肺癌診療指引

胸腔腫瘤暨食道癌多專科團隊

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參考資料：

Non-small Cell Lung Cancer NCCN Guidelines V1.2015

Small Cell Lung Cancer NCCN Guidelines V1.2015

全民健康保險藥品給付規定 行政院衛生署一百零三年版

Physicians' Cancer Chemotherapy Drug Manual 2010

☆：選項

EUS：Endoscopic ultrasound
EBUS：Endobronchial ultrasound
SABR：Stereotactic ablative radiotherapy
SRS：Stereotactic radiosurgery
WBRT：Whole brain radiotherapy
SVC：Superior vena cava

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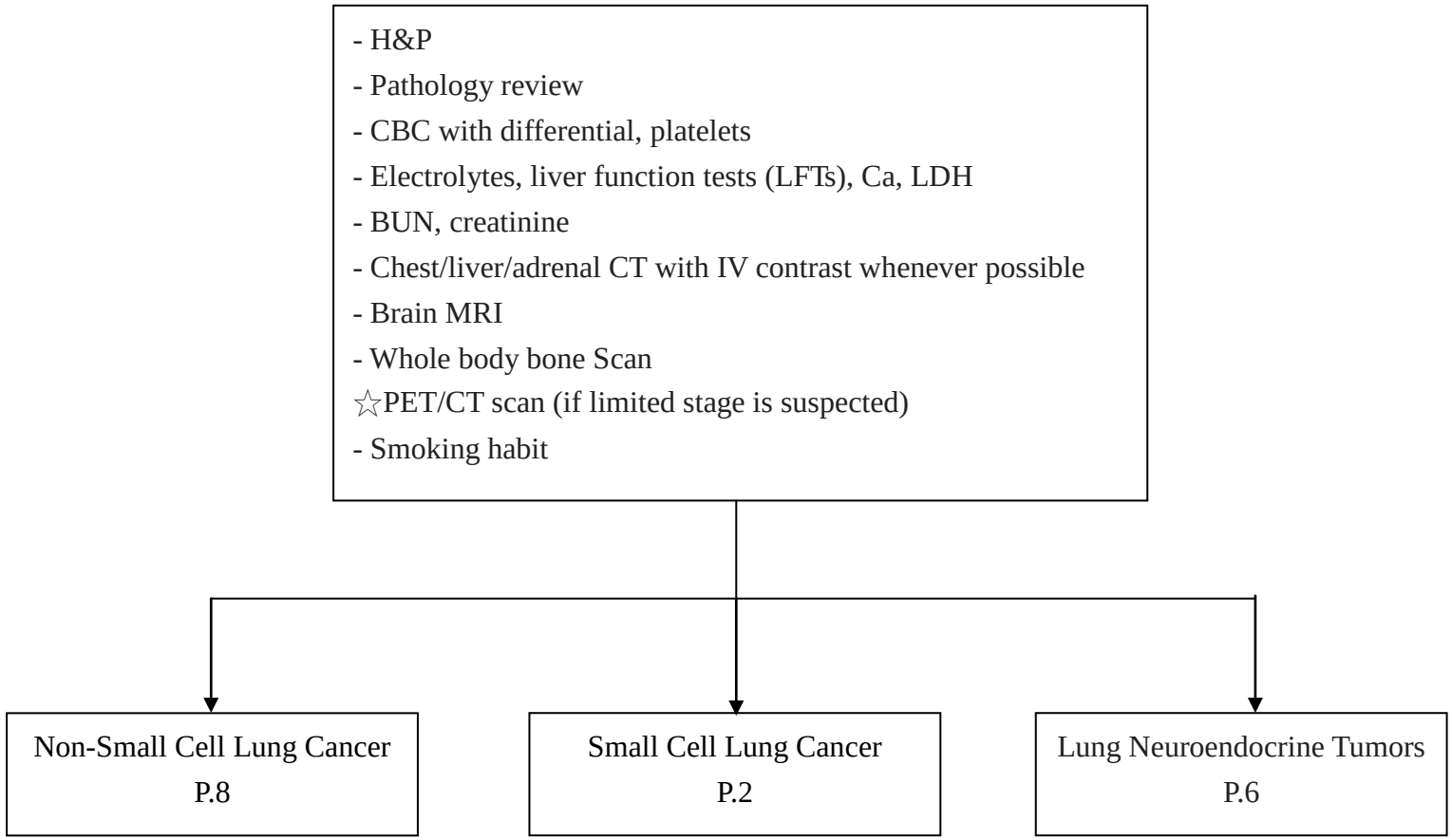
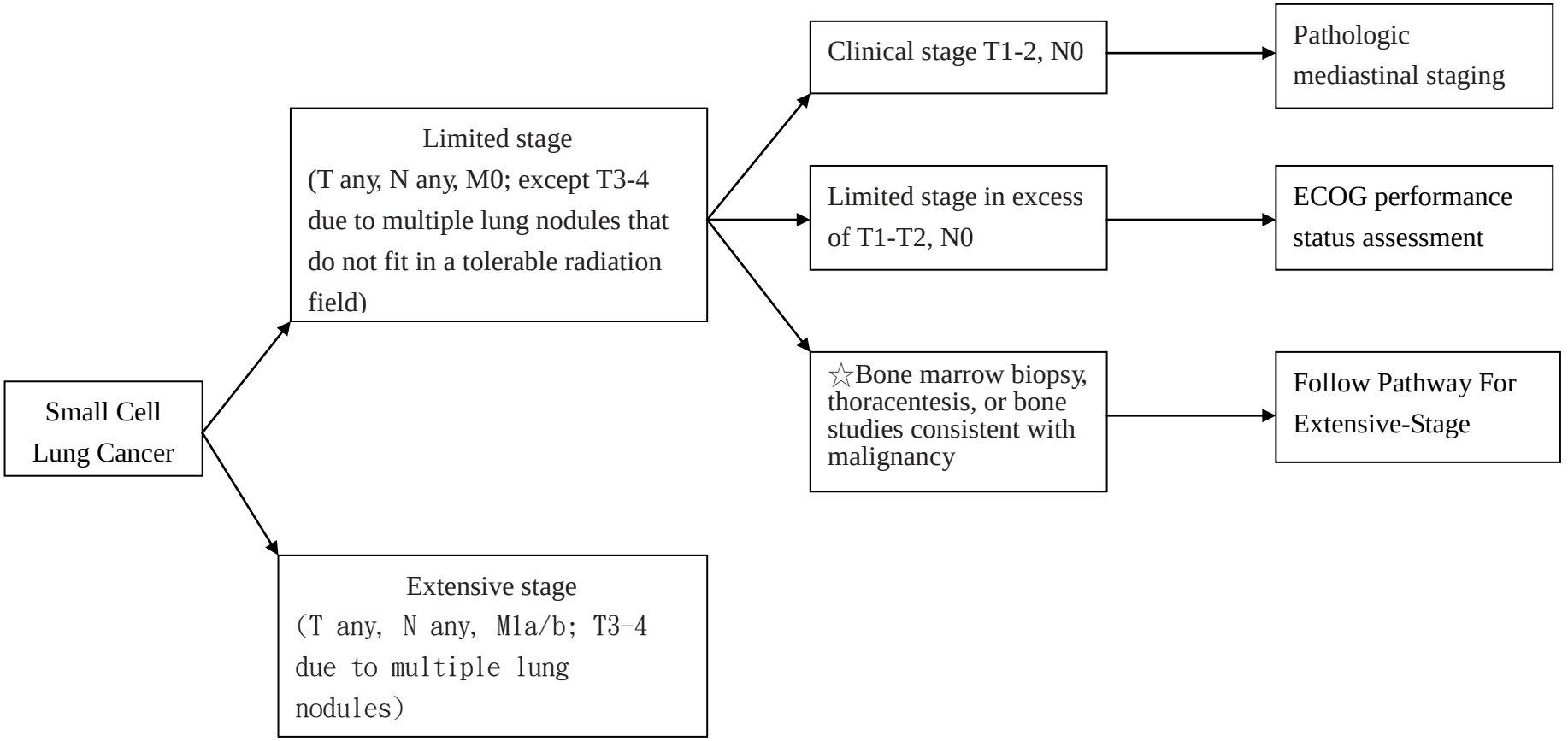
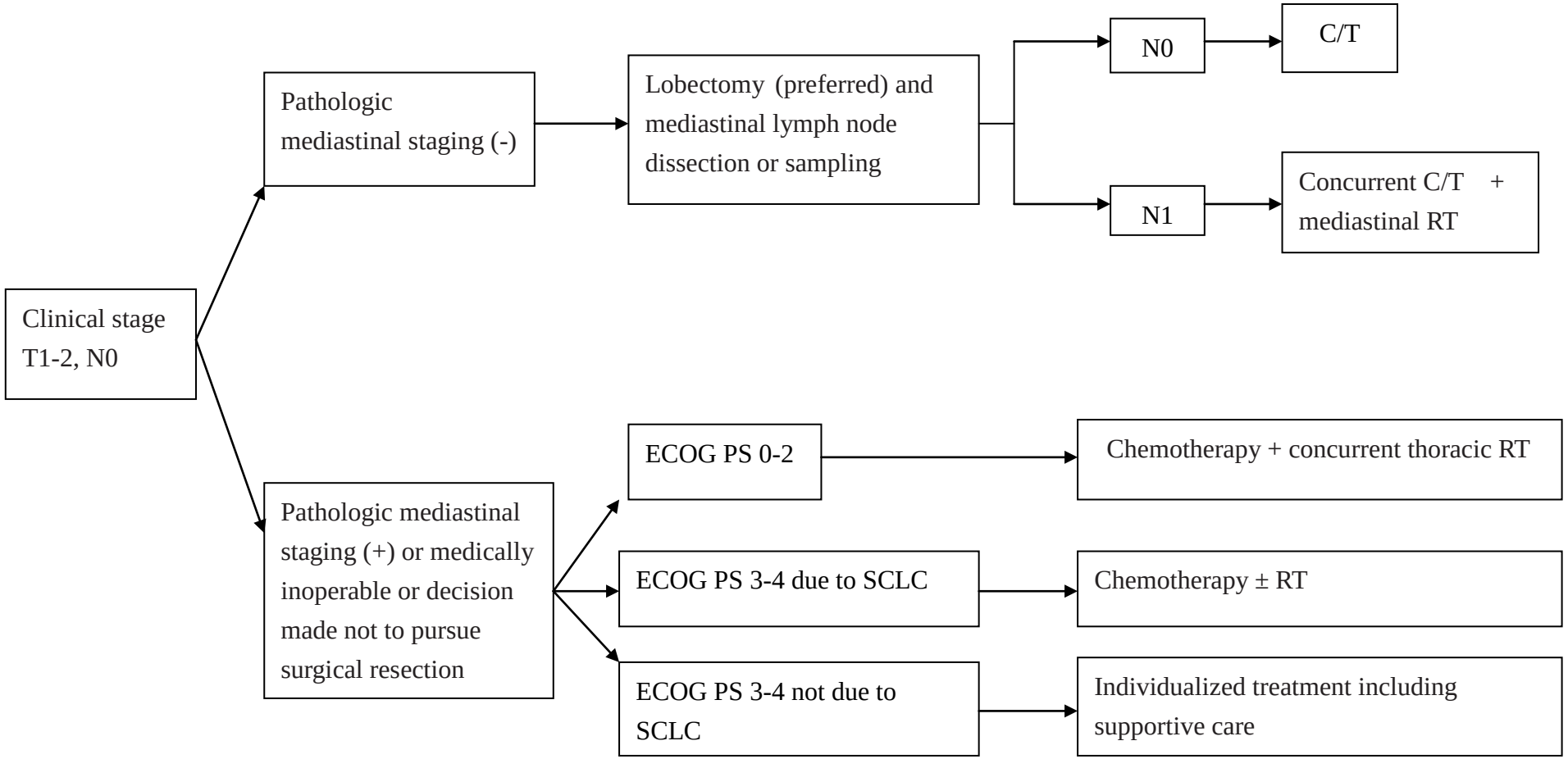
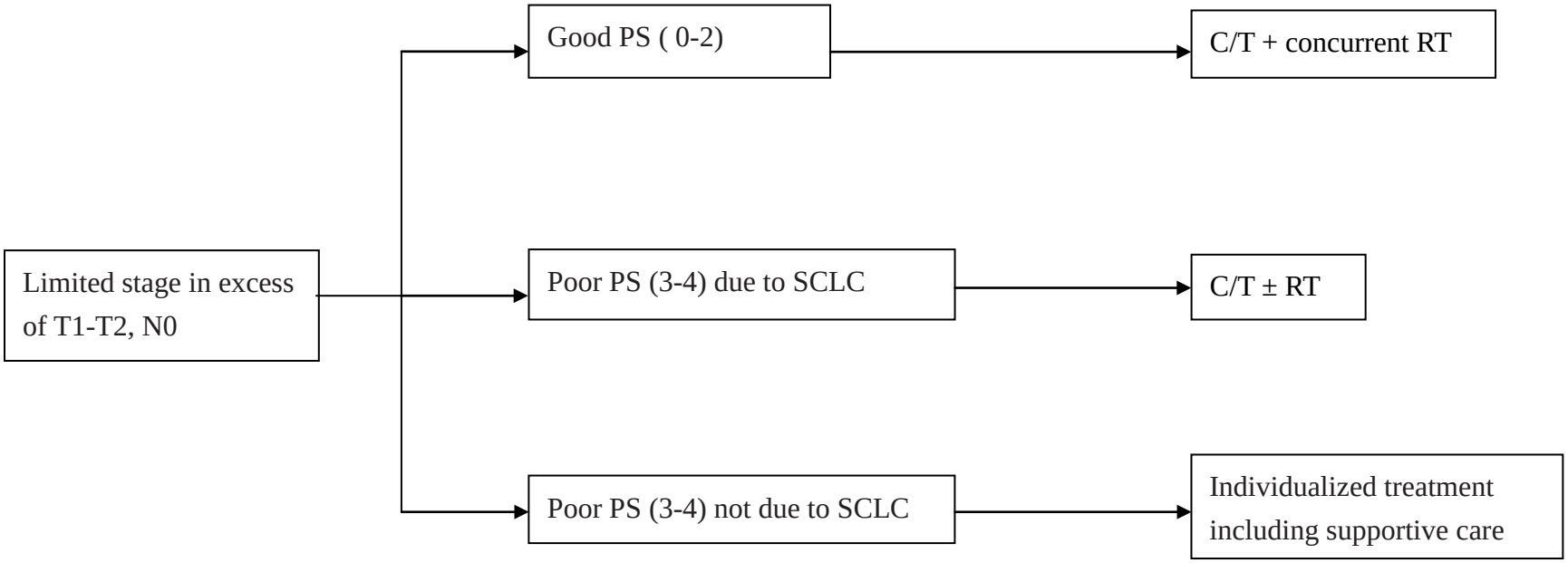
Initial Evaluation

