臺北榮總肺癌診療共識

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臺北榮總胸腔腫瘤團隊

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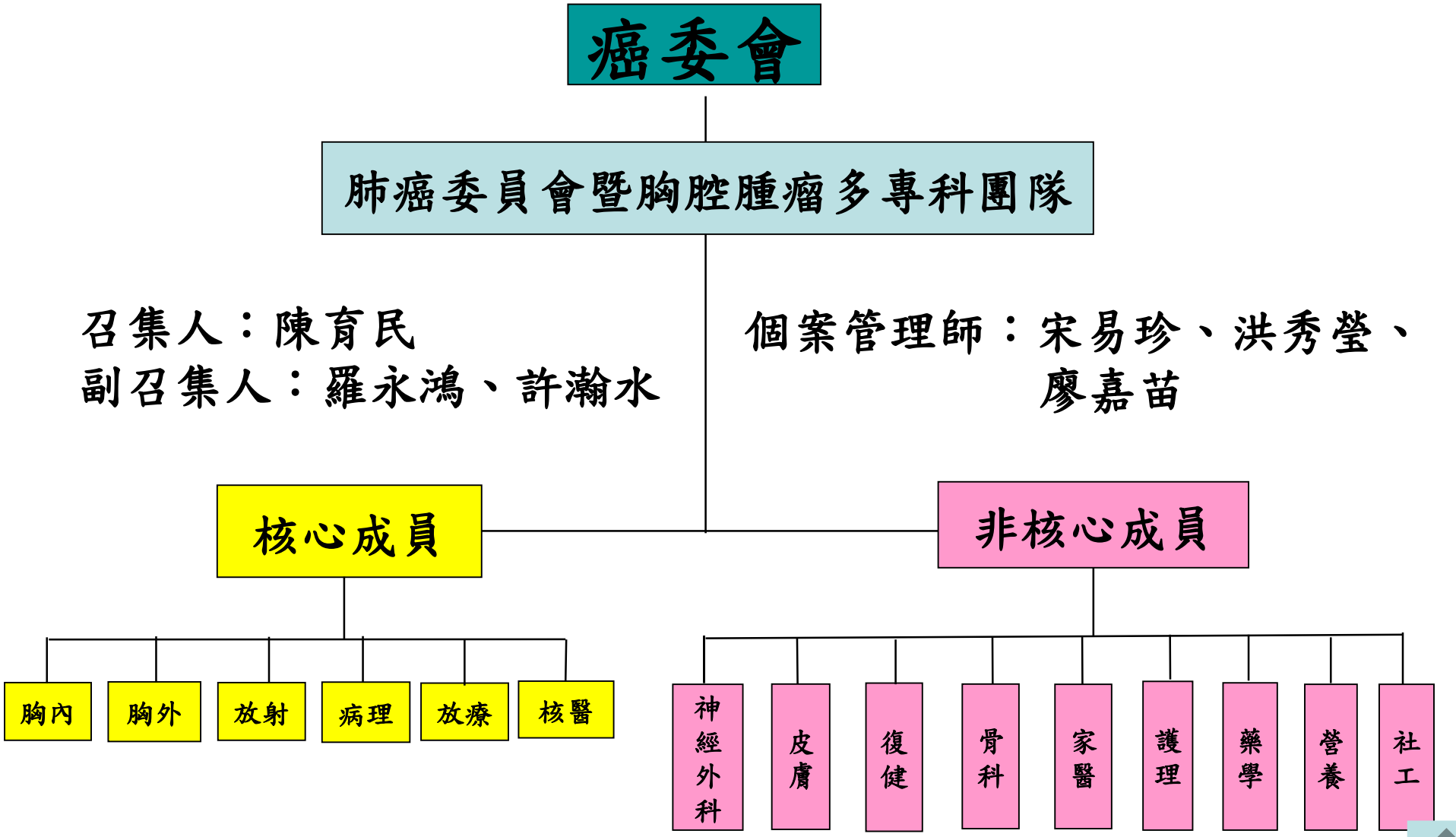
臺北榮總肺癌診療共識

- Multidisciplinary Team
- Taipei VGH Lung Cancer Panel Members
- TNM staging
  - Taipei VGH supplement to TNM staging
  - Table of stage grouping
- Evaluation and treatment
  - Stage o (Tis)
  - Stage I (T1abc-2a, N0), Stage II (T1abc-2abc, N1; T2b, N0), Stage IIB (T3, N0), and Stage IIIA (T3, N1)
  - Stage IIB (T3 invasion, N0) and Stage IIIA (T4 extension, N0-1; T3, N1)
  - Stage IIIA (T1-2, N2); Stage IIIB (T3, N2); Separate Pulmonary Nodules (Stage IIB, IIIA, IV)
  - Multiple Lung Cancers
  - Stage IIIB (T1-2, N3); Stage IIIC (T3, N3)
  - Stage IIIB (T4, N2); Stage IIIC (T4N3); Stage IVA, M1a: Pleural or Pericardial effusion
  - Stage IVA, M1b: Limited Sites
- Surveillance
- Therapy for Recurrence and Metastases
- Principles of Pathology
- Principles of Surgical Resection
- Principles of Radiation Therapy
  - Recommended Radiation Doses
  - Dose Volume Data for Radiation Pneumonitis
- Principles of CCRT
- Principles of Chemotherapy
  - Non-Small Cell Lung Cancer
  - Small Cell Lung Cancer
- Adjuvant Chemotherapy
- Neoadjuvant Chemotherapy
- Clinical Trials for Advanced/ Metastatic NSCLC
- Tracheal cancer
- References
- 關於此臨床指引：肺癌的診療仍在發展階段，本指引主要在呈現目前肺癌診療的進展與共識，醫師應鼓勵病患參與臨床試驗，使其有機會得到最好的治療。在本指引中的化療用藥建議是基於現有的臨床證據，和目前的衛服部或健保署規定無關。

臺北榮總肺癌委員會暨胸腔腫瘤多專科團隊組織架構



臺北榮總胸腔腫瘤多專科團隊核心人員

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NSCLC &SCLC TNM Staging (AJCC 8th edition)

T Category	T Criteria
TX	Primary tumor cannot be assessed, or tumor proven by the presence of malignant cells in sputum or bronchial washings but not visualized by imaging or bronchoscopy
T0	No evidence of primary tumor
Tis	Carcinoma *in situ* Squamous cell carcinoma *in situ* (SCIS) Adenocarcinoma *in situ* (AIS): adenocarcinoma with pure lepidic pattern, ≤3 cm in greatest dimension
T1	Tumor ≤3 cm in greatest dimension, surrounded by lung or visceral pleura, without bronchoscopic evidence of invasion more proximal than the lobar bronchus (i.e., not in the main bronchus)
T1mi	Minimally invasive adenocarcinoma: adenocarcinoma (≤3 cm in greatest dimension) with a predominantly lepidic pattern and ≤5 mm invasion in greatest dimension
T1a	Tumor ≤1 cm in greatest dimension. A superficial, spreading tumor of any size whose invasive component is limited to the bronchial wall and may extend proximal to the main bronchus also is classified as T1a, but these tumors are uncommon.
T1b	Tumor >1 cm but ≤2 cm in greatest dimension
T1c	Tumor >2 cm but ≤3 cm in greatest dimension
T2	Tumor >3 cm but ≤5 cm or having any of the following features: • Involves the main bronchus regardless of distance to the carina, but without involvement of the carina • Invades visceral pleura (PL1 or PL2) • Associated with atelectasis or obstructive pneumonitis that extends to the hilar region, involving part or all of the lung T2 tumors with these features are classified as T2a if ≤4 cm or if the size cannot be determined and T2b if >4 cm but ≤5 cm.
T2a	Tumor >3 cm but ≤4 cm in greatest dimension
T2b	Tumor >4 cm but ≤5 cm in greatest dimension
T3	Tumor >5 cm but ≤7 cm in greatest dimension or directly invading any of the following: parietal pleura (PL3), chest wall (including superior sulcus tumors), phrenic nerve, parietal pericardium; or separate tumor nodule(s) in the same lobe as the primary
T4	Tumor >7 cm or tumor of any size invading one or more of the following: diaphragm, mediastinum, heart, great vessels, trachea, recurrent laryngeal nerve, esophagus, vertebral body, or carina; separate tumor nodule(s) in an ipsilateral lobe different from that of the primary

*** MX has been removed by a general rule from UICC/AJCC.**

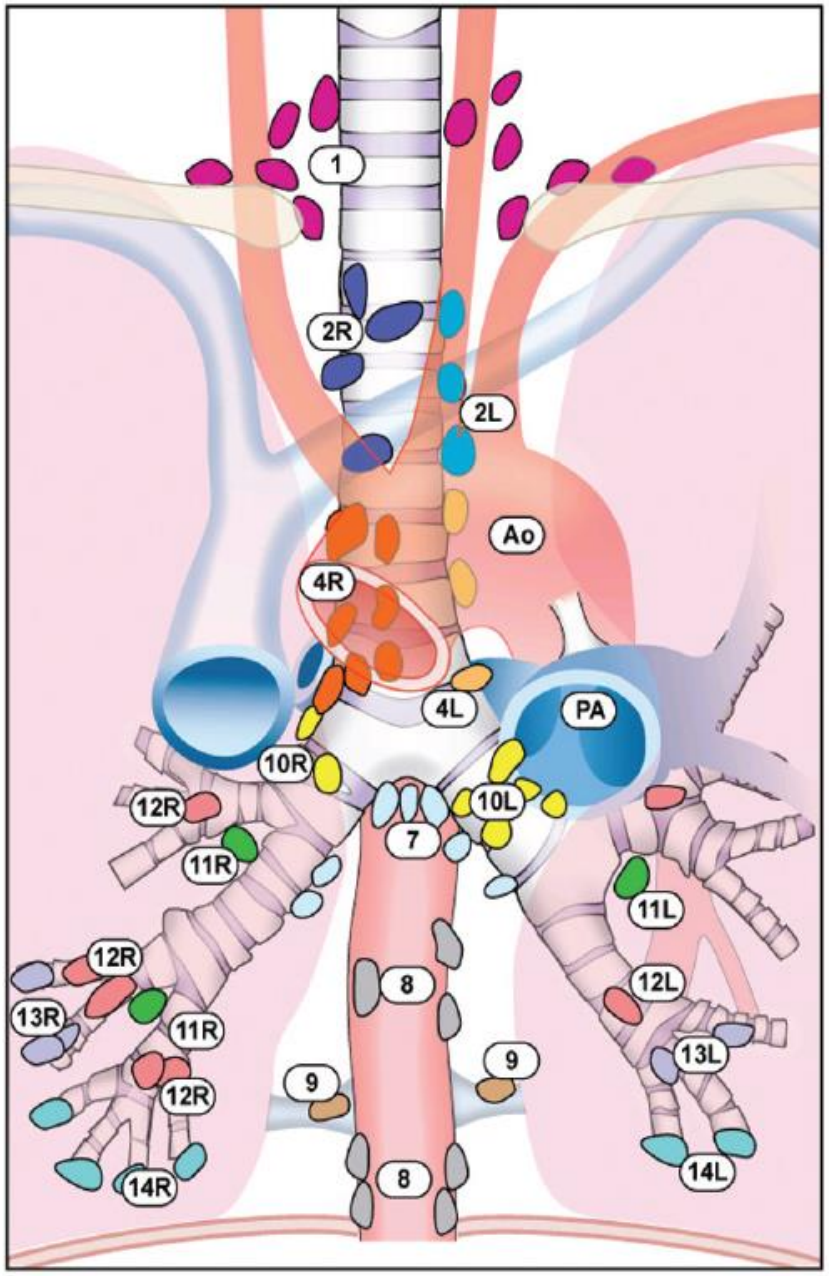
Lung Cancer

N Category	N Criteria
NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis in ipsilateral peribronchial and/or ipsilateral hilar lymph nodes and intrapulmonary nodes, including involvement by direct extension
N2	Metastasis in ipsilateral mediastinal and/or subcarinal lymph node(s)
N3	Metastasis in contralateral mediastinal, contralateral hilar, ipsilateral or contralateral scalene, or supraclavicular lymph node(s)

