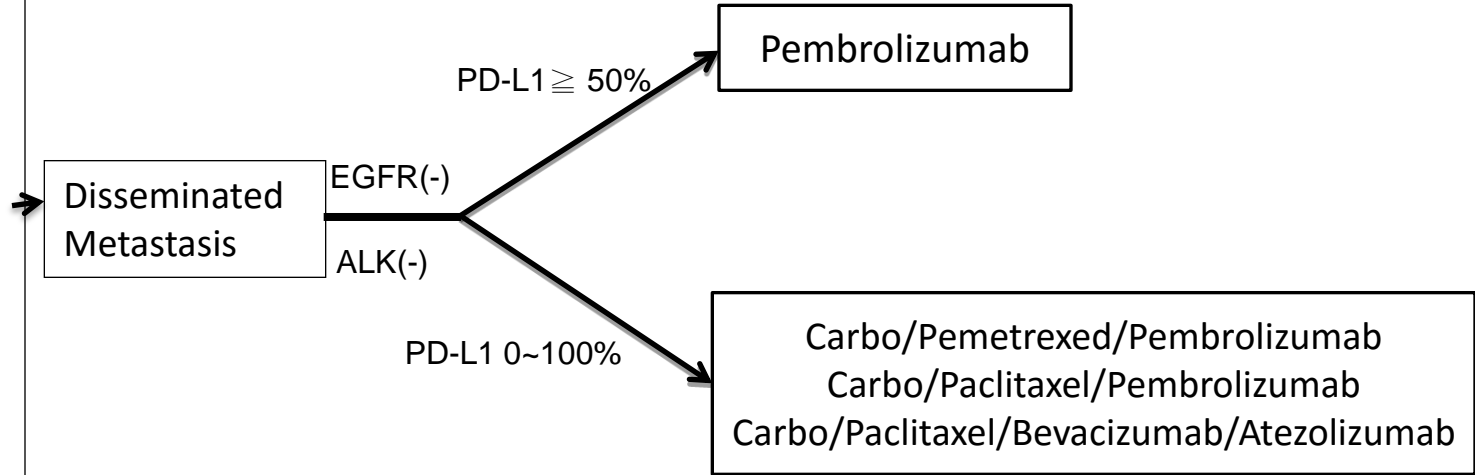
高雄榮民總醫院
臨床診療指引

2020年第一版

| 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

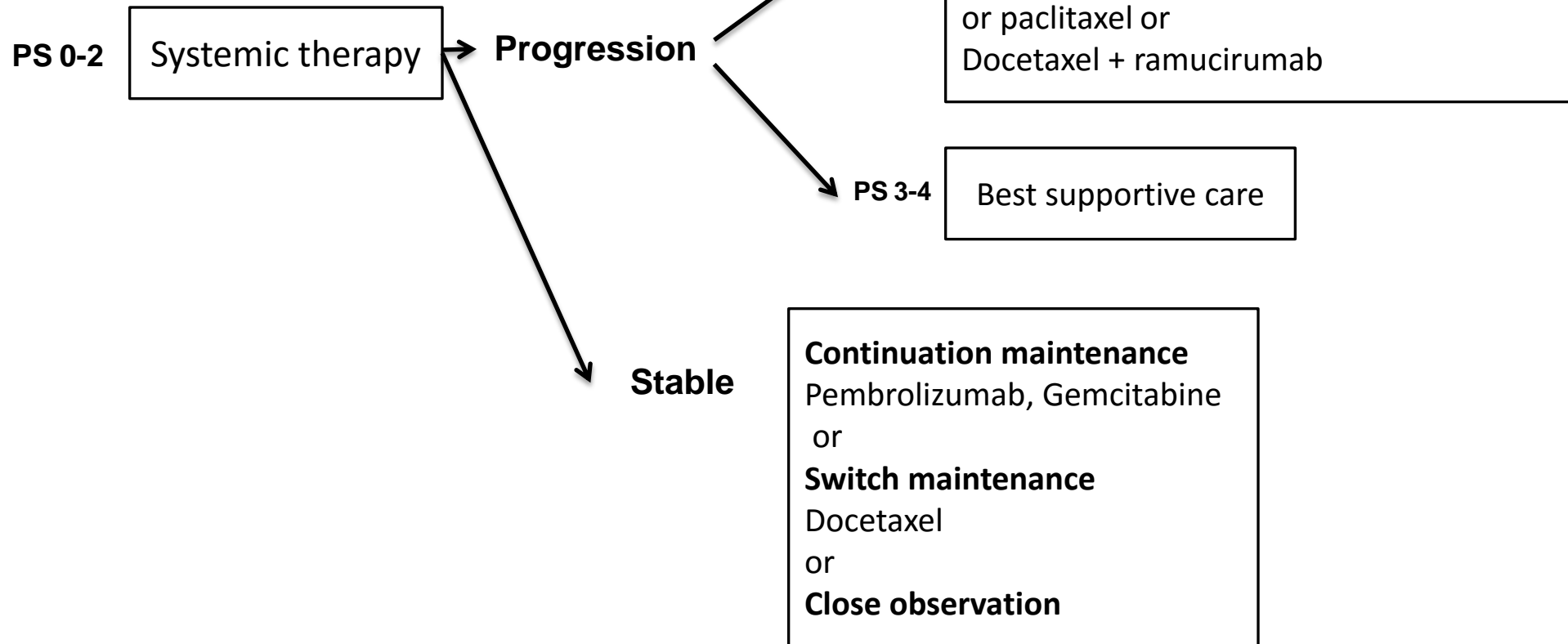


非小細胞肺癌

高雄榮民總醫院
臨床診療指引

2020年第一版

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



非小細胞肺癌

高雄榮民總醫院
臨床診療指引

2020年第一版

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 |
| 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 |
| 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 |

非小細胞肺癌

高雄榮民總醫院
臨床診療指引

2020年第一版

一線化學治療處方（二）

| Published C/T Regimens | Schedule |
|---|---------------------|
| Pembrolizumab # 2mg/kg IV or Pembrolizumab 200 mg IV | Q3w until PD or 2yr |
| 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

非小細胞肺癌

高雄榮民總醫院
臨床診療指引

2020年第一版

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。

非小細胞肺癌

高雄榮民總醫院
臨床診療指引

2020年第一版

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。

非小細胞肺癌

高雄榮民總醫院
臨床診療指引

2020年第一版

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 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 |

非小細胞肺癌

高雄榮民總醫院
臨床診療指引

2020年第一版

二線及二線之後的化學治療處方（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 |

* 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

非小細胞肺癌

高雄榮民總醫院
臨床診療指引

2020年第一版

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 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 Docetaxel 30 mg/m ² , IV, D1,8,15 | Q28 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, D15. Gemcitabine 900-1000 mg/m ² , IV, D1,8,15. | Q28 d x 2-4 cycles |
| Cisplatin 60-75 mg/m ² , IV, D1 #Pemetrexed 500 mg/m ² , IV, D1 | Q21 d 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

2020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, 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