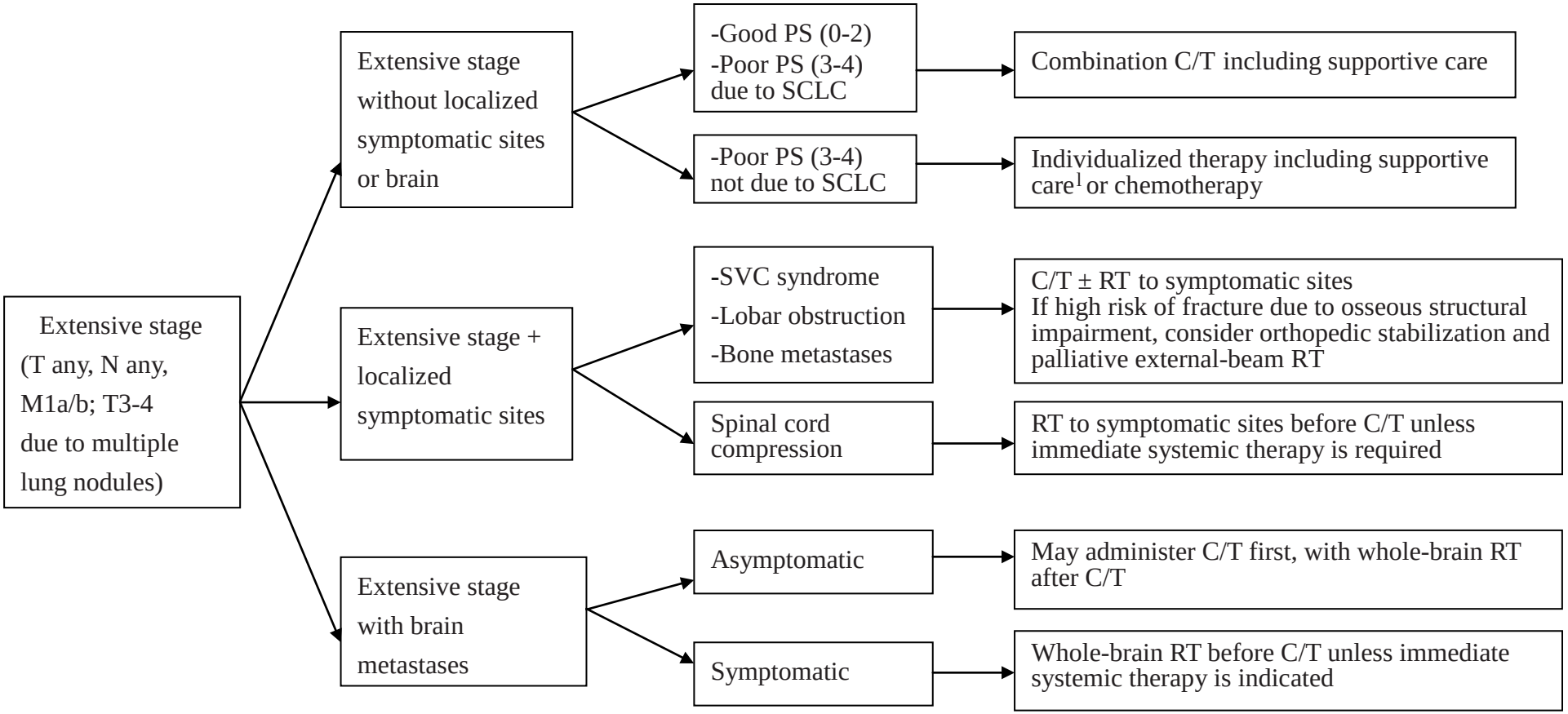



Small Cell Lung Cancer
Limited stage (T any, N any, M0; except T3-4 due to multiple lung nodules that do not fit in a tolerable radiation field)
Extensive stage (T any, N any, M1a/b; T3-4 due to multiple lung nodules)
Clinical stage T1-2, N0
Limited stage in excess of T1-T2, N0
☆Bone marrow biopsy, thoracentesis, or bone studies consistent with malignancy
Pathologic mediastinal staging
ECOG performance status assessment
Follow Pathway For Extensive-Stage