M Category	M Criteria
M0	No distant metastasis
M1	Distant metastasis
M1a	Separate tumor nodule(s) in a contralateral lobe; tumor with pleural or pericardial nodules or malignant pleural or pericardial effusion. Most pleural (pericardial) effusions with lung cancer are a result of the tumor. In a few patients, however, multiple microscopic examinations of pleural (pericardial) fluid are negative for tumor, and the fluid is nonbloody and not an exudate. If these elements and clinical judgment dictate that the effusion is not related to the tumor, the effusion should be excluded as a staging descriptor.
M1b	Single extrathoracic metastasis in a single organ (including involvement of a single nonregional node)
M1c	Multiple extrathoracic metastases in a single organ or in multiple organs

	N0	N1	N2	N3	M1a any N	M1b any N	M1c any N
T1a	IA1	IIB	IIIA	IIIB	IVA	IVA	IVB
T1b	IA2	IIB	IIIA	IIIB	IVA	IVA	IVB
T1c	IA3	IIB	IIIA	IIIB	IVA	IVA	IVB
T2a	IB	IIB	IIIA	IIIB	IVA	IVA	IVB
T2b	IIA	IIB	IIIA	IIIB	IVA	IVA	IVB
T3	IIB	IIIA	IIIB	IIIC	IVA	IVA	IVB
T4	IIIA	IIIA	IIIB	IIIC	IVA	IVA	IVB

Lung Cancer



Supraclavicular zone

- 1 Low cervical, supraclavicular, and sternal notch nodes

SUPERIOR MEDIASTINAL NODES

Upper zone

- 2R Upper Paratracheal (right)
- 2L Upper Paratracheal (left)
- 3a Prevascular
- 3p Retrotracheal
- 4R Lower Paratracheal (right)
- 4L Lower Paratracheal (left)

AORTIC NODES

AP zone

- 5 Subaortic
- 6 Para-aortic (ascending aorta or phrenic)

INFERIOR MEDIASTINAL NODES

Subcarinal zone

- 7 Subcarinal

Lower zone

- 8 Paraesophageal (below carina)
- 9 Pulmonary ligament

N1 NODES

Hilar/Interlobar zone

- 10 Hilar
- 11 Interlobar

Peripheral zone

- 12 Lobar
- 13 Segmental
- 14 Subsegmental

Summary of Evaluation and Treatment

- **PFT: 1.Necessary for all operable stages**

  2.胸腔腫瘤放射治療，於轉介放射腫瘤科之前,常規性安排肺功能檢查(Spirometry 及 DLCO)

- **PET (PET/CT) : recommend for all clinical stages, except**
  - Non-operable stage IV
- **Mediastinoscopy: recommend for all clinical stages, except**
  - Peripheral stage IA and non-operable stage IV

    p.s. N2 or N3 disease can be confirmed by methods including mediastinotomy, thoracoscopy, EBUS-FNA, EUS-FNA, CT-guided-FNA, supraclavicle LN biopsy
- **Brain MRI: recommend for all clinical stages, except**
  - Stage IA, Stage IB (options)
- **Pre-operative diagnosis**
  - It may not be necessary for those with high probability of malignancy and surgical resection is feasible. Intra-operative histological examination can be considered.

Diagnostic Imaging

- **For incidental nodules detected on CT, the diagnostic algorithm updated based on accordance of Fleischner criteria (2017).**
- **For lung cancer screening detected nodules, the guideline were based on LUNG-RADS v 1.1 (2019).**
- **Brain MRI with contrast**
  - For stage IVA, M1a, pretreatment evaluation.
  - Clarified with “Brain MRI with contrast” to recurrence after completion of definitive therapy.

2024

偶然發現之大於8毫米之實質性結節或實質性部分大於或等於六毫米的部分實質性結節處理流程：

- 考慮於三個月時追蹤電腦斷層或FDG-PET/CT或切片。
- 如考慮FDG-PET/CT呈偽陰性是因腫瘤活性低及/或疑細胞少，電腦斷層追蹤或是切片是合理的選項

偶然發現之大於8毫米之實質性結節或實質性部分大於或等於六毫米的部分實質性結節處理流程：

於治療前，需

多專科(包含治療的主治醫師以及取得診斷組織的專家(胸腔外科、介入胸腔科、介入放射科)評估較安全及較有效的切片方式

或

經共識為切片為高風險或高困難而肺癌的臨床診斷為適切而治療為合理。

Follow up for incidental finding: solid nodules on chest CT > 8 mm (DIAG-2) or the solid component of a part-solid nodule >=6 mm (DIAG-3)：

Prior to treatment, multidisciplinary evaluation that includes treating physicians and specialists in obtaining tissue diagnosis (thoracic surgery, interventional pulmonology, and interventional radiology) is required to determine the safest and most efficient approach for biopsy, or to provide consensus that a biopsy is too risky or difficult, that a clinical diagnosis of lung cancer is appropriate, and that treatment is warranted.

診斷評估原則

- 風險評估包含影像特徵(含與舊片比較及如有PET/CT者納入評估)、居住於感染症流行區域。
- 臨床強烈懷疑IA期肺癌(基於危險因子及影像學特徵)者手術前不需切片
- 手術前切片對臨床分期IB或以上且為潛在可接受系統性治療者、進行術中診斷困難者、接受SABR治療前建立診斷者可能合理。。

治療前評估

Stage IA, peripheral T1abc, negative mediastinal lymph nodes者

- 經胸腔外科醫師認定為病灶無法手術或手術高風險***或病患諮詢胸腔外科後拒手術者***考慮RT(SABR)，而影像導引消融(IGTA)為另一選項。

診斷評估原則

對於疑似I至III期肺癌者

- 優化診斷步驟應由投入顯著臨床工作時間於胸腔腫瘤疾病的胸腔放射科、介入放射科、胸腔外科及胸腔內科醫師決定。多專科評估亦應包括胸腔外科或胸腔內科精於進階支氣管鏡技術的專家。

多發性肺癌(疑似或確診)(且N0-1)者

- 經多專科評估流程
- 處理方式的分類依據去除症狀相關因素並改為主要根據
  - 穩定病灶或非常慢速成長病灶者→ Observation
  - Dominant結節且有成長徵象者分成下列兩種：
    - 可Definitive local therapy者→肺實質保留之切除(優先)或放射治療或影像導引消融
    - 無法Definite local therapy者→Palliative chemotherapy +- local palliative therapy
      或
      觀察

EGFR EXON 19 缺失或 EXON 21 L858R 突變者

- **In patients with symptomatic systemic limited progression on osimertinib, IGTA may be an option for select patients**

NSCLC 診斷治療流程

Required:
- Detail H&P, baseline lab (CBC/DC, chemistry, etc.)
- Chest CT scan
- Brain Image (CT or MRI)
- either Bone scan or PET-CT

Optional:
- PFT
- Bronchoscopy
- Thoracic sonography
- Thoracentesis
- Pathologic mediastinal lymph node evaluation (mediastinoscopy, mediastinotomy, EBUS, etc.)

→

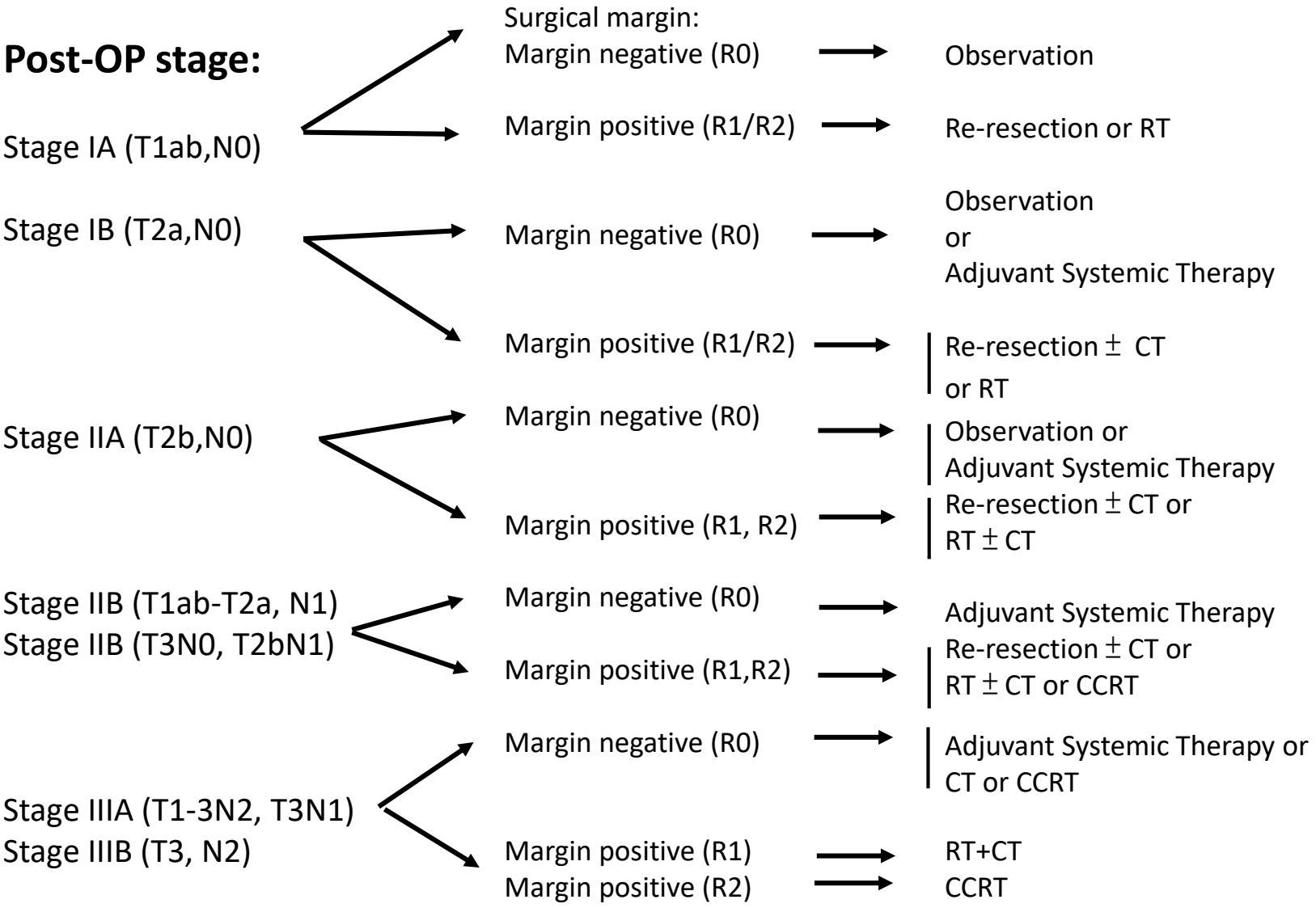
Clinical stage:

Stage IA (T1ab**c**, N0) →
Operation
or
Definitive RT preferably SABR (if medically inoperable surgical risk as determined by thoracic surgeon, and those who decline surgery after thoracic surgical consultation)

Stage IB (T2a,N0)
Stage IIA (T2b,N0)
Stage IIA (T1-2a, N1)
Stage IIB (T3, N0)
Stage IIIA (T3, N1) →
Operation ± adjuvant CT (for high-risk stage IB-IIIA*) followed by atezolizumab or pembrolizumab or TKI (Osimertinib or Alectinib)
or
Neoadjuvant Nivo or Pemb + chemo for tumor >4cm (IB-IIIA)
or
Definitive RT/SABR (if medically inoperable) + adjuvant CT (for high risk stage IB-IIIA*)
or
Definitive CCRT (for N1 disease)
± Durvalumab if non-PD after CCRT

- *High risk factors: poorly-differentiated tumors, neuroendocrine tumors, vascular invasion, wedge resection, visceral pleural invasion, Unknown lymph node status(Nx), pulmonary adenocarcinoma with a micropapillary/solid–predominant pattern
- Neoadjuvnt Pembro or Nivo is not reimbursed by NHI
- Adjuvant Pembro or Nivo or Osimertinib or Alectinib is not reimbursed by NHI

NSCLC 診斷治療流程



Adjuvant Treatment 請參閱 Regimens for Adjuvant Therapy

NSCLC 診斷治療流程

Required:
- Detail H&P, baseline lab (CBC/DC, chemistry, etc.)
- Chest CT scan
- Brain Image (CT or MRI)
- Either bone scan or PET-CT

Optional:
- PFT
- PET-CT
- Bronchoscopy
- Thoracic sonography
- Thoracentesis
- Pathologic mediastinal lymph node evaluation (mediastinoscopy, mediastinotomy, EBUS, etc.)