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

2020年第一版

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

References

1. American Society of Clinical Oncology clinical practice guidelines: Opportunities and challenges. *J Clin Oncol* 26:4022-4026, 2008
2. Goldstraw P, Crowley J, Chansky K, et al: The IASLC Lung Cancer Staging Project: Proposals for the revision of the TNM stage groupings in the forthcoming (seventh) edition of the TNM Classification of malignant tumours. *J Thorac Oncol* 2:706-714, 2007
3. Gridelli C, Ardizzoni A, Ciardiello F, et al: Second-line treatment of advanced non-small cell lung cancer. *J Thorac Oncol* 3:430-440, 2008
4. D'Addario G, Felip E: Non-small-cell lung cancer: ESMO clinical recommendations for diagnosis, treatment and follow-up. *Ann Oncol* 19:ii39-ii40, 2008 (suppl 2)
5. Ettinger D, Johnson B: Update: NCCN small cell and non-small cell lung cancer Clinical Practice Guidelines. *J Natl Compr Canc Netw* 3:S17-S21, 2005 (suppl 1)
6. Noble J, Ellis PM, Mackay JA, et al: Secondline or subsequent systemic therapy for recurrent or progressive non-small cell lung cancer: A systematic review and practice guideline. *J Thorac Oncol* 1:1042-1058, 2006
7. Socinski MA, Crowell R, Hensing TE, et al: Treatment of non-small cell lung cancer, stage IV: ACCP evidence-based clinical practice guidelines (2nd edition). *Chest* 132:277S-289S, 2007
8. Pfister DG, Johnson DH, Azzoli CG, et al: American Society of Clinical Oncology treatment of unresectable non-small-cell lung cancer guideline: Update 2003. *J Clin Oncol* 22:330-353, 2004
9. Spiro SG, Rudd RM, Souhami RL, et al: Chemotherapy versus supportive care in advanced non-small cell lung cancer: Improved survival without detriment to quality of life. *Thorax* 59:828-836, 2004
10. NSCLC Meta-Analyses Collaborative Group: Chemotherapy in addition to supportive care improves survival in advanced non-small-cell lung cancer: A systematic review and meta-analysis of individual patient data from 16 randomized controlled trials. *J Clin Oncol* 26:4617-4625, 2008
11. Pisters KM, Evans WK, Azzoli CG, et al: Cancer Care Ontario and American Society of Clinical Oncology adjuvant chemotherapy and adjuvant radiation therapy for stages I-IIIa resectable non-small-cell lung cancer guideline. *J Clin Oncol* 25:5506-5518, 2007
12. Georgoulas V, Ardavanis A, Tsiadaki X, et al: Vinorelbine plus cisplatin versus docetaxel plus gemcitabine in advanced non-small-cell lung cancer: A phase III randomized trial. *J Clin Oncol* 23:2937-2945, 2005
13. Lilenbaum RC, Herndon JE 2nd, List MA, et al: Single-agent versus combination chemotherapy in advanced non-small-cell lung cancer: The Cancer and Leukemia Group B (study 9730). *J Clin Oncol* 23:190-196, 2005
14. Lilenbaum R, Axelrod R, Thomas S, et al: Randomized phase II trial of erlotinib or standard chemotherapy in patients with advanced non-small-cell lung cancer and a performance status of 2. *J Clin Oncol* 26:863-869, 2008
15. Cullen MH, Zatloukal P, Sorenson S, et al: A randomized phase III trial comparing standard and high-dose pemetrexed as second-line treatment in patients with locally advanced or metastatic non-small-cell lung cancer. *Ann Oncol* 19:939-945, 2008