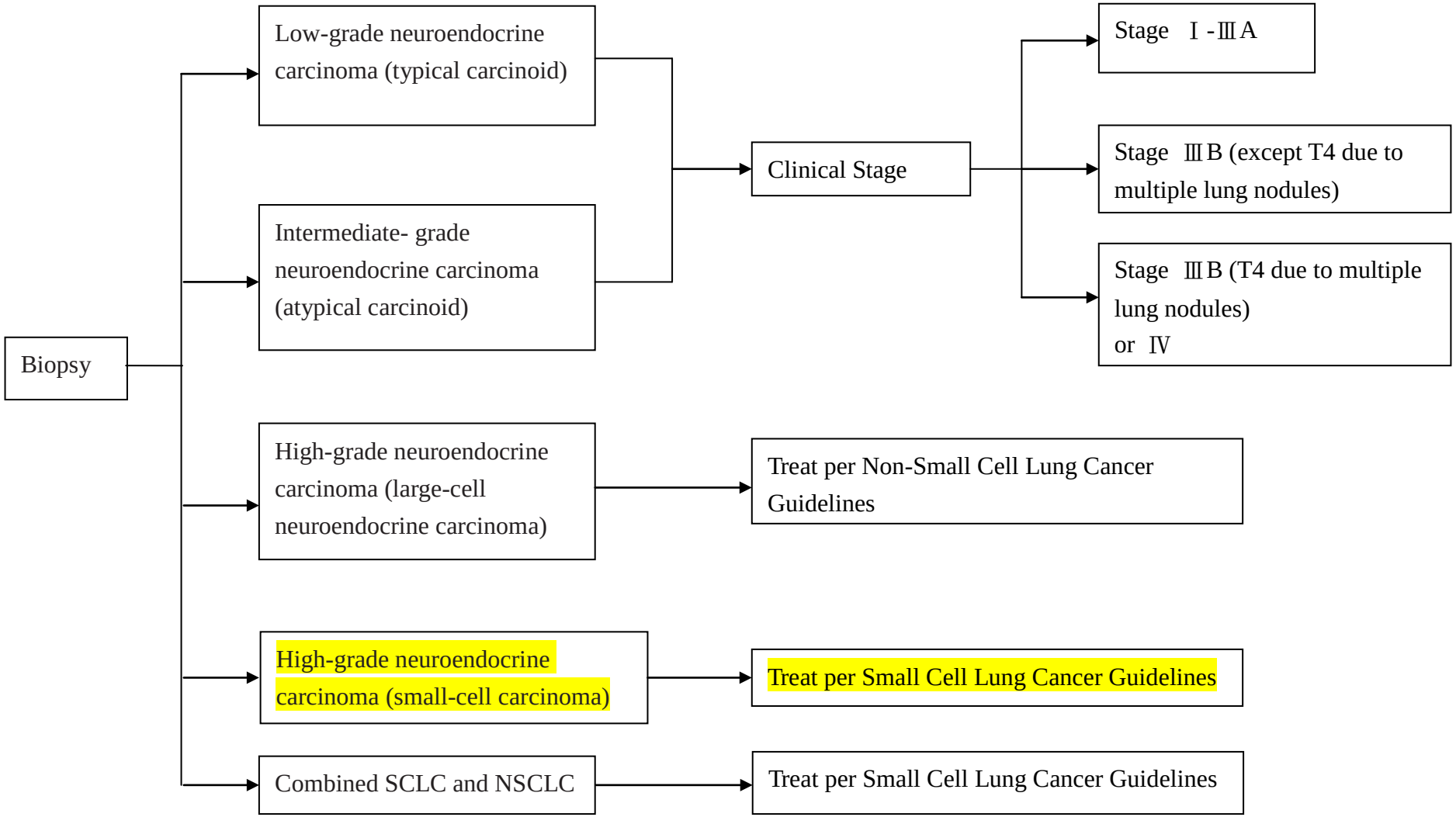

Clinical stage
T1-2, N0
Pathologic mediastinal staging (-)
Lobectomy (preferred) and mediastinal lymph node dissection or sampling
N0
C/T
N1
Concurrent C/T + mediastinal RT
Pathologic mediastinal staging (+) or medically inoperable or decision made not to pursue surgical resection
ECOG PS 0-2
Chemotherapy + concurrent thoracic RT
ECOG PS 3-4 due to SCLC
Chemotherapy ± RT
ECOG PS 3-4 not due to SCLC
Individualized treatment including supportive care

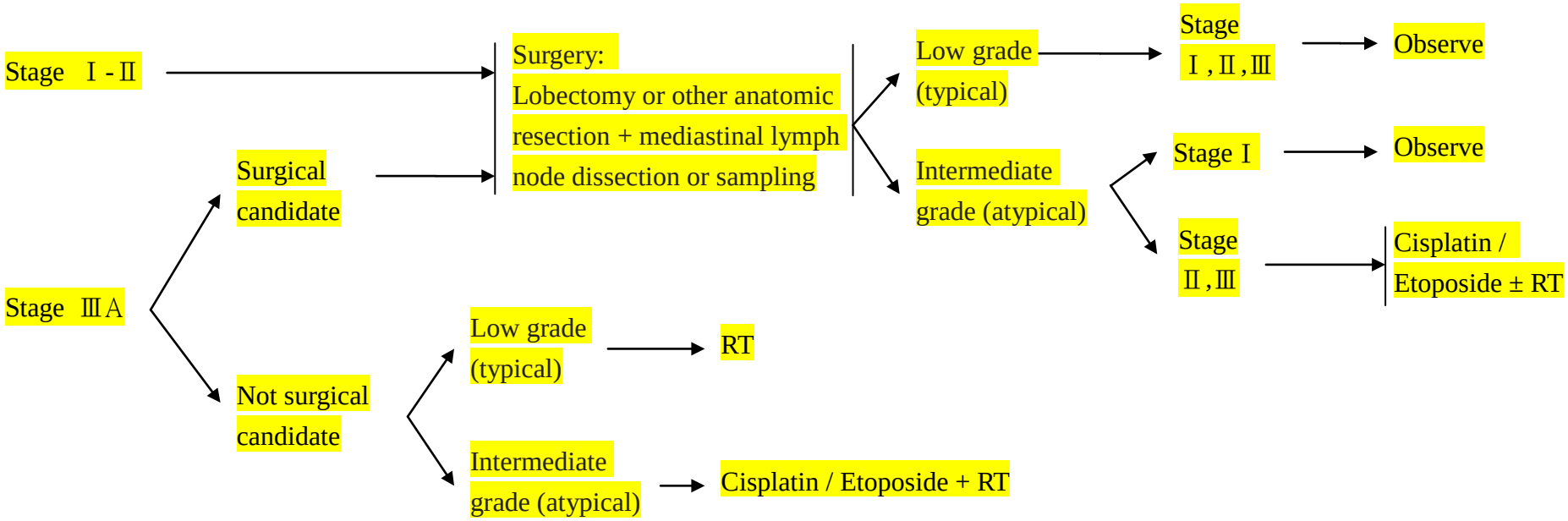


Prophylactic Cranial Irradiation (PCI)is recommended for patients with either limited-stage or extensive-stage disease who attain a complete or partial response. The recommended regimens for PCI include: 25 Gy in 10 daily fractions (2.5 Gy/fraction), 30 Gy in 10-15 daily fractions, or 24Gy in 8 daily fractions.