Clinical stage:

Superior sulcus tumor Stage IIB (T3-invasion, N0) Stage IIIA (T4 extension, N0-1, T3N1) → Pre-OP CCRT/CT/RT, then re-evaluation; OP + Adjuvant Systemic Therapy or definitive CCRT (IIIA unresectable) ± Durvalumab/if non-PD after CCRT

Chest wall, trachea / carina, or mediastinum, Stage IIB-IIIA (T3 invasion N0-1) (T4, N0-1 resectable) → OP first or Pre-OP CCRT/CT, then: OP (if resectable) + Adjuvant Systemic Therapy (R0 resection) or CCRT (R1,R2 resection) or definitive CCRT (if unresectable) ± Durvalumab if non-PD after CCRT

Stage IIIA (T4, N0-1 unresectable) Stage IIIBC, unresectable (T1-4 N3) → CCRT or CT or RT (according to patient's condition); then consider maintenance CT ± Durvalumab if non-PD after CCRT

Stage III建議多專科團隊會議論，Adjuvant Treatment 請參閱 Regimens for Adjuvant Therapy
Durvalumab is not reimbursed by NHI

NSCLC 診斷治療流程

Required:
- Detail H&P, baseline lab (CBC/DC, chemistry, etc.)
- Chest CT scan
- Brain Image (CT or MRI)
- Bone scan

Optional:
- PFT
- Bronchoscopy
- Thoracic sonography
- Thoracentesis
- Bone scan
- Pathologic mediastinal lymph node evaluation (mediastinoscopy, mediastinotomy, EBUS, etc.)

Clinical stage:

Stage IIIA
(T1-3 N2)
(T3 invasive N2)
→ Definitive CCRT ± Durvalumab
or
Systemic therapyp,y ± RT

Stage IIIB
(T1-2 N3)
Stage IIIC
(T3 N3)

Stage IIIB
(T4 N0-2)
Stage IIIC
(T4 N3)
→ Definitive CCRT ± Durvalumab

Stage III建議多專科團隊會議論，Neoadjuvant Treatment 請參閱 Regimens for Neoadjuvant Therapy; Adjuvant Treatment 請參閱 Regimens for Adjuvant Therapy
Durvalumab are not covered by the national health insurance.

NSCLC 診斷治療流程

Required:
- Detail H&P, baseline lab (CBC/DC, chemistry, etc.)
- Chest CT scan
- Brain Image (CT or MRI)
- Bone scan

Optional:
- PFT
- PET-CT
- Bronchoscopy
- Thoracic sonography
- Thoracentesis
- Pathologic mediastinal lymph node evaluation (mediastinoscopy, mediastinotomy, EBUS, etc.)

Clinical stage:

Separate pulmonary nodules, T3, N0-1 or T4, N0-1 → Neoadjuvant treatment or not, then OP+LND if operable, then consider:
If pN0-1: adjuvant systemic therapy
If pN2, R0 resection: adjuvant systemic therapy or Sequential chemotherapy + Consider RT
If pN2, R1 resection: SCRT or CCRT
If pN2, R2 resection: CCRT

Stage IV, contralateral nodules, N0, M1a → Treat as two primary lung tumors if both curable

Suspected multiple lung cancers (based on the presence of biopsy proven synchronous lesions or history of lung cancer) → Observation (if Stable or very slow-growing disease)
or definitive local therapy if possible (parenchymal sparing resection or RT or Ablation)
or palliative CT ± local therapy if definitive local therapy not possible

NSCLC 診斷治療流程

Required:
- Detail H&P, baseline lab (CBC/DC, chemistry, etc.)
- Chest CT scan
- Brain Image (CT or MRI)
- Bone scan

Optional:
- PFT
- PET-CT
- Bronchoscopy
- Thoracic sonography
- Thoracentesis
- Pathologic mediastinal lymph node evaluation (mediastinoscopy, mediastinotomy, EBUS, etc.)

→ Clinical stage:

→ Stage IV-M1b, limited sites, potentially resectable

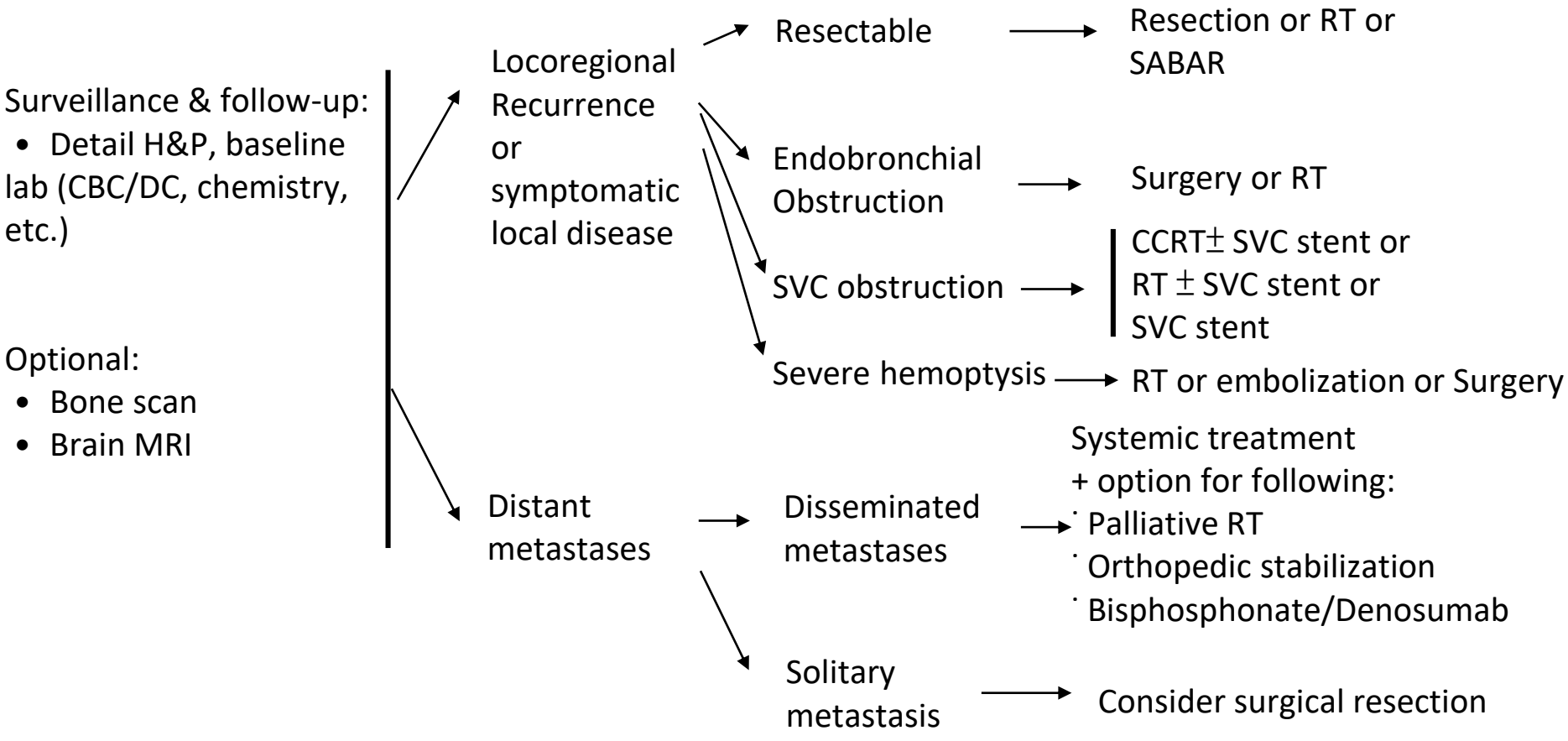
Brain mets+ →

If medically operable:
Stereotactic radiosurgery (SRS) alone
or Surgical resection, if symptomatic or warranted for diagnosis, followed by SRS or whole brain RT (WBRT)
then consider lung OP or SABR ± adjuvant CT/RT

→ Stage IV-M1b, limited sites, unresectable or medically inoperable →

Systemic Therapy for Metastatic Disease

NSCLC surveillance



Advanced NSCLC 診斷治療流程

Required:
- Detail H&P, baseline lab (CBC/DC, chemistry, etc.)
- Chest CT scan
- Brain Image (CT or MRI)
- Bone scan

Optional:
- PFT
- PET-CT
- Bronchoscopy
- EBUS
- Thoracic sonography
- Thoracentesis

→ Histologic subtype:

- Adenocarcinoma
- Large cell
- NSCLC not otherwise specified (NOS)

→ -Molecular testing:
- Next Generation Sequencing
- EGFR mutation
- ALK testing
- ROS1 testing
- BRAF, METex14 skipping, RET, KRAS, NTRK1/2/3 , ERBB2 ,HER2

-PD-L1 testing

→ Squamous cell carcinoma →

-Consider Molecular testing (Optional):
- EGFR, ALK, ROS1
- BRAF, METex14 skipping, RET, KRAS, NTRK1/2/3 , ERBB2 ,HER2

-PD-L1 testing

Next Generation Sequencing is partial reimbursed by NHI if EGFR(-)

EGFR mutation positive metastatic NSCLC

EGFR m+ known before 1st line CT →

First line therapy:

- Osimertinib*
- Osimertinib + pemetrexed + (cisplatin or carboplatin
- Afatinib (preferred if S768I, L861Q, and/ or G719X mutations)
- Gefitinib
- Erlotinib +/- Bevacizumab / Ramucirumab
- Dacomitinib

→ PD (Asymptomatic or Limited Progression) → Consider local therapy (SABR or surgery) and continue EGFR-TKI or 2nd line therapy (see below)

EGFR m+ known during 1st line CT → Interrupt or complete planned CT, followed by EGFR TKI → PD (Multiple lesions) →

2nd line therapy:

- Osimertinib* (if T790M+, preferred)
- Systemic therapy
- BSC (if PS 3-4)

*Osimertinib first line use is conditionally reimbursed by NHI.
*Osimertinib + Chemotherapy are not covered by the NHI
*ramucirumab are not covered by the NHI.

EGFR exon 20 insertion mutation positive metastatic NSCLC

First line therapy:

EGFR exon 20 insertion mutation positive →

- ● Systemic therapy → PD → Amivantamab or systemic treatment

or

- ● Amivantamab-vmjw + carboplatin/ pemetrexedqq (nonsquamous) → PD → systemic treatment

*Amivantamab is not reimbursed by NHI.