References

16. Shepherd FA, Rodrigues Pereira J, Ciuleanu T, et al: Erlotinib in previously treated non-small-cell lung cancer. *N Engl J Med* 353:123-132, 2005
17. Hanna N, Shepherd FA, Fossella FV, et al: Randomized phase III trial of pemetrexed versus docetaxel in patients with non-small-cell lung cancer previously treated with chemotherapy. *J Clin Oncol* 22:1589-1597, 2004
18. Weiss GJ, Langer C, Rosell R, et al: Elderly patients benefit from second-line cytotoxic chemotherapy: A subset analysis of a randomized phase III trial of pemetrexed compared with docetaxel in patients with previously treated advanced non-small-cell lung cancer. *J Clin Oncol* 24:4405-4411, 2006
19. D'Addario G, Pintilie M, Leighl NB, et al: Platinum-based versus non-platinum-based chemotherapy in advanced non-small-cell lung cancer: A meta-analysis of the published literature. *J Clin Oncol* 23:2926-2936, 2005
20. Pujol JL, Barlesi F, Daures JP: Should chemotherapy combinations for advanced non-small cell lung cancer be platinum-based? A meta-analysis of phase III randomized trials. *Lung Cancer* 51:335-345, 2006
21. Sculier JP, Lafitte JJ, Lecomte J, et al: A phase III randomised trial comparing sequential chemotherapy using cisplatin-based regimen and paclitaxel to cisplatin-based chemotherapy alone in advanced non-small-cell lung cancer. *Ann Oncol* 18:1037-1042, 2007
22. Belani CP, Ramalingam S, Perry MC, et al: Randomized, phase III study of weekly paclitaxel in combination with carboplatin versus standard every-3-weeks administration of carboplatin and paclitaxel for patients with previously untreated advanced non-small-cell lung cancer. *J Clin Oncol* 26:468-473, 2008
23. Scagliotti GV, Parikh P, von Pawel J, et al: Phase III study comparing cisplatin plus gemcitabine with cisplatin plus pemetrexed in chemotherapy-naïve patients with advanced-stage non-small-cell lung cancer. *J Clin Oncol* 26:3543-3551, 2008
24. Gridelli C: The ELVIS trial: A phase III study of single-agent vinorelbine as first-line treatment in elderly patients with advanced non-small cell lung cancer—Elderly Lung Cancer Vinorelbine Italian Study. *Oncologist* 6:4-7, 2001 (suppl 1)
25. Gridelli C, Langer C, Maione P, et al: Lung cancer in the elderly. *J Clin Oncol* 25:1898-1907, 2007 Azzoli et al
26. Pallis AG, Polyzos A, Boukovinas I, et al: Pooled analysis of elderly patients with non-small cell lung cancer treated with front line docetaxel/ gemcitabine regimen: The Hellenic Oncology Research Group experience. *J Thorac Oncol* 3:505-510, 2008
27. Jiang J, Liang X, Zhou X, et al: A metaanalysis of randomized controlled trials comparing carboplatin-based to cisplatin-based chemotherapy in advanced non-small cell lung cancer. *Lung Cancer* 57:348-358, 2007
28. Belani CP, Pereira JR, von Pawel J, et al: Effect of chemotherapy for advanced non-small cell lung cancer on patients' quality of life: A randomized controlled trial. *Lung Cancer* 53:231-239, 2006
29. Fidias PM, Dakhil SR, Lyss AP, et al: Phase III study of immediate compared with delayed docetaxel after front-line therapy with gemcitabine plus carboplatin in advanced non-small-cell lung cancer. *J Clin Oncol* 27:591-598, 2009