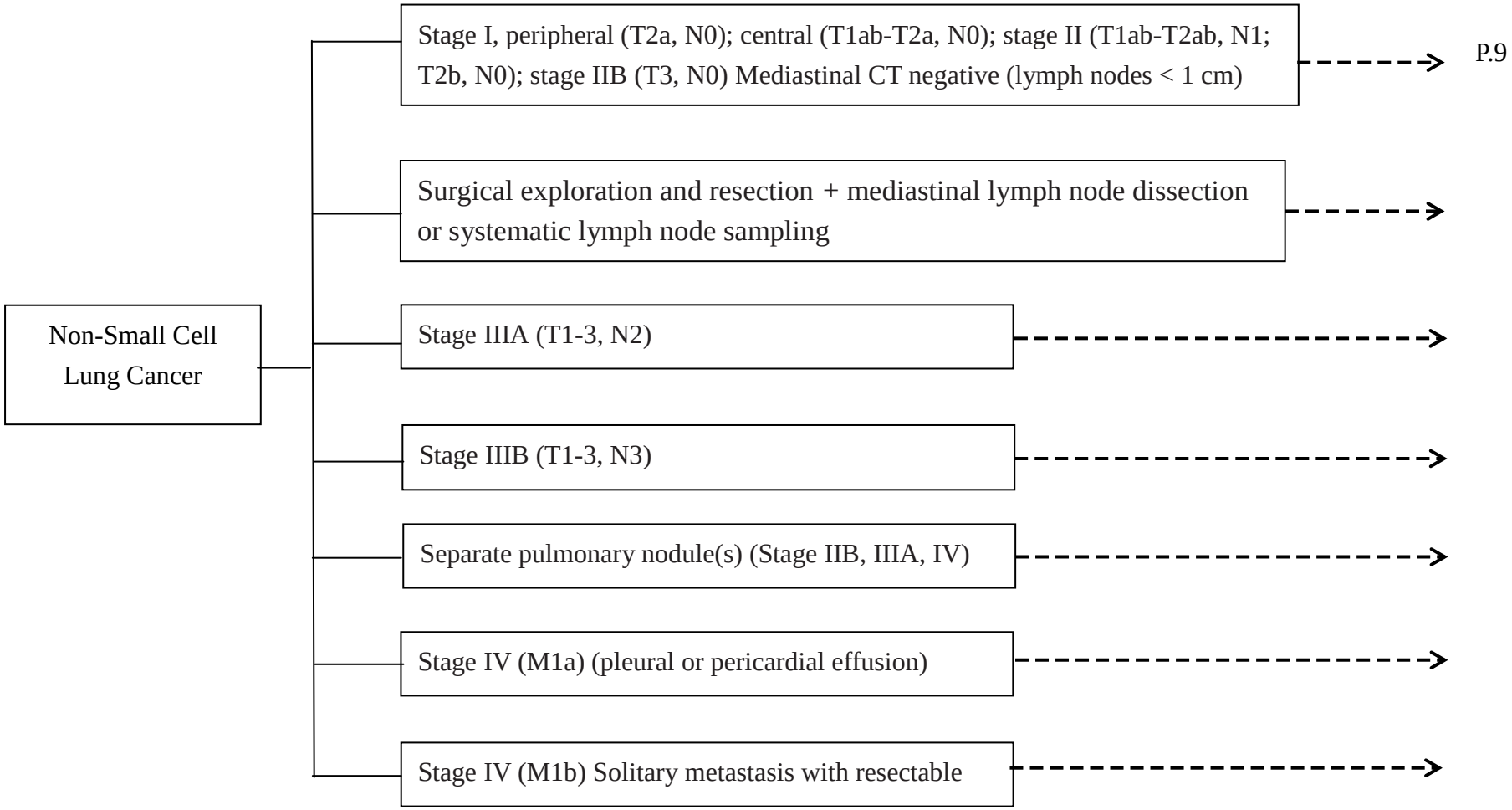
Prophylactic Cranial Irradiation (PCI) is recommended for patients with either limited-stage or extensive-stage disease who attain a complete or partial response. The recommended regimens for PCI include: 25 Gy in 10 daily fractions (2.5 Gy/fraction), 30 Gy in 10-15 daily fractions, or 24Gy in 8 daily fractions.