ALK rearrangement positive metastatic NSCLC

ALK rearrangement (+):

First line therapy:

- Alectinib
- Brigatinib
- Lorlatinib
- Ceritinib
- Crizotinib

→ PD (Brain or limited progression) → Consider local therapy (SABR or surgery) and continue ALK-TKI

or 2nd line therapy (see below)

→ PD (Multiple lesions) → 2nd line therapy:

- Ceritinib, Alectinib, Brigatinib (if 1st line Crizotinib)
- Lorlatinib (if not previously given)
- Systemic therapy
- BSC (if PS 3-4)

NSCL-25

KRAS G12C mutation positive metastatic NSCLC

KRAS G12C mutation (+) → **First line therapy:**
- Systemic therapy

PD →

2nd line therapy:
- Sotorasib or Adagrasib
- Systemic treatment
- BSC (if PS 3-4)

* Sotorasib is not reimbursed by NHI.
* Adagrasib is not approved by TFDA.

ROS1 rearrangement positive metastatic NSCLC

ROS1 rearrangement (+) →

First line therapy:
- Crizotinib
- Entrectinib
- Repotrectinib
- Ceritinib

PD →

2nd line therapy:
- Entrectinib (if previously treated with crizotinib or ceritinib) or lorlatinib (if not previously given)
- Systemic therapy
- BSC (if PS 3-4)

* Treatment with ceritinib, lorlatinib, repotrectinib for ROS-1 is not approved by TFDA.

BRAF mutation positive metastatic NSCLC

BRAF V600E mutation (+) →

First line therapy:
- Dabrafenib+Trametinib
- Encorafenib+binimetinib
- Dabrafenib
- Vemurafenib
- Systemic Therapy

PD →

2nd line therapy:
- Dabrafenib + trametinib or Encorafenib + binimetinib if not used
- Systemic Therapy
- BSC (if PS 3-4)

- First-line treatment with Dabrafenib + Trametinib is not covered by the NHI(健保目前給付於一線含鉑類化療失敗病患)
- Vemurafenib, Encorafenib, Binimetinib are not approved by TFDA for the treatment of NSCLC yet .

NTRK fusion positive metastatic NSCLC

NTRK fusion (+) → **First line therapy**:
- Larotrectinib
- Entrectinib
- Systemic Therapy

→ PD →

2nd line therapy:
- Larotrectinib or Entrectinib if not previously used
- Systemic Therapy
- BSC (if PS 3-4)

- Treatment with entrectinib is not reimbursed by NHI
- Treatment with larotrectinib is conditionally covered by NHI

MET exon 14 Skipping mutation positive metastatic NSCLC

MET exon 14 skipping mutation (+) →

First line therapy:
- Tepotinib
- Capmatinib
- Crizotinib
- Systemic Therapy

PD →

2nd line therapy:
- Tepotinib or Capmatinib or Crizotinib if not previously used
- Systemic Therapy
- BSC (if PS 3-4)

- Treatment with capmatinib is not reimbursed by NHI
- crizotinib is not approved by TFDA for METex14 skipping mutation.

RET rearrangement positive metastatic NSCLC

RET rearrangement (+) →

First line therapy:
- Selpercatinib
- Pralsetinib
- Carbozantinib
- Systemic Therapy

PD →

2nd line therapy:
- Selpercatinib or Pralsetinib or Carbozantinib if not previously used
- Systemic Therapy
- BSC (if PS 3-4)

- Treatment with selpercatinib or cabozantinib is not approved by TFDA
- Treatment with pralsetinib is not reimbursed by NHI

ERBB2 (HER2) Mutation positive metastatic NSCLC

ERBB2 (HER2) mutation → First line therapy:
- systemic therapy

→ PD →

2nd line therapy:
(Preferred)
Trastuzumab deruxtecan (T-Dxd)
or
Trastuzumab emtansine (T-DM1)

- Treatment with is or Ado-trastuzumab Emtansine is not approved by TFDA
- Treatment with Fam-trastuzumab deruxtecan-nxki is not reimbursed by NHI

Systemic Therapy for PD-L1 expression ≧ 50% metastatic NSCLC

First line therapy:

Adenocarcinoma, Large cell ,NSCLC NOS →

Preferred
- Pembrolizumab
- (Carboplatin or cisplatin) + pemetrexed + pembrolizumab
- Atezolizumab
- Cemiplimab-rwlc
- Cemiplimab-rwlc + pemetrexed + (carboplatin or cisplatin)

Other Recommended
- Carboplatin + paclitaxel + bevacizumab + atezolizumab
- Carboplatin + albumin-bound paclitaxel + atezolizumab
- Nivolumab + ipilimumab + pemetrexed + (carboplatin or cisplatin)
- Cemiplimab-rwlc + paclitaxel + (carboplatin or cisplatin)
- Tremelimumab-actl + durvalumab + carboplatin + albumin-bound paclitaxel
- Tremelimumab-actl + durvalumab + (carboplatin or cisplatin) + pemetrexed

Useful in Certain Circumstances
- Nivolumab + ipilimumab

Squamous Cell Carcinoma →

Preferred
- Pembrolizumab
- Carboplatin + (paclitaxel or albumin-bound paclitaxel) + pembrolizumab
- Atezolizumab
- Cemiplimab-rwlc
- Cemiplimab-rwlc + paclitaxel + (carboplatin or cisplatin)

Other Recommended
- Nivolumab + ipilimumab + paclitaxel + carboplatin
- Tremelimumab-actl + durvalumab + carboplatin + albumin-bound paclitaxel
- Tremelimumab-actl + durvalumab + (carboplatin or cisplatin) + gemcitabine

Useful in Certain Circumstances
- Nivolumab + ipilimumab

* Treatment with Cemiplimab is neither available nor approved by TFDA.
* Use of anti-CTLA4, anti-PD-1/PD-L1 was conditionally reimbursed by NHI.

Systemic Therapy for PD-L1 expression ≧ 1-49% metastatic NSCLC

Adenocarcinoma, Large cell ,NSCLC NOS →

Preferred
- (Carboplatin or cisplatin) + pemetrexed + pembrolizumab
- Cemiplimab-rwlc + pemetrexed + (carboplatin or cisplatin)

Other Recommended
- Carboplatin + paclitaxel + bevacizumab + atezolizumab
- Carboplatin + albumin-bound paclitaxel + atezolizumab57
- Nivolumab + ipilimumab + pemetrexed + (carboplatin or cisplatin)
- Nivolumab + ipilimumab
- Cemiplimab-rwlc + paclitaxel + (carboplatin or cisplatin)
- Tremelimumab-actl + durvalumab + carboplatin + albumin-bound paclitaxel
- Tremelimumab-actl + durvalumab + (carboplatin or cisplatin) +

Useful in Certain Circumstances
- Pembrolizumab

Squamous Cell Carcinoma →

Preferred
- Carboplatin + (paclitaxel or albumin-bound paclitaxel) + pembrolizumab
- Cemiplimab-rwlc + paclitaxel + (carboplatin or cisplatin

Other Recommended
- Nivolumab + ipilimumab + paclitaxel + carboplatin
- Nivolumab + ipilimumab
- Tremelimumab-actl + durvalumab + carboplatin + albumin-bound paclitaxel
- Tremelimumab-actl + durvalumab + (carboplatin or cisplatin) + gemcitabine

Useful in Certain Circumstances
- Pembrolizumab

* Treatment with Cemiplimab is neither available nor approved by TFDA.
* Use of anti-CTLA4, anti-PD-1/PD-L1 was conditionally reimbursed by NHI.

PRINCIPLES OF PATHOLOGICAL REVIEW

病理評估

- 病理評估的目的包括:
  - 使用WHO肺癌組織分類，正確診斷肺癌組織型態
  - 依循AJCC建議確定所有分期參數，包括腫瘤大小、侵犯範圍、手術切除邊緣適當性及淋巴結轉移評估

- Non-small cell carcinoma(NSCC)或NSCC-NOS這個診斷應盡量避免使用，除非是型態學與免疫染色無法明確診斷之病例。

- 福馬林固定石臘包埋之腫瘤可適用於多數分子病理分析。

- 在小標本應謹慎使用免疫及特殊染色，以儘量保存腫瘤組織用於分子檢測。

PRINCIPLES OF PATHOLOGICAL REVIEW

肺腺癌分類 (WHO classification 2021)

- Preinvasive lesions
  - Atypical adenomatous hyperplasia
  - Adenocarcinoma in situ (AIS): ≤ 3cm nodule, lepidic growth
- Minimally invasive adenocarcinoma (MIA): ≤ 3cm nodule with ≤ 5mm invasion, predominantly lepidic growth
- Invasive adenocarcinoma: > 5mm of invasion, with lepidic, acinar, papillary, micropapillary or solid growth pattern, classified according to predominant pattern
- Invasive adenocarcinoma variants: mucinous adenocarcinomas, colloid, fetal and enteric adenocarcinoma
- 對於 non-mucinous adenocarcinoma，以 size of invasive component 做為AJCC T category 分期的依據

PRINCIPLES OF PATHOLOGICAL REVIEW

免疫組織化學染色

- 原發性肺腺癌
  - TTF-1對區分原發或轉移肺腺癌很重要。大部分(70-90%)的non-mucinous原發肺腺癌TTF-1為陽性，轉移腺癌(甲狀腺癌除外)幾乎均為陰性反應。
  - Napsin A於>80%的肺腺癌表現，可用於輔助TTF-1。
  - 使用一個鱗狀上皮癌的標記(例如p40)加上一個腺癌的標記(例如TTF-1)，搭配黏液染色(mucicarmine)的組合可用於進一步分類小標本型態為NSCC-NOS的肺癌。
- 神經內分泌分化
  - CD56, chromogranin, synaptophysin及INSM1可用於辨識神經內分泌分化。
- 惡性間皮細胞癌vs.肺腺癌
  - 建議使用兩個已知的間皮細胞癌免疫陽性抗體及兩個已知的腺癌免疫陽性抗體來做鑑別。
  - 間皮細胞癌的免疫陽性抗體：WT-1, calretinin, CK5/6, D2-40
  - 肺腺癌的免疫陽性抗體：CEA, Claudin4, TTF-1, Napsin A, B72.3, Ber-EP4, MOC31, CD15

PRINCIPLES OF PATHOLOGICAL REVIEW

肺癌之分子病理診斷

- 檢測方法學
  - 若可能的話，建議使用多基因套組檢測 (broad panel testing)。Next generation sequencing (NGS) 是最常用的檢測方法。
  - 如果 DNA-based 多基因套組檢測沒有找到 driver oncogene，可考慮加做 RNA-based NGS 來提升 fusion 偵測的能力。
  - Real-time PCR 可用於偵測特定的突變 (specific mutations)。除了這些特定突變以外的變異則無法偵測。
  - Sanger sequencing 不適合用於腫瘤比例低於 25-30% 的檢體，也不適合用來偵測 subclonal events (如抗藥性突變)。
  - Variant of uncertain significance (VUS) 不能用來當做標靶治療藥物選擇的依據。
  - Fluorescence in situ hybridization (FISH) 可用於偵測 copy number, amplification, 以及 gene rearrangement。