30. Ciuleanu T, Brodowicz T, Belani CP, et al: Maintenance pemetrexed plus best supportive care (BSC) versus placebo plus BSC: A phase III study. *J Clin Oncol* 26:426s, 2008 (suppl; abstr 8011)

References

31. Herbst RS, Prager D, Hermann R, et al: TRIBUTE: A phase III trial of erlotinib hydrochloride (OSI-774) combined with carboplatin and paclitaxel chemotherapy in advanced non–small-cell lung cancer. *J Clin Oncol* 23:5892-5899, 2005
32. Gatzemeier U, Pluzanska A, Szczesna A, et al: Phase III study of erlotinib in combination with cisplatin and gemcitabine in advanced non–smallcell lung cancer: The Tarceva Lung Cancer Investigation Trial. *J Clin Oncol* 25:1545-1552, 2007
33. Mok TS, Wu YL, Thongprasert S, et al: Gefitinib or carboplatin-paclitaxel in pulmonary adenocarcinoma. *N Engl J Med* 361:947-957, 2009
34. Pirker R, Pereira JR, Szczesna A, et al: Cetuximab plus chemotherapy in patients with advanced non-small-cell lung cancer (FLEX): An open-label randomised phase III trial. *Lancet* 373:1525-1531, 2009
35. Scagliotti G, Hanna N, Fossella F, et al: The differential efficacy of pemetrexed according to NSCLC histology: A review of two phase III studies. *Oncologist* 14:253-263, 2009
36. Yang CH, Shih JY, Chen KC, et al: Survival outcome and predictors of gefitinib antitumor activity in East Asian chemo-naïve patients with advanced nonsmall cell lung cancer. *Cancer* 107:1873-1882, 2006
37. Eberhard DA, Johnson BE, Amler LC, et al: Mutations in the epidermal growth factor receptor and in KRAS are predictive and prognostic indicators in patients with non–small-cell lung cancer treated with chemotherapy alone and in combination with erlotinib. *J Clin Oncol* 23:5900-5909, 2005
38. Harrington SE, Smith TJ: The role of chemotherapy at the end of life: “When is enough, enough?” *JAMA* 299:2667-2678, 2008
39. Curran WJ et al. Sequential vs concurrent chemoradiation for stage III non-small cell lung cancer: a randomized phase III trial RTOG 9410. *J Natl Cancer Inst.* 2011;103:1452-1460
40. Sequist LV, Yang JC et al. Phase III study of afatinib or cisplatin plus pemetrexed in patients with metastatic lung adenocarcinoma with EGFR mutations. *J Clin Oncol* 2013;31:3327-3334.
41. Shaw AT et al. Ceritinib in ALK-rearranged non-small-cell lung cancer. *N Engl J Med* 2014;370:1189-1197
42. Soria JC, Ohe Y, Vansteenkiste J, et al. Osimertinib in untreated EGFR-mutated advanced non-small-cell lung cancer. *N Engl J Med* 2018;378:113-125.
43. Ramalingam SS, Yang JC, Lee CK, et al. Osimertinib as first-line treatment for EGFR mutation positive advanced non-small cell lung cancer. *J Clin Oncol* 2018;36:841-849.
44. Horn L, Spigel DR, Vokes EE, et al. Nivolumab versus docetaxel in previously treated patients with advanced non-small-cell lung cancer: two-year outcomes from two randomized, open-label, phase III trials (CheckMate 017 and CheckMate 057). *J Clin Oncol* 2017;35:3924-3933.
45. Browning ET, Weickhardt AJ, Camidge DR. Response to crizotinib rechallenge after initial progression and intervening chemotherapy in ALK lung cancer. *J Thorac Oncol* 2013;8:e21.
46. Larkins E, Scepura B, Blumenthal GM, et al. U.S. Food and Drug Administration Approval Summary: ramucirumab for the treatment of metastatic non-small cell lung cancer following disease progression on or after platinum-based chemotherapy. *Oncologist* 2015;20:1320-1325