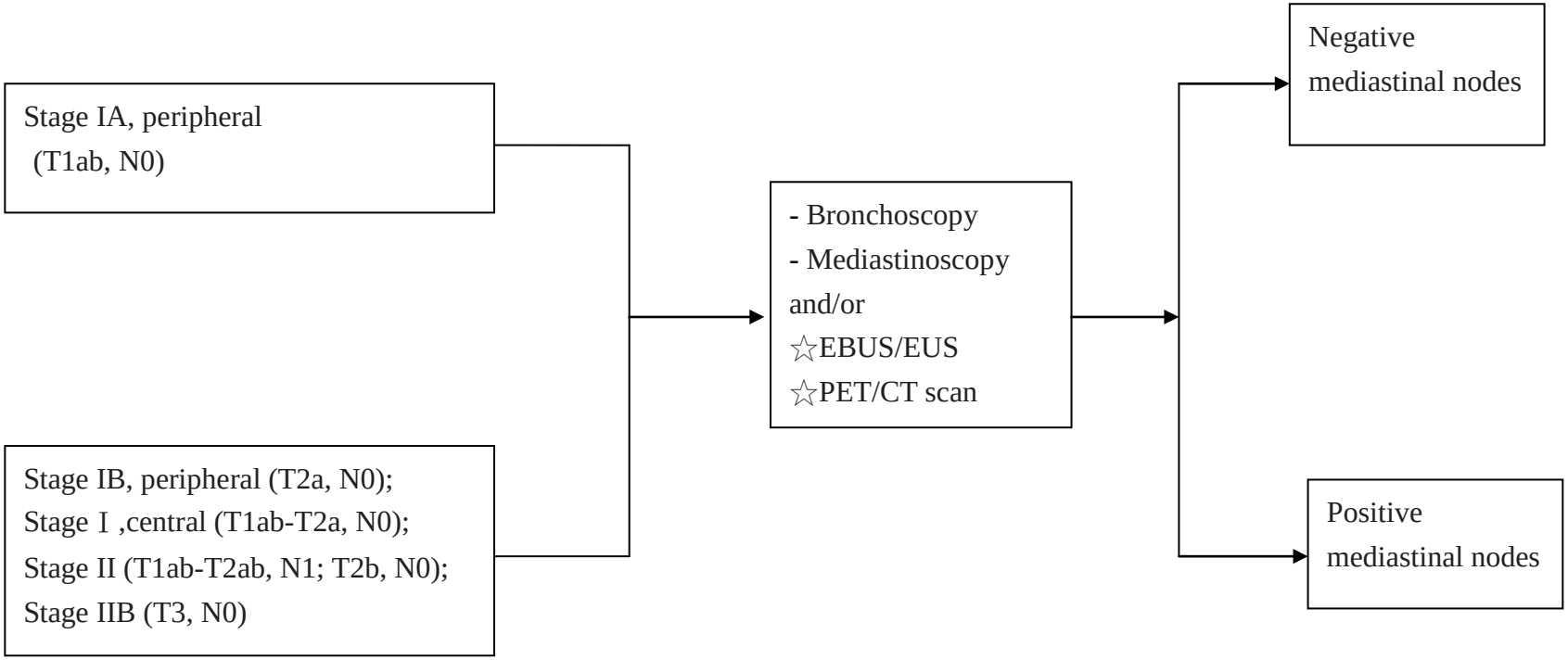

Biopsy
Low-grade neuroendocrine carcinoma (typical carcinoid)
Intermediate- grade neuroendocrine carcinoma (atypical carcinoid)
High-grade neuroendocrine carcinoma (large-cell neuroendocrine carcinoma)
High-grade neuroendocrine carcinoma (small-cell carcinoma)
Combined SCLC and NSCLC
Clinical Stage
Stage Ⅰ-ⅢA
Stage ⅢB (except T4 due to multiple lung nodules)
Stage ⅢB (T4 due to multiple lung nodules) or Ⅳ
Treat per Non-Small Cell Lung Cancer Guidelines
Treat per Small Cell Lung Cancer Guidelines
Treat per Small Cell Lung Cancer Guidelines