PRINCIPLES OF PATHOLOGICAL REVIEW

肺癌之分子病理診斷

- EGFR 突變
  - 腺癌EGFR突變的盛行率在西方人為10%，而在亞洲病人高達50%，且在非吸菸者、女性及非黏液腫瘤有較高EGFR突變頻率
  - EGFR突變與TKI治療之反應相關。
  - 對治療有反應的突變種類包括常見的L858R及exon 19 deletions，以及較不常見的exon 19 insertions, L861Q, G719X與S768I
  - T790M突變與第一代及第二代EGFR TKI的抗藥性相關，而對第三代的EGFR TKI 有療效反應。
  - Exon 20 insertion是一群異質性的變異，不同的變異類型對於標靶治療有不同的療效反應。PCR-based 檢測方法對於 Exon 20 insertion 的檢測靈敏度較低，NGS-based 檢測方法是較佳的選擇。
  - 檢測方法: Real-time PCR, Sanger sequencing, Next generation sequencing是檢測 EGFR 突變最常用的檢測方法。

PRINCIPLES OF PATHOLOGICAL REVIEW

肺癌之分子病理診斷

- ALK基因轉位
  - ALK基因轉位與ALK TKI的療效反應相關
  - 檢測方法: Fluorescence in situ hybridization (FISH) 是廣為使用的方法。美國 FDA 認可的免疫染色 (ALK D5F3 CDx Assay) 可做為獨立的檢測方式，不需再做 FISH 確認。Next generation sequencing 可用於偵測 ALK基因轉位。Real-time PCR 檢測亦可使用，但可能無法偵測 novel partner fusion。

- ROS1 基因轉位
  - ROS1基因轉位與ROS1 TKI的療效反應相關
  - 檢測方法: Fluorescence in situ hybridization (FISH)可做為診斷的方法，但可能較難偵測 FIG-ROS1 基因轉位。免疫染色可做為screening modality，但由於specificity不佳，需再做confirmatory testing。Next generation sequencing 可用於偵測 ROS1 基因轉位。Real-time PCR 檢測亦可使用，但可能無法偵測 novel partner fusion。

PRINCIPLES OF PATHOLOGICAL REVIEW

肺癌之分子病理診斷

- BRAF突變
  - BRAF V600突變與combined BRAF及MEK inhibitor療效反應相關
  - 其他型式的BRAF突變與療效反應的相關性目前仍不明確
  - 檢測方法: Real-time PCR, Sanger sequencing, next generation sequencing是最常用的檢測方法。使用anti-BRAF V600E-specific antibody免疫染色來檢測需要經過廣泛的驗證研究。

- KRAS突變
  - 由於 KRAS 突變與其他 targetable 突變同時出現的機率很低，帶有KRAS突變的腫瘤再進行其他 targetable 突變檢測的效益不高
  - KRAS G12C 突變與 KRAS G12C inhibitor 的療效反應相關
  - 檢測方法: Real-time PCR, Sanger sequencing, next generation sequencing 是最常用的檢測方法。

PRINCIPLES OF PATHOLOGICAL REVIEW

肺癌之分子病理診斷

- MET exon 14 skipping
  - MET exon 14 skipping 突變與 MET TKI 的療效相關
  - 檢測方法: Next generation sequencing (NGS)是主要的檢測方式，其中又以 RNA-based NGS 具有較好的表現。免疫染色不能用來檢測 MET exon 14 skipping 突變。

- RET 基因轉位
  - RET基因轉位與 RET TKI 的療效相關
  - 常見的基因轉位 partner 包括: KIF5B, NCOA4, CCDC6
  - 檢測方法: Fluorescence in situ hybridization (FISH) 可用於偵測 RET 基因轉位。Next generation sequencing (NGS) 可用於偵測 RET 基因轉位，而 RNA-based NGS 比 DNA-based NGS 具有較好的表現。Real-time PCR 檢測亦可使用，但可能無法偵測 novel partner fusion。

PRINCIPLES OF PATHOLOGICAL REVIEW

肺癌之分子病理診斷

- ERBB2/HER2 突變
  - ERBB2在癌症的變異包括基因突變、基因擴增等等。
  - ERBB2基因突變最常見的類型是exon20 insertion/duplication。
  - ERBB2 activating mutation與anti-HER2 targeted therapy療效反應相關。
  - 檢測方法：雖然Sanger sequencing和PCR可用於偵測ERBB2突變，但由於突變的種類繁多，NGS是較佳的檢測方法。

PRINCIPLES OF PATHOLOGICAL REVIEW

肺癌之分子病理診斷

- NTRK 基因轉位
  - NTRK 基因轉位與 TKI 的療效相關。
  - NTRK 1/2/3 基因轉位是罕見的癌症基因變異，有許多不同的 fusion partners。
  - NTRK 1/2/3 的點突變通常不會活化癌細胞，目前無證據顯示與 TKI 的療效相關。
  - 檢測方法: Fluorescence in situ hybridization (FISH)、免疫染色、PCR、Next generation sequencing可用於偵測NTRK基因轉位。免疫染色的判讀會受到組織中NTRK baseline expression的影響。Next generation sequencing可偵測廣泛的基因變異，但DNA-based NGS有可能出現偽陰性。

PRINCIPLES OF PATHOLOGICAL REVIEW

肺癌之分子病理診斷

- 標靶治療產生抗藥性之後的分子檢測
  - 對於使用標靶治療後產生抗藥性的病患，由於組織型態轉變(例如 small cell transformation)是可能的抗藥性機轉之一，應考慮對 progressing lesion進行組織切片來評估病理型態及分子檢測。
  - 對於使用 EGFR TKI 治療後產生抗藥性的病患，需進行 T790M 的檢測。檢測方法需具有能夠偵測 5% allele frequency 的靈敏度。
  - Broad genomic profiling 對於檢測可能的抗藥性機轉可以提供最豐富的資訊。

- 分子檢測用於鑑別多顆原發性肺癌或肺內轉移：
  - 研究顯示 broad gene coverage NGS 可能有助於鑑別多顆原發性肺癌或肺內轉移。

PRINCIPLES OF PATHOLOGICAL REVIEW

肺癌之分子病理診斷

- PD-L1
  - PD-L1免疫染色可用於選出較有可能對第一線免疫治療有反應的病人
  - PD-L1免疫染色有多種不同的抗體及染色平台，各自對陽性與陰性有不同的定義，且對應到不同的checkpoint inhibitor

PRINCIPLES OF PATHOLOGICAL REVIEW

肺癌之分子病理診斷

- 循環腫瘤DNA檢測
  - 循環腫瘤DNA檢測不應用來取代組織診斷。
  - 循環腫瘤DNA檢測建議用於晚期/轉移肺癌。早期肺癌使用組織檢體來進行基因檢測是較佳的選擇。
  - 循環腫瘤DNA檢測及組織基因檢測具有高特異性，但都有可能出現偽陰性，兩者互相輔助併用可提高偵測敏感度。

PRINCIPLES OF PATHOLOGICAL REVIEW

小細胞癌

- 小細胞癌(SCLC)是一種惡性上皮腫瘤，由高核質比、極少細胞質、細緻顆粒狀的核染色質及沒有或不明顯的核仁的小細胞所組成。腫瘤細胞呈圓形、橢圓或梭狀，核相嵌現象明顯，且有很高的mitotic counts。
- 區分小細胞癌與大細胞神經內分泌癌(large cell neuroendocrine carcinoma)最有用的特徵是小細胞癌具有高核質比，且核仁不明顯。
- 幾乎所有小細胞癌對Keratin免疫染色如AE1/AE3、CAM5.2均呈陽性反應
- 大多數小細胞癌表現神經內分泌分化，對如CD56、synaptophysin、chromogranin A、INSM1等免疫染色呈陽性反應。小於5%的小細胞癌對上述的神經內分泌免疫染色均呈陰性反應。
- TTF-1免疫染色在85%-90%的小細胞癌呈陽性反應。
- Ki-67免疫染色有助於區分小細胞癌與carcinoid tumors，特別是在細胞呈現crush artifact，無法計數mitotic counts的情況下尤其有幫助。
- 小細胞癌的Ki-67 proliferative index通常在50%-100%之間。
- 擴散期(extensive stage)的小細胞癌病患若屬於不抽煙、少量抽煙(<10根/天)、診斷不明確或治療方針不易決定，或是疾病復發時，可考慮進行分子檢測。

肺癌之手術治療原則

評估

- 應當由通過專科認證並且以肺癌手術為主要執業項目的胸腔外科醫生來決定腫瘤可否以手術切除。

- 手術切除(包括楔形切除術)優於腫瘤消融術 (射頻消融、微波消融、冷凍療法、立體定位放療)。每一位考慮行根治性局部治療的患者在接受評估時，都應諮詢胸腔腫瘤外科醫生的意見。手術切除高風險患者考慮以立體定位放射治療時，建議由包含放射腫瘤醫師之多專科團隊評估之。

肺癌之手術治療原則

- 在任何非緊急治療前，應完成完整治療計畫的制訂和必要的影像學檢查。

- 胸腔外科醫生應積極參加針對肺癌患者的多專科團隊討論和會議 (如多專科綜合治療門診和/或腫瘤委員會)。

- 應向吸菸的患者提供諮詢和戒菸支持。雖然主動吸煙的患者術後肺部併發症的發生率略有增加，但不應將這些認為是導致無法手術的風險。外科醫生不應僅僅因為吸煙狀況而拒絕對患者進行手術，因為手術提供了早期肺癌患者的主要治療方法。

肺癌之手術治療原則

切除

- 對於大多數非小細胞肺癌患者，解剖性肺切除術為首選。

- 對於位於周邊 T1ab、N0 腫瘤，可考慮進行亞肺葉切除術(肺節切除術和楔形切除術)。

- 亞肺葉切除術應當達到肺實質切緣大於等於2 公分或者大於等於結節的大小。除非技術不可行性，亞肺葉切除術術中在不顯著增加手術風險的情況下，應對Nl和N2淋巴結進行取樣活檢。

肺癌之手術治療原則

切除

- 肺節切除術（首選）或楔形切除術適用於肺儲備能力差或有其他主要合併症而導致無法進行肺葉切除術的特定患者。

- T3 (侵犯) 及T4 局部擴展腫瘤需要總括性(En-Bloc)切除所有腫瘤涉及之組織構造，以達到切緣陰性為目的。

肺癌之手術治療原則

- 如患者無解剖學和手術方面的禁忌症，只要不違反腫瘤治療標準和胸腔手術切除原則，建議考慮微創手術（VATS 或機器人輔助方法）。

- 在高個案量醫學中心(high volume centers)並具有相當的胸腔鏡外科手術經驗，選擇某些病人施行胸腔鏡肺葉切除可以改善短期結果(疼痛，住院天數，回復正常功能時間)而不會危及癌症預後。

- 如解剖位置合適且能夠做到切緣(resection margin)陰性，保留肺組織的解剖性切除術(袖狀切除術)優於全肺切除術。

肺癌之手術治療原則

切緣及淋巴評估

- 外科及病理的聯繫(Surgical pathologic correlation)對於評估顯然接近(apparent close)或陽性切緣非常重要，因為這些並不一定代表真正的切緣或代表真正會局部復發的區域(例如當隆凸下淋巴結分開廓清時，主支氣管或間支氣管的內面，或當沒有附著主動脈時鄰近主動脈的肋膜切緣) 。
- N1和N2淋巴結切除並標明位置(最少對3個N2站的淋巴結進行取樣或行完全淋巴結清除術) 應為肺癌切除手術之例行組成部分。
- N2患者在接受切除術時應行正規的同側縱隔淋巴結清除術。

肺癌之手術治療原則

- 完整切除需達到手術切緣陰性、系統性淋巴擴清或取樣、及最高位縱膈腔淋巴結為陰性。如果切緣陽性、有無法移除的陽性淋巴結、或陽性肋膜或心包膜積液，則定義為非完整切除。完整切除歸類為R0 ，病理顯微鏡檢陽性為R1，肉眼可見殘餘腫瘤則為R2 。