References

47. Garon EB, Rizvi NA, Hui R, et al. Pembrolizumab for the treatment of non-small-cell lung cancer. *N Engl J Med* 2015;372:2018-2028.
48. Rittmeyer A, Barlesi F, Waterkamp D, et al. Atezolizumab versus docetaxel in patients with previously treated non-small-cell lung cancer (OAK): a phase 3, open-label, multicentre randomised controlled trial. *Lancet* 2017;389:255-265.
49. Langer CJ, et al. Carboplatin and pemetrexed with or without pembrolizumab for advanced, non-squamous non-small-cell lung cancer: a randomised, phase 2 cohort of the open-label KEYNOTE-021 study. *The Lancet Oncology*. 2016;17:1497-1508.
50. Gandhi L, Rodriguez-Abreu D, Gadgeel S, et al. Pembrolizumab plus chemotherapy in metastatic non-small-cell lung cancer. *N Engl J Med* 2018;378:2078-2092.
51. Barlesi F, Scherpereel A, Gorbunova V, et al. Maintenance bevacizumab-pemetrexed after first-line cisplatin-pemetrexed-bevacizumab for advanced nonsquamous non-small-cell lung cancer: updated survival analysis of the AVAPERL (MO22089) randomized phase III trial. *Ann Oncol* 2014;25:1044-1052.
52. Peters S, Camidge DR, Shaw AT et al. Alectinib versus crizotinib in untreated ALK-positive non-small cell lung cancer. *N Engl J Med* 2017;377:829-838.
53. Borghaei H, Paz-Ares L, Horn L, et al. Nivolumab versus docetaxel in advanced nonsquamous non-small-cell lung cancer. *N Engl J Med* 2015;373:1627-1639.
54. Soria JC, Tan DS, Chiari R, et al. First-line ceritinib versus platinum-based chemotherapy in advanced ALK-rearranged non-small-cell lung cancer (ASCEND-4): a randomised, open-label, phase 3 study. *Lancet* 2017;389:917-929.
55. Antonia SJ, Villegas A, Daniel D, et al. Durvalumab after chemoradiotherapy in stage III non-small-cell lung cancer. *N Engl J Med* 2017;377:1919-1929.
56. Kato H, Ichinose Y, Ohta M et al. A randomized trial of adjuvant chemotherapy with uracil-tegafur for denocarcinoma of the lung. *N Engl J Med* 2004, Apr 22;350(17):1713-21
57. Arriagada R, Bergman B, Dunant A, et al. The International Adjuvant Lung^aWinton T, Livingston R, Johnson D, et al. Vinorelbine plus cisplatin Cancer Trial Collaborative Group. Cisplatin-based adjuvant chemotherapy in patients with completely resected non-small cell lung cancer. *N Engl J Med* 2004;350:351-360.
58. Douillard JY, Rosell R, De Lena M, et al. Adjuvant vinorelbine plus cisplatin versus observation in patients with completely resected stage IB-III A non-small-cell lung cancer (Adjuvant Navelbine International Trialist Association [ANITA]): a randomised controlled trial. *Lancet Oncol* 2006;7:719-727
59. Strauss GM, Herndon III JE, Maddaus MA, et al. Adjuvant paclitaxel plus carboplatin compared with observation in stage IB non-small cell lung cancer: CALGB 9633 with the Cancer and Leukemia Group B, Radiation Therapy Oncology Group, and North Central Cancer Treatment Group Study Groups. *J Clin Oncol* 2008;26:5043- 5051.