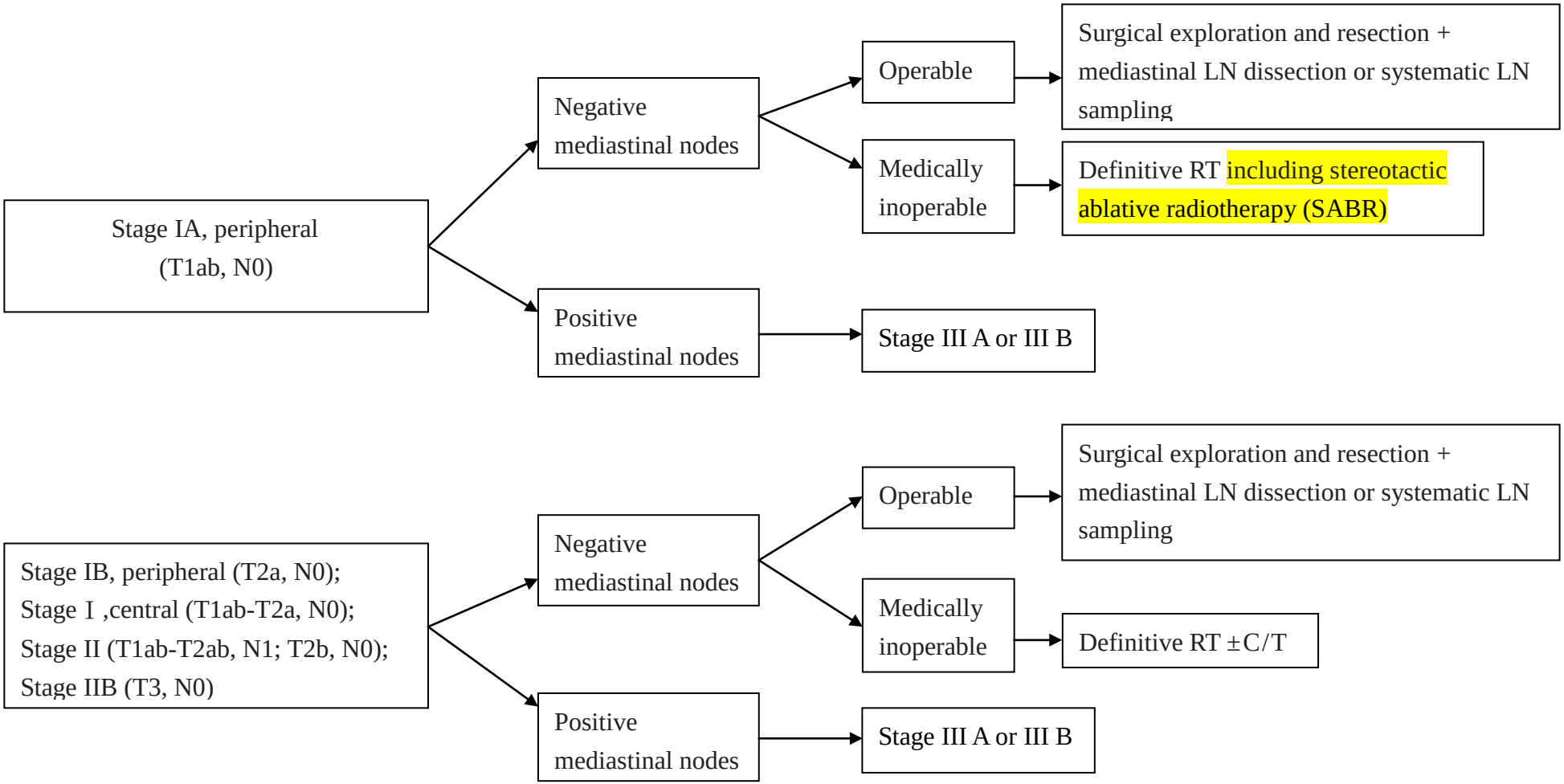


Stage ⅢB (except T4 due to multiple lung nodules) → Cisplatin / Etoposide ± RT

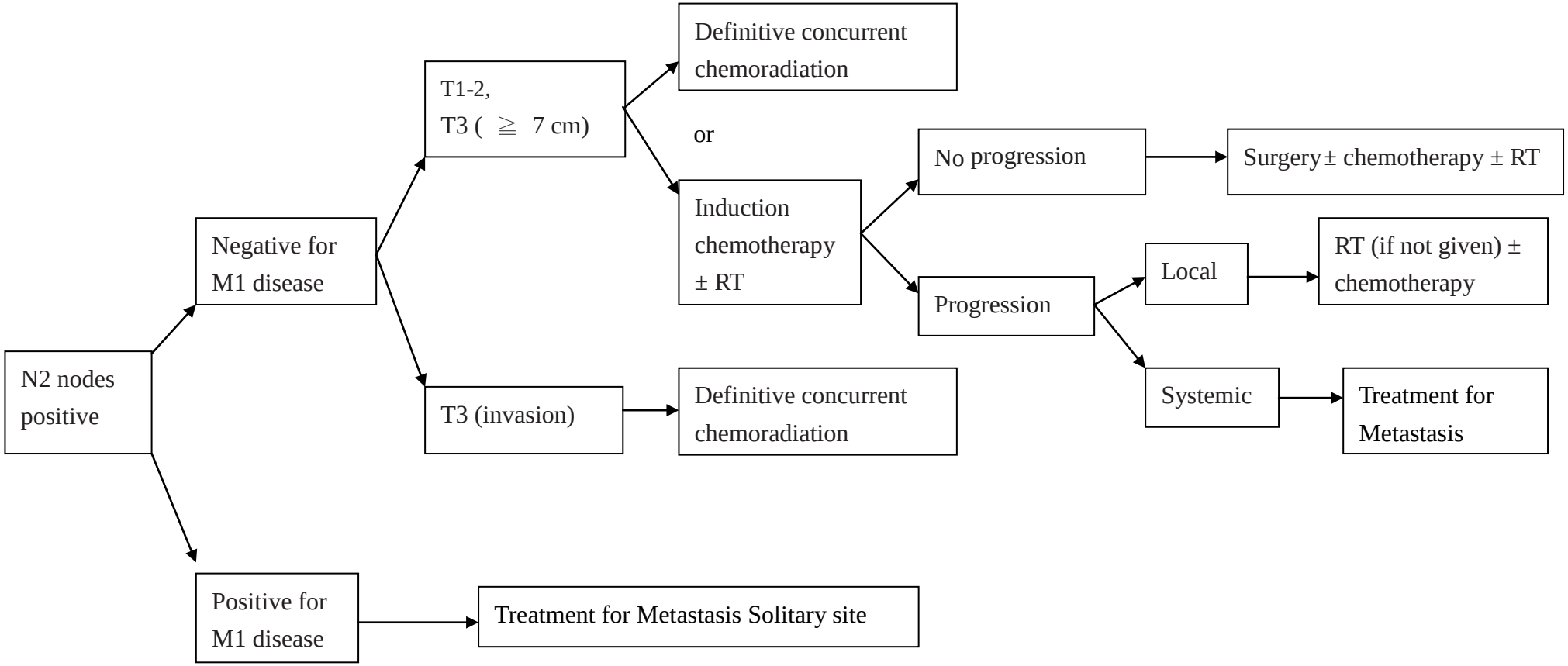
Stage ⅢB (T4 due to multiple lung nodules) or Ⅳ →
Systemic therapy
Consider octreotide (including LAR), if octreotide scan positive or symptoms of carcinoid syndrome

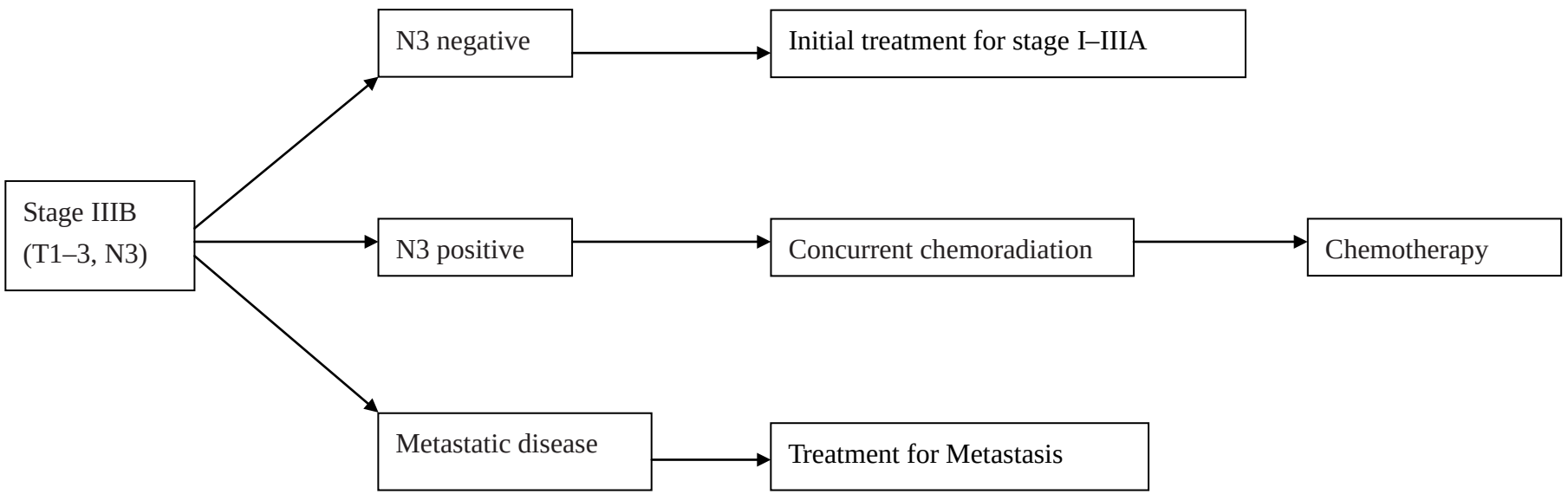

Non-Small Cell Lung Cancer
Stage I, peripheral (T2a, N0); central (T1ab-T2a, N0); stage II (T1ab-T2ab, N1; T2b, N0); stage IIB (T3, N0) Mediastinal CT negative (lymph nodes < 1 cm)
P.9
Surgical exploration and resection + mediastinal lymph node dissection or systematic lymph node sampling
Stage IIIA (T1-3, N2)
Stage IIIB (T1-3, N3)
Separate pulmonary nodule(s) (Stage IIB, IIIA, IV)
Stage IV (M1a) (pleural or pericardial effusion)
Stage IV (M1b) Solitary metastasis with resectable