- 術後患者之臨床分期為IB期或以上，或具有高危險因子者，應轉診至胸腔腫瘤內科進行評估。

- N2患者可考慮轉診至放射腫瘤科。

肺癌之手術治療原則

手術在IIIA期(N2)患者之角色

- N2疾病之有無，應在開始治療前以影像及侵入性分期來加以確認。

- 若患者在手術進行中發現有隱匿性陽性(occult-positive)之N2淋巴結，應進行原定之腫瘤切除，並輔以縱膈腔淋巴結廓清術。若在接受VATS之病患發現有N2疾病，可以考慮停止手術，讓病患接受誘導治療後再行手術;然而繼續原定手術亦是治療選項。

肺癌之手術治療原則

- 手術在N2淋巴結陽性病患之治療角色，應在啟動治療前，於包含胸腔外科醫師在內的多專科團隊評估。

- 影像學懷疑陽性N2淋巴結之存在大幅增加N3淋巴結陽性之可能性。縱膈腔之病理評估必須包括氣管隆凸下(subcarinal)淋巴結及對側淋巴結。支氣管鏡超音波 +/- 內視鏡超音波可作為輔助縱膈腔鏡檢之微創病理縱膈腔分期之技術。

肺癌之手術治療原則

- 具有單一淋巴結且小於3公分之N2陽性病患，可以考慮包括手術在內的多樣性治療。
- 誘導治療後的再分期，應包含電腦斷層 +/- 正子掃描，以便排除疾病進展或轉移發生。
- 誘導治療後縱膈腔呈陰性的患者，有較佳之預後。

2021

影像導引消融術原則
Image-guided thermal ablation therapy (IGTA) principle

- 介入放射科醫師參加肺癌多專科討論，並決定IGTA是否可行。
- IGTA包含射頻、微波、冷凍治療。
- IGTA可經多專科評估後考慮用於病灶可手術切除但因共病症之無法手術之高風險族群或於可手術邊緣之患者。
- 高風險客觀定義為符合列一主要條件(FEV1 or DLCO ≤ 50%), 及或兩個或以上之次要條件(FEV1 or DLCO 51-60%, ≥ 70 歲，肺動脈高壓、LVEF≤ 40%, 休息或運動PaO2 < 55 mmHg, 或PCO2>45mmHg

2021

影像導引消融術原則
Image-guided thermal ablation therapy (IGTA) principle

- 較適用於 < 3 cm 病灶。
- 於下列NSCLC疾病範圍，適合手術但無接受手術或SABR或definitive RT者可考慮使用IGTA:
  - 特定Stage 1A NSCLC
  - Multiple lung cancer (N0-1)
  - Locoregional recurrence of symptomatic local thoracic disease
  - Thoracic disease (T1-3, N0) for Stage IVA, M1b, PS 0-2, limited metastases (≤3-5) other than brain
  - Limited lesion, in advanced or metastatic disease with progression on Osimertnib
  - Limited lesion , in asymptomatic patients or symptomatic patient with limited metastases, no brain metastases, on progression on
    - EGFR (+), progression on erlotinib +-(ramucirumab or bevacizumab), afatinib, gefitinib, or dacomitinib (NSCL-22).
    - ALK (+), progression on alectinib or brigatinib or ceritinib or lorlatinib
    - ALK (+), progression on crizotinib

Taipei Veterans General Hospital Practices Guidelines Radiation Oncology

Lung Cancer

Version 2024

General principles

- **More advanced technologies are appropriate when needed to deliver curative RT safely.**
- **These technologies include (but are not limited to) 4D-CT and/or PET/CT simulation, IMRT/VMAT, IGRT, and motion management.**
- **Nonrandomized comparisons of using advanced technologies versus older techniques demonstrate reduced toxicity and improved survival.**
- **In a prospective trial of definitive chemo/RT for stage III NSCLC (RTOG 0617), IMRT was associated with a nearly 60% decrease in high-grade radiation pneumonitis and similar survival and tumor control outcomes despite a higher proportion of stage IIIB and larger treatment volumes compared to 3D-CRT; as such, IMRT is preferred over 3D-CRT in this setting.**

General principles

- **The interaction of strong VEGF inhibitors with prior or subsequent dose-intensive RT involving the proximal bronchial tree, hilar vessels, or esophagus can lead to serious toxicity. Careful coordination of medical and radiation oncology on the therapeutic strategy is important.**

Early-stage NSCLC(Stage I, node negative Stage IIA)

- **SABR(also known as SBRT) is recommended for patients who are medically inoperable or who refuse to have surgery after thoracic surgery evaluation.**
- **Although SABR is not proven equivalent to lobectomy, some prospective series have demonstrated similar overall and cancer-specific survival.**
- **Close follow-up and salvage therapy for isolated local and/or locoregional recurrence after SABR have been shown to improved overall survival in a large retrospective study.**
- **SABR is most commonly used for tumors up to 5 cm in size, though selected larger isolated tumors can be treated safely if normal tissue constraints are respected.**
- **In patients treated with surgery, postoperative radiotherapy is not recommended unless there are positive margins or upstaging to N2.**

Locally advanced NSCLC(Stage II-III)

- **The standard of care for patients with inoperable stage II (node positive) and stage III is currently CCRT.**
- **RT interruptions and dose reductions for manageable acute toxicities should be avoided by employing supportive care.**
- **Although the optimal sequence is not established, post-operative radiotherapy (PORT) is generally administered after postoperative chemotherapy and concurrently with chemotherapy for positive resection margins.**

Locally advanced NSCLC(Stage II-III)

- **In patients with clinical stage I/II upstaged surgically to N2 with completely resected disease, two randomized studies did not show an overall survival benefit of PORT, although locoregional control was significantly improved.**
- **PORT (generally following postoperative chemotherapy) may be considered for selected patients with high-risk N2 disease, such as extracapsular extension, multi-station involvement, inadequate lymph node dissection/sampling, and/or refusal or intolerance of adjuvant systemic therapy.**
- **In patients with completely resected pN1 receiving adjuvant systemic therapy, PORT is not recommended.**
- **PORT may be considered for these patients if they are unable to receive adjuvant systemic therapy.**

Advanced/Metastatic NSCLC(Stage IV)

- **Definitive local therapy to isolated or limited metastatic sites (oligometastasis) (including not limited to brain, lung, and adrenal gland) achieves prolonged survival in a small proportion of well-selected patients with good performance status who have also received radical therapy to the intrathoracic disease. Definitive RT to oligomestasis(limited number is not universally defined but clinical trials have included up to 3-5 metastases), particularly SABR, is an appropriate option in such cases if it can be delivered safely to the involved sites.**
- **In the setting of progression at a limited number of sites on a given line of systemic therapy(oligoprogression), local ablative therapy to the oligoprogressive sites may extend the duration of benefit of the current line of systemic therapy.**
- **When treating oligometastatic/oligoprogressive lesions, if SABR is not feasible, other dose-intensive accelerated/hypofractionated conformal radiation therapy regimes may be used.**

Principles of Radiation Therapy

Radiation Simulation, Planning and Delivery

Treatment planning should be performed by CT scans obtained in the treatment position, with a slice thickness of 3~5mm. IV contrast may be considered for better target delineation whenever possible, especially in patients with central tumors or with nodal disease. PET-CT is preferable in cases with significant atelectasis. PET-CT can significantly improve the target accuracy. A randomized trial of PET/CT versus CT-only RT planning demonstrated improved preemption of futile radical RT, decreased recurrence, and a trend toward improved overall survival with PET/CT RT planning.(*)

Principles of Radiation Therapy

Radiation Simulation, Planning and Delivery

Recommended methods of accounting for tumor motion, per guideline, include:

1) Motion-encompassing methods such as slow CT scanning, **inhale and exhale breath-hold CT**, four-dimensional (4-D) respiration-correlated CT;

2) Respiratory gating methods using an external respiration signal or using internal fiducial markers;

3) **Breath-hold methods by deep-inspiration breath-hold**, active-breathing control (ABC) device, SDX spirometric voluntary breath hold system, surface guided radiotherapy, or self breath-hold with or without respiratory monitoring; forced shallow breathing with abdominal compression; and real-time tumor-tracking methods.

Principles of Radiation Therapy

Dose, Volume, and Normal Tissue Constraints for Conventionally Fractionated Radiation Therapy

- Postoperative radiation dose should be based on margin status. Lung tolerance to radiation after surgery is remarkably smaller than those with the presence of both lungs.

- For patients receiving postoperative RT, more strict DVH parameters should be considered for the lung.
- Pre-radiotherapy and post-radiotherapy lung function tests should be obtained.

Principle of Target volume delineation

Gross Target Volume (GTV) delineation

- The pulmonary extent of lung tumors should be delineated on pulmonary windows, and the mediastinal extent of tumors should be delineated using mediastinal windows.

- The PET images can help to categorize suspected mediastinal and hilar adenopathy and differentiate between collapsed lung tissue from tumor. However, false-positive PET scans can be caused by inflammation, and a biopsy is recommended if there is any question.

Principle of Target volume delineation

Clinical Target Volume (CTV) delineation

- –includes the area of subclinical involvement around the GTV. For the lung parenchymal disease, a margin of 5-10 mm is recommended.
- –In the absence of radiographic proof of invasion, the CTV of the primary lesion should not extend into the chest wall or mediastinum.
- –5-10 mm expansions of involved nodes of the CTV is recommended, but not extend into the major airways or lung, chest wall, or vertebral body without evidence of invasion.

Principle of Target volume delineation

Clinical Target Volume (CTV) delineation

- Regarding CTV of nodal regions, elective nodal irradiation (ENI) remains controversial and should be individualized based on tumor volume, dosimetric parameters of adjacent normal structures, and comorbid conditions. Involved field RT to high dose without ENI has been shown to allow higher dose radiation with acceptable toxicity and low risk of isolated nodal relapse.

- In patients who receive PORT, CTV should consist of the bronchial stump and high-risk draining lymph node stations.(**)

Principle of Target volume delineation

Planning Target Volume (PTV)

–When patients are immobilized with a Vac-Loc bag or other devices, expansion along all axes of 7 mm is recommended.

–When daily image-guided setup is used, the setup uncertainty can be reduced.

–Typically CTV could be expanded 0.5-1 cm in all directions (**)

Commonly Used Doses for Conventionally Fractionated and Palliative RT (NCCN v3. 2024)

Table 4. Commonly Used Doses for Conventionally Fractionated and Palliative RT

Treatment Type	Total Dose	Fraction Size	Treatment Duration
Definitive RT with or without chemotherapy	60–70 Gy	2 Gy	6–7 weeks
Preoperative RT	45–54 Gy	1.8–2 Gy	5 weeks
Postoperative RT			
• Negative margins	50–54 Gy	1.8–2 Gy	5–6 weeks
• Extracapsular nodal extension or microscopic positive margins	54–60 Gy	1.8–2 Gy	6 weeks
• Gross residual tumor	60–70 Gy	2 Gy	6–7 weeks
Palliative RT			
• Obstructive disease (SVC syndrome or obstructive pneumonia)	30–45 Gy	3 Gy	2–3 weeks
• Bone metastases with soft tissue mass	20–30 Gy	4–3 Gy	1–2 weeks
• Bone metastases without soft tissue mass	8–30 Gy	8–3 Gy	1 day–2 weeks
• Brain metastases	CNS GLs*	CNS GLs*	CNS GLs*
• Symptomatic chest disease in patients with poor PS	17 Gy	8.5 Gy	1–2 weeks
• Any metastasis in patients with poor PS	8–20 Gy	8–4 Gy	1 day–1 week

*NCCN Guidelines for Central Nervous System Cancers

→

- RTOG 0617 (74 Gy vs. 60 Gy, CCRT): no overall survival benefit.
- While optimal RT dose intensification remains a valid question, higher doses of 74 Gy are not currently recommended for routine use.