References

60. Usami N, Yokoi K, Hasegawa Y, et al. Phase II study of carboplatin and gemcitabine as adjuvant chemotherapy in patients with completely resected non-small cell lung cancer: a report from the Central Japan Lung Study Group, CJLSG 0503 trial. *Int J Clin Oncol* 2010;15:583-587.
61. Zhang L, Ou W, Liu Q, et al. Pemetrexed plus carboplatin as adjuvant chemotherapy in patients with curative resected non-squamous non-small cell lung cancer. *Thorac Cancer* 2014;5:50-56.
62. Albain KS, Crowley JJ, Turrisi AT III, et al. Concurrent cisplatin, etoposide, and chest radiotherapy in pathologic stage IIIB non-small-cell lung cancer: A Southwest Oncology Group Phase II Study, SWOG 9019. *J Clin Oncol* 2002;20:3454-3460.
63. Govindan R, Bogart J, Stinchcombe T, et al. Randomized phase II study of pemetrexed, carboplatin, and thoracic radiation with or without cetuximab in patients with locally advanced unresectable non-small-cell lung cancer: Cancer and Leukemia Group B trial 30407. *J Clin Oncol* 2011;29:3120-3125.
64. Bradley JD, Paulus R, Komaki R, et al. Standard-dose versus high-dose conformal radiotherapy with concurrent and consolidation carboplatin plus paclitaxel with or without cetuximab for patients with stage IIIA or IIIB non-small-cell lung cancer (RTOG 0617): a randomised, two-by-two factorial phase 3 study. *Lancet Oncol* 2015;16:187-199.
65. Okamoto I., Yoshioka H., Morita S., Ando M., Takeda K., Seto T., et al. (2010) Phase III trial comparing oral S-1 plus carboplatin with paclitaxel plus carboplatin in chemotherapy-naïve patients with advanced non-small-cell lung cancer: results of a West Japan Oncology Group study. *J Clin Oncol* 28: 5240–5246
66. Camidge DR, Tiseo M, Ahn M-J, et al. P3.02a-013 Brigatinib in crizotinib-refractory ALK+ NSCLC: central assessment and updates from ALTA, a pivotal randomized phase 2 trial [abstract]. *J Thorac Oncol* 2017;12:S1167–S1169.
67. Larkins E, Scepura B, Blumenthal GM, et al. U.S. Food and Drug Administration Approval Summary: Ramucirumab for the Treatment of Metastatic Non-Small Cell Lung Cancer Following Disease Progression On or After Platinum-Based Chemotherapy. *Oncologist* 2015;20:1320-1325.
68. Ramalingam SS, Reungwetwattana T, Chewaskulyong B, et al. Osimertinib versus standard-of-care EGFR-TKI as first-line treatment in patients with EGFRm advanced NSCLC: FLAURA [abstract] [abstract]. Presented at the ESMO Congress; Madrid. Abstract LBA2_PR
69. Wu YL, Yang JC, Kim DW, et al. Phase II Study of Crizotinib in East Asian Patients With ROS1-Positive Advanced Non-Small-Cell Lung Cancer. *J Clin Oncol* 2018;36:1405-1411.