Recommended Dose/Volume Limit for Lung

- **QUANTEC is recommended by NCCN guideline 2024**
- **For conventional fractionation, definitive RT:**
  - V20 ≦ 30–35% and MLD ≦ 20–23 Gy to limit the risk of radiation pneumonitis to ≦ 20%
  - Limiting the dose to the central airways to ≦ 80 Gy to reduce the risk of bronchial stricture

- **Reference : *Radiation dose-volume effects in the lung.*** *Int J Radiat Oncol Biol Phys. 2010 Mar 1;76(3 Suppl):S70-6.*

QUANTEC = Quantitative Analysis of Normal Tissue Effects in the Clinic
V20 = % of whole lung receiving ≥ 20 Gy
MLD = Mean Lung Dose

Normal Tissue Constraints (NCCN v3. 2024)

Table 5. Normal Tissue Dose-Volume Constraints for Conventionally Fractionated RT with Concurrent Chemotherapy*

OAR	Constraints in 30–35 fractions
Spinal cord	Max ≤50 Gy
Lung	V20 ≤35%–40%†; MLD ≤20 Gy
Heart**	V50 ≤25%; Mean ≤20 Gy
Esophagus	Mean ≤34 Gy; Max ≤105% of prescription dose; V60 ≤17%; contralateral sparing is desirable
Brachial plexus	Median dose ≤69 Gy

Vxx = % of the whole OAR receiving ≥xx Gy.

*These constraints represent doses that generally should not be exceeded. Because the risk of toxicity increases progressively with dose to normal tissues, a key principle of radiation treatment planning is to keep normal tissue doses "as low as reasonably achievable" while adequately covering the target. The doses to any given organ at risk should typically be lower than these constraints, approaching them only when there is close proximity to the target volume.

†Use V20 <35%, especially for the following: elderly ≥70 years, taxane chemotherapy, and poor PFTs (such as FEV1 or DLCO <50% normal). Use more conservative limits with a diagnosis or radiologic evidence of idiopathic pulmonary fibrosis (IDP)/usual interstitial pneumonia (UIP) (the tolerance of these patients is lower though not well characterized).

Atlas:
http://www.rtog.org/CoreLab/ContouringAtlases/LungAtlas.aspx

Node-Negative Early-Stage SABR

- **SABR is recommended for patients who are medically inoperable or who refuse to have surgery after thoracic surgery evaluation.**
- **SABR is also an appropriate option for patients with high surgical risk.**
- **Intensive regimens of BED_{10} ≥100 Gy are associated with significantly better local control and survival than less intensive regimens.**
- **For centrally located tumors (within 2 cm of the proximal bronchial tree), 4 to 10 fraction risk-adapted SABR regimens appear to be effective and safe, while 54 to 60 Gy in 3 fractions is unsafe and should be avoided.**
- **Treatment-related mortality was 1.0% when the biologically equivalent normal tissue dose (BED_3) of the radiation schedule was ⩽210 Gy**

Node-Negative Early-Stage SABR

- **Most commonly used for tumors up to 5 cm in size.**
- **Prescription doses incompletely describe the actual delivered doses, which also depend strongly on how the dose is prescribed (to the isocenter vs. an isodose volume covering a proportion of the PTV), the degree of dose heterogeneity, whether tissue density heterogeneity corrections are used, and the type of dose calculation algorithm. All of these must be considered when interpreting or emulating regimens from prior studies.**

SABR (NCCN v3. 2024)

Table 2. Commonly Used Doses for SABR

Total Dose	# Fractions	Example Indications
25–34 Gy	1	Peripheral, small
45–60 Gy	3	Peripheral tumors
48–50 Gy	4	Central or peripheral tumors <4–5 cm
50–55 Gy	5	Central or peripheral tumors
60–70 Gy	8–10	Central tumors

Table 3. Maximum Dose Constraints for SABR*

OAR/Regimen	1 Fraction	3 Fractions	4 Fractions	5 Fractions
Spinal Cord	14 Gy	18 Gy (6 Gy/fx)	26 Gy (6.5 Gy/fx)	30 Gy (6 Gy/fx)
Esophagus	15.4 Gy	27 Gy (9 Gy/fx)	30 Gy (7.5 Gy/fx)	105% of PTV prescription^
Brachial Plexus	17.5 Gy	24 Gy (8 Gy/fx)	27.2 Gy (6.8 Gy/fx)	32 Gy (6.4 Gy/fx)
Heart/ Pericardium	22 Gy	30 Gy (10 Gy/fx)	34 Gy (8.5 Gy/fx)	105% of PTV prescription^
Great Vessels	37 Gy	NS	49 Gy (12.25 Gy/fx)	105% of PTV prescription^
Trachea & Proximal Bronchi	20.2 Gy	30 Gy (10 Gy/fx)	34.8 Gy (8.7 Gy/fx)	105% of PTV prescription^
Rib	30 Gy	30 Gy (10 Gy/fx)	40 Gy (10 Gy/fx)	NS
Skin	26 Gy	24 Gy (8 Gy/fx)	36 Gy (9 Gy/fx)	32 Gy (6.4 Gy/fx)
Stomach	12.4 Gy	NS	27.2 Gy (6.8 Gy/fx)	NS

*Based on constraints used in recent RTOG SABR trials (RTOG 0618, 0813, & 0915).
^for central tumor location. NS = not specified

Principles of Radiation Therapy for Small cell lung cancer

Definitive RT for limited disease:

Simulation, planning and delivery similar to NSCLC

ENI may be considered (No ENI in current trials: RTOG 0538, EORTC 08072)

Dose: 45-60 Gy (1.5 Gy bid) or **56-70** Gy (1.8-2.0 Gy qd)

Prophylactic cranial irradiation (PCI)

30Gy / 15 Fx or
25Gy / 10 Fx

Consolidative thoracic RT

Consolidative thoracic RT is beneficial for selected patients with extensive-stage SCLC with good response to systemic therapy. Dosing may be individualized within the range of 30 Gy/ 10 Fx to 60 Gy/ 30 Fx.

Indication of carbon ion radiotherapy

Disease	Indication
Lung cancer without metastasis or invasion of adjacent organs	Clinical stage Tis, T1-T4N0 primary lung cancer (excluding T4 due to invasion of nearby organs)
Primary non-small cell lung cancer with regional lymph node metastasis or invasion of adjacent organs, and tracheal/bronchial cancer without distant metastasis	Clinical stage T0-4N1-3M0 or T4N0M0 (invasion of nearby organs)
Metastatic lung tumors	Oligometastatic lung tumors (5 or fewer)

***: Dose-fractionation of each indication is listed in CIRT guideline.**
****: Indication for each candidate will be discussed in CIRT tumor board.**

Acronym

- **3D-CRT: 3D Conformal Radiation Therapy**
- **CCRT: Concurrent chemoradiotherapy**
- **CT: computed tomography**
- **CTV: Clinical Target Volume**
- **DVH: dose-volume histogram**
- **ENI: elective nodal irradiation**
- **Fx: fraction**
- **GTV: Gross Tumor Volume**
- **HDR: High dose rate**
- **IGRT: Image-Guided Radiation Therapy**
- **IMRT: Intensity Modulated Radiation Therapy**
- **LDR: Low dose rate**
- **MRI: Magnetic Resonance Image**
- **PET: Positron Emission Tomography**
- **PTV: Planning Target Volume**
- **RT: Radiation Therapy**
- **SABR: Stereotactic Ablative RT, also known as Stereotactic Body RT (SBRT)**
- **BED: Biologically effective dose**

References:

- **(*) Ung, Y., et al. "An Ontario Clinical Oncology Group (OCOG) randomized trial (PET START) of FDG PET/CT in patients with stage III non-small cell lung cancer (NSCLC): Predictors of overall survival." *Journal of Clinical Oncology* 29.15_suppl (2011): 7018-7018**
- **(**) Cox, James D., Joe Y. Chang, and Ritsuko Komaki, eds. Image-Guided Radiotherapy of Lung Cancer. CRC Press, 2007.**

肺癌治療用藥準則 – 非小細胞肺癌

◎ 第一線

- **Gemcitabine (GC-G)**
  G (1000-1250 mg/m^2) + Cisplatin (60-75 mg/m^2), Q3-4W.
- **Vinorelbine (NC-N)**
  Vinorelbine (25-30 mg/m^2 i.v. or 60-80 mg/m^2 p.o.) + C (60-75 mg/m^2), Q3-4W.
- **Paclitaxel (TaC or TaC-Ta-Ta)**
  1. **Paclitaxel (160-175 mg/m^2) + Cisplatin (60- 75 mg/m^2) +- Bevacizumab[a] (15 mg/kg)-D1,Q3W.**
  2. **Paclitaxel (60-80 mg/m^2)-D1,8,15 + Cisplatin (60-75 mg/m^2)-D1, Q4W.**
- **Docetaxel (TC or TC-T)**
  1. **Docetaxel (60-75 mg/m^2)-D1 + Cisplatin (60-75 mg/m^2)-D1, Q3W.**
  2. **Docetaxel (30-35 mg/m^2)-D1,8 + Cisplatin (60-75 mg/m^2)-D1,Q3W.**
- **Pemetrexed (AC)**
  Pemetrexed (500 mg/m^2) + Cisplatin (60-75 mg/m^2) +- Bevacizumab[a] (15 mg/kg)-D1, Q3W.
- **TS-1[a] (80-120 mg in 2 divided doses)-D1~14 +Carboplatin (AUC = 4-6)-D1, Q3W**
- **TS-1[a] (80-120 mg in 2 divided doses)-D1~21 + Cisplatin (60-75 mg/m^2)-D8, Q4-5W**
- **UFUR (300-600 mg as tegafur in 2-3 divided doses daily)-D1~21 + Cisplatin (60-75 mg/m^2)-D8, Q4W**
- **Pembrolizumab[b] (200 mg)-D1, Q3W. (**PD-L1≥ 50%**)**
- **Pembrolizumab[a] (200 mg) + Pemetrexed (500 mg/m^2) + Cisplatin (60-75 mg/m^2)-D1, Q3W.** (Nonsquamous NSCLC)
- **Pembrolizumab[a] (200 mg) + Paclitaxel (160-175 mg/m^2) + carboplatin (AUC = 4-6)-D1, Q3W.** (Squamous NSCLC)
- **Atezolizumab[a] (1200 mg) + bevacizumab[a] (7.5-15 mg/kg) + Paclitaxel (160-175 mg/m^2) + carboplatin (AUC = 4-6)-D1, Q3W. (Nonsquamous NSCLC)**
- **Atezolizumab[a] (1200 mg), Q3W. (**PD-L1≥ 50%, IC>10%**)**
- **Ipilimumab[c] (1mg/kg, Q6w)+ Nivolumab[a] (3mg/kg, Q2W)**
- **Ipilimumab[c] (1mg/kg, Q6w)+ Nivolumab[a] (360mg, Q3W) +-platinum–based doublet chemotherapy**
- **Amivantamab[a] + carboplatin (AUC = 4-6) + Pemetrexed (500 mg/m2) - D1, Q3W. (**EGFR exon 20 insertion(+)**)**
- **Gefitinib 250 mg, QD**.[if EGFR sensitizing mutation(+)]
- **Erlotinib 150 mg, QD.** [if EGFR sensitizing mutation(+)]
- **Erlotinib 150mg QD + Bevacizumab[b] (15 mg/kg q3w)**
- **Erlotinib 150mg QD + Ramucirumab[a] (10mg/kg, Q2W)**
- **Afatinib 40 mg, QD**. [if EGFR sensitizing mutation(+)]
- **Dacomitinib 45mg, QD** [if EGFR sensitizing mutation(+)]
- **Osimertinib[b] 80mg QD** [if EGFR sensitizing mutation(+)]
- **Crizotinib[e] 250 mg, BID**.[ALK/ROS1 rearrangement(+)/METex14 skipping mutation(+)]
- **Alectinib 600mg BID.** [ALK rearrangement(+)]
- **Ceritinib[d] 450 mg, QD**. [ALK/ROS-1 rearrangement(+)]
- **Lorlatinib[b] 100mg QD.** [ALK rearrangement(+)]
- **Brigatinib[b] 90mg QD x 7days, then 180m QD** [ALK rearrangement(+)]
- **Entrectinib[b] 600mg QD** [ROS-1/NTRK rearrangement(+)]
- **Dabrafenib[a]150 mg, BID + trametinib[a] 2 mg, QD [if BRAF V600E mutation (+)]**
- **Tepotinib[a] 450mg QD** [if METex14 skipping mutation(+)]
- **Capmatinib[a] 400mg, BID**.[if METex14 skipping mutation(+)]
- **Selpercatinib[c]** [if RET rearrangement(+)]
- **Pralsetinib[a]** [if RET rearrangement(+)]

*** 病患若參加本院 IRB 同意之臨床試驗，則依該臨床試驗之治療計畫進行**

[a] 健保不給付

[b] 健保特殊條件給付

[c] TFDA尚未核準其適應症

[d] TFDA尚未核準其適應症於ROS-1 rearrangement

[e] TFDA尚未核準其適應症於METex 14 skipping mutation

備註: 1. Elderly or poor performance status：cisplatin omitted. 2. Cisplatin 若改成 Carboplatin, 劑量為 (CCr+25) x AUC, AUC = 4-6. 3. Bevacizumab 7.5 mg/kg 可與 chemotherapy併用於第一線治療, 但限於non-squamous cell carcinoma, no hemoptysis 4. Pemetrexed/cisplatin用於第一線治療以及 pemetrexed用於第二線療都僅限於non-squamous cell carcinoma 5. Ramucirumab 10 mg/kg可與 docetaxel併用於第二線(後)之治療。

肺癌治療用藥準則 – 非小細胞肺癌

◎ 第二線以上

- **Docetaxel**
  1. **Docetaxel (60 – 75 mg/m^2)-D1, Q3W.**
  2. **Docetaxel (30 – 35 mg/m^2)-D1,8, Q3W.**
  3. **Docetaxel (60 – 75 mg/m^2) + Ramucirumab[a] (10mg/kg)-D1,Q3W**
- **Pemetrexed (500 mg/m^2)-D1,Q3W.**
- **TS-1 (80–120 mg)-D1~28, Q6W**
- **Gefitinib 250 mg, QD.** (if Adeno**)**
- **Erlotinib 150 mg, QD.** (if Adeno, if NSCLC 3rd line)
- **Afatinib 40mg QD (if squamous)**
- **Osimertinib[b] 80 mg, QD.** [if T790M EGFR mutation (+)]
- **Lorlatinib[c] 100mg QD [**ALK/ROS-1 rearrangement(+)**]**
- **Pembrolizumab[b] (2 mg/kg)-D1, Q3W.**
- **Nivolumab[b] (3 mg/kg)-D1, Q2W.**
- **Atezolizumab[b] (1200 mg)-D1, Q3W.**
- **Larotrectinib[a] 100mg BID** [NTRK rearrangement(+)]
- **Amivantamab[b] (<80kg: Week 1, Day 1: 350 mg IV x 1 dose, Day 2: 700 mg IV x 1 dose, Weeks 2-4: 1050 mg IV QW, Week 5 and thereafter: 1050 mg Q2W)**[EGFR exon 20 insertion(+)]
- **Fam-trastuzumab deruxtecan-nxki[a] (5.4 mg/kg)-D1, Q3W** [HER2 (+)]

*** 病患若參加本院 IRB 同意之臨床試驗，則依該臨床試驗之治療計畫進行**

[a] 健保不給付

[b] 健保特殊條件給付

[c] TFDA尚未核準其適應症於ROS-1 rearrangement

備註: 1. Elderly or poor performance status：cisplatin omitted. 2. Cisplatin 若改成 Carboplatin, 劑量為 (CCr+25) x AUC, AUC = 4-6. 3. Bevacizumab 7.5 mg/kg 可與 chemotherapy併用於第一線治療, 但限於non-squamous cell carcinoma, no hemoptysis 4. Pemetrexed/cisplatin用於第一線治療以及 pemetrexed用於第二線療都僅限於non-squamous cell carcinoma 5. Ramucirumab 10 mg/kg可與 docetaxel併用於第二線(後)之治療。

小細胞肺癌治療原則 (NEW)（臨床試驗病例除外）

◎ Limited-stage small cell lung cancer (SCLC):

1. Clinical stage I-IIA (T1-2, N0, M0) should consider pathological mediastinal staging, then lobectomy and mediastinal lymph node dissection or sampling should be considered in pathologic mediastinal staging negative.
2. Limited stage IIB-IIIC (T3-4, N0, M0; T1-4, N1-3, M0) with good performance status (ECOG 0-2), systemic therapy with concurrent radiotherapy should be considered.
3. Limited stage IIB-IIIC (T3-4, N0, M0; T1-4, N1-3, M0) with poor performance status (ECOG 3-4) due to SCLC, systemic therapy with/without radiotherapy (concurrent or sequential) should be considered.
4. Four cycles of systemic therapy are recommended.

◎ Standard regimens for Limited-stage SCLC:

1. Cisplatin (60-75 mg/m^2) + etoposide (60-80 mg/m^2) D1,2,3/ Q3W
2. Carboplatin (AUC = 4-6) D1 + etoposide (60-80 mg/m^2) D1,2,3/ Q3W

小細胞肺癌治療原則 NEW（ 臨床試驗病例除外 ）

◎ Standard regimens for Extensive-stage SCLC* :

1. Cisplatin (60-75 mg/m^2) + etoposide (60-80 mg/m^2) D1,2,3/ Q3W
2. Carboplatin (AUC = 4-6) D1 + etoposide (60-80 mg/m^2) D1,2,3/ Q3W
3. Carboplatin (AUC 5) day 1 and etoposide 100 mg/m^2 day 1,2,3 and atezolizumab 1200mg day 1 every 21 days x 4 cycles followed by maintenance atezolizumab 1200 mg (category 1)
4. Carboplatin (AUC 5-6) day 1 and etoposide 80-100 mg/m^2 day 1,2,3 and durvalumab 1500 mg day 1 every 21 days x 4 cycles followed by maintenance durvalumab 1500 mg every 28 days(category 1,but durvalumab was not covered by NHI)
5. Cisplatin (75-80 mg/m^2) day 1 and etoposide 80-100 mg/m^2 day 1,2,3 and durvalumab 1500 mg day 1 every 21 days x 4 cycles followed by maintenance durvalumab 1500 mg every 28 days (category 1,but durvalumab was not covered by NHI)

◎ Relapsed regimens:

1. Topotecan 1.5 mg/m^2 D1-5/ Q3W
2. Ifosfamide 1000 mg/m^2 D1-3 + oral etoposide 50 mg D4-13/ Q3W
3. Topotecan 1.5 mg/m^2 D1-3 + epirubicin 30 mg/m^2 D1/ Q3W
4. Lurbinectedin 3.2 mg/m^2 Q3W (not covered by NHI)

*** Extensive-stage: Stage IV (T any, N any, M 1a/b/c), or T3-4 due to multiple lung nodules that are too extensive or have tumor/nodal volume that is too large to be encompassed in a tolerable radiation plan.**

* 治療先前至少已接受兩種化學治療

Regimens for Neoadjuvant Therapy

	Published Chemotherapy Regimens	Schedules
NC-N	Vinorelbine (25-30 mg/m^2 i.v. or 60-80 mg/m^2 p.o.)-D1,8 + Cisplatin (60-75 mg/m^2)-D1	Q3W for 2-4 cycles
	Nivolumab 360 mg + platinum based chemotherapy (as following) - Carboplatin (AUC = 4-6) -D1 + Paclitaxel (160-175 mg/m2) -D1 (any histology) - Cisplatin (60-75 mg/m2) -D1 + Pemetrexed (500 mg/m2) -D1 (non-SqCC histology) - Cisplatin (60-75 mg/m2) -D1 + Gemcitabine (1000-1250 mg/m2)-D1,8 (squamous histology) - Cisplatin (60-75 mg/m2) -D1 + Paclitaxel (160-175 mg/m2)-D1 (any histology)	Q3W for 3 cycles
	Pembrolizumab (200 mg)-D1 + platinum based chemotherapy (as following) - Cisplatin (60-75 mg/m2) -D1 + Pemetrexed (500 mg/m2) -D1 (non-SqCC histology) - Cisplatin (60-75 mg/m2) -D1 + Gemcitabine (1000-1250 mg/m2)-D1,8 (squamous histology)	
GC-G	Gemcitabine (1000-1250 mg/m^2)-D1,8 + Cisplatin (60-75 mg/m^2)-D1	Q3W for 2-4 cycles
TC	Docetaxel (60-75 mg/m^2)-D1 + Cisplatin (60-75 mg/m^2)-D1	Q3W for 2-4 cycles
TaC*	Paclitaxel (160-175 mg/m^2)-D1 + Cisplatin (60-75 mg/m^2)-D1	Q3W for 2-4 cycles
AC	Pemetrexed (500 mg/m^2) –D1+ Cisplatin (60-75 mg/m^2)-D1	Q3W for 2-4 cycles

Neoadjuvant treatment with Nivolumab, pembrolizumab and Pemetrexed is not reimbursed by NHI

Regimens for Adjuvant Therapy

[Indication: pathological IB (high-risk patients, 健保不給付), stage II and IIIA]

	Published Chemotherapy Regimens	Schedules
NC-N	Vinorelbine (25-30 mg/m^2 i.v. or 60-80 mg/m^2 p.o.)-D1,8 + Cisplatin (60-75 mg/m^2)-D1	Q3W for 2-4 cycles
	Other Acceptable Chemotherapy Regimens (健保不給付)	**Schedules**
GC-G	Gemcitabine (1000-1250 mg/m^2)-D1,8 + Cisplatin (60-75 mg/m^2)-D1	Q3W for 2-4 cycles
TC	Docetaxel (60-75 mg/m^2)-D1 + Cisplatin (60-75 mg/m^2)-D1	Q3W for 2-4 cycles
TaC*	Paclitaxel (160-175 mg/m^2)-D1 + Cisplatin (60-75 mg/m^2)-D1	Q3W for 2-4 cycles
AC	Pemetrexed (500 mg/m^2) + Cisplatin (60-75 mg/m^2)-D1	Q3W for 2-4 cycles
	Osimertinib 80 mg (EGFR(+) after platinum based chemotherapy)	QD for 3 years
	Atezolizumab 840mg/1200mg/1680mg (EGFR(-))	Q2W/Q3W/Q4W for 1 year
	Pembrolizumab 200 mg (EGFR(-))	Q3W for 1 year

Chemotherapy Regimens for Adjuvant Therapy-non platintinum based

(Indication: Adeno, pT2 and tumor size > 3 cm)

UFUR(for adeno)	300-600 mg as tegafur, divided by 2-3 times daily	2 years

Cisplatin 若改成 Carboplatin, 劑量為 (CCr+25) x AUC, AUC = 4-6

***Paclitaxel+carboplatin regimen showed survival benefit in stage IB, > 4 cm**

Adjuvant treatment with Osimertinib/Atezolizumab/Pembrolizumab is not reimbursed by NHI

臺北榮總肺癌診療共識

1. 主要依據- **NCCN Version v1. 2024**
2. 本治療指引將每年檢討修訂一次
   預定下次修訂日期: **2025**年**05**月

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