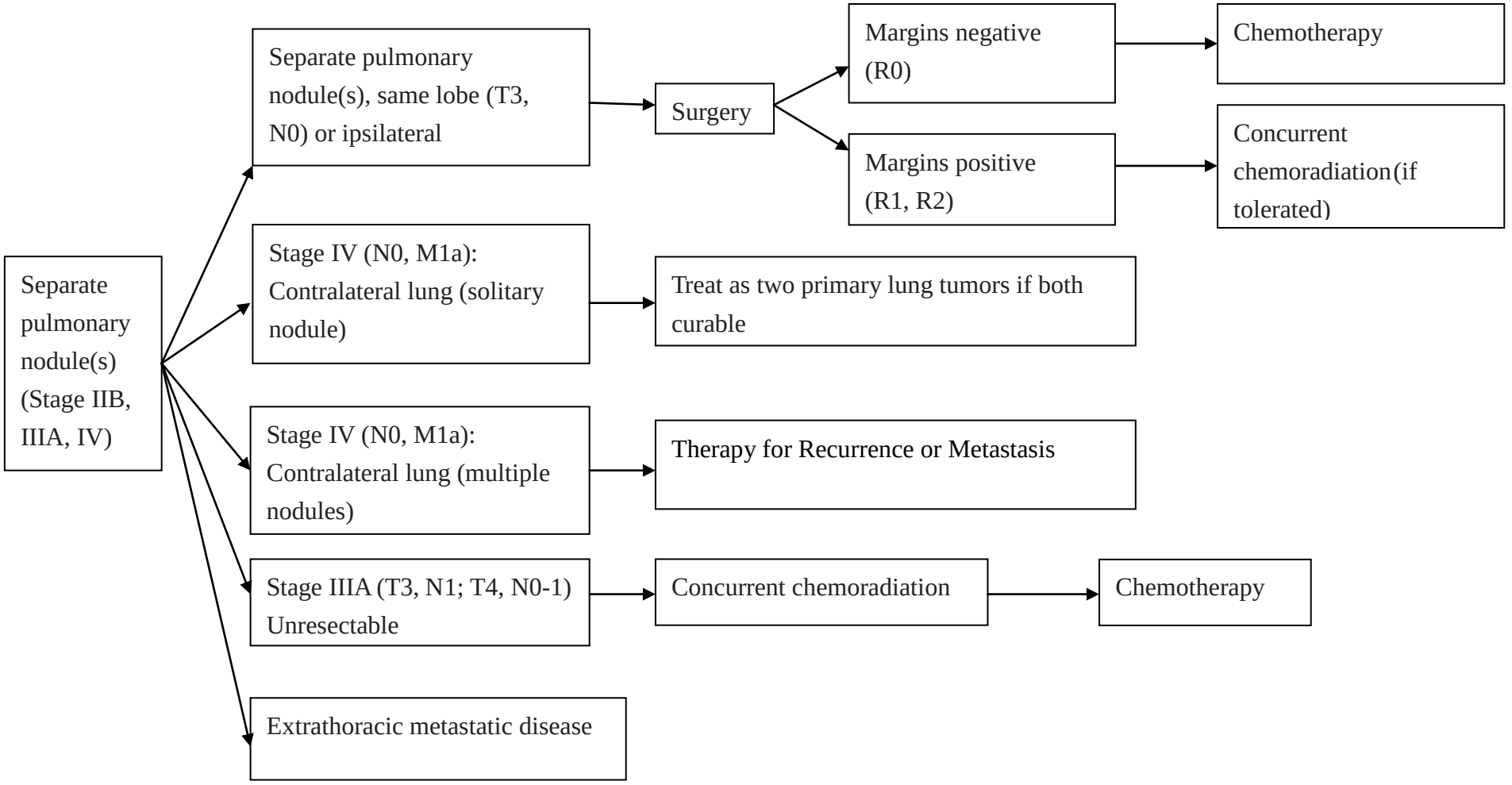

Stage IA, peripheral
(T1ab, N0)
Stage IB, peripheral (T2a, N0);
Stage Ⅰ,central (T1ab-T2a, N0);
Stage II (T1ab-T2ab, N1; T2b, N0);
Stage IIB (T3, N0)
- Bronchoscopy
- Mediastinoscopy
and/or
☆EBUS/EUS
☆PET/CT scan
Negative
mediastinal nodes
Positive
mediastinal nodes

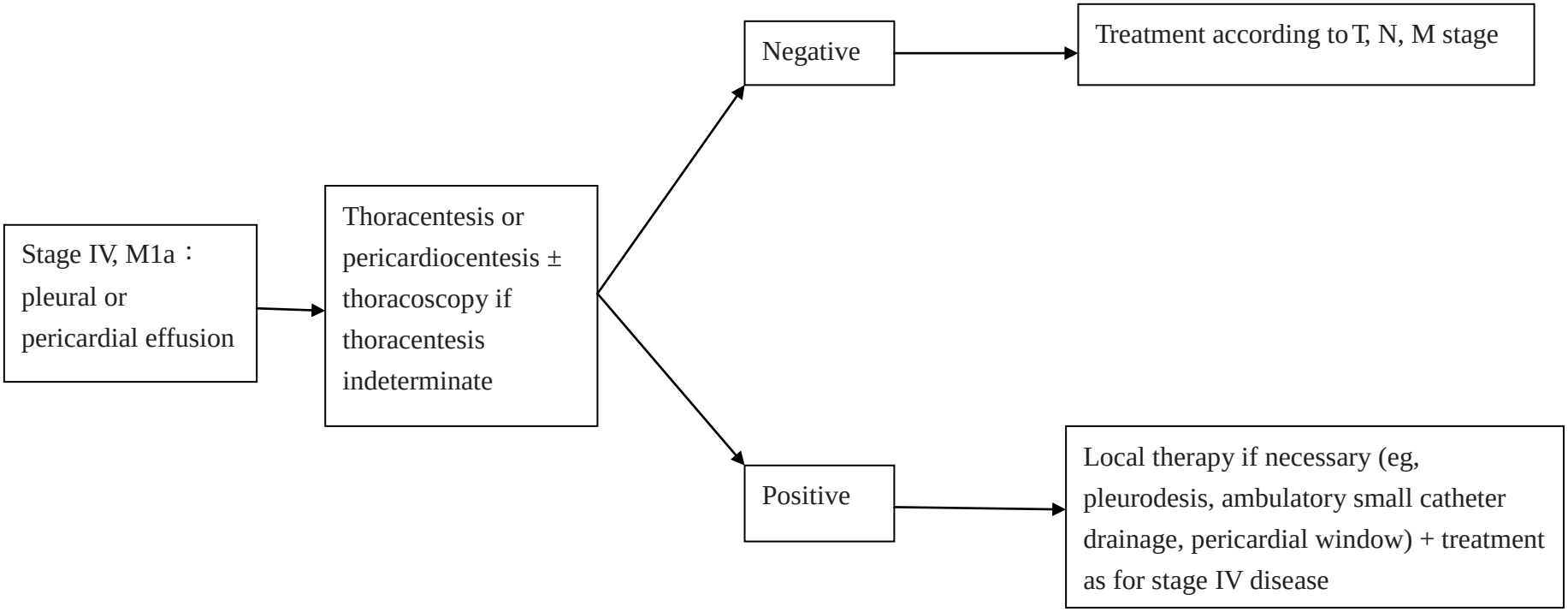

Stage IA, peripheral (T1ab, N0)
Negative mediastinal nodes
Operable
Surgical exploration and resection + mediastinal LN dissection or systematic LN sampling
Medically inoperable
Definitive RT including stereotactic ablative radiotherapy (SABR)
Positive mediastinal nodes
Stage III A or III B
Stage IB, peripheral (T2a, N0);
Stage Ⅰ,central (T1ab-T2a, N0);
Stage II (T1ab-T2ab, N1; T2b, N0);
Stage IIB (T3, N0)
Negative mediastinal nodes
Operable
Surgical exploration and resection + mediastinal LN dissection or systematic LN sampling
Medically inoperable
Definitive RT ±C/T
Positive mediastinal nodes
Stage III A or III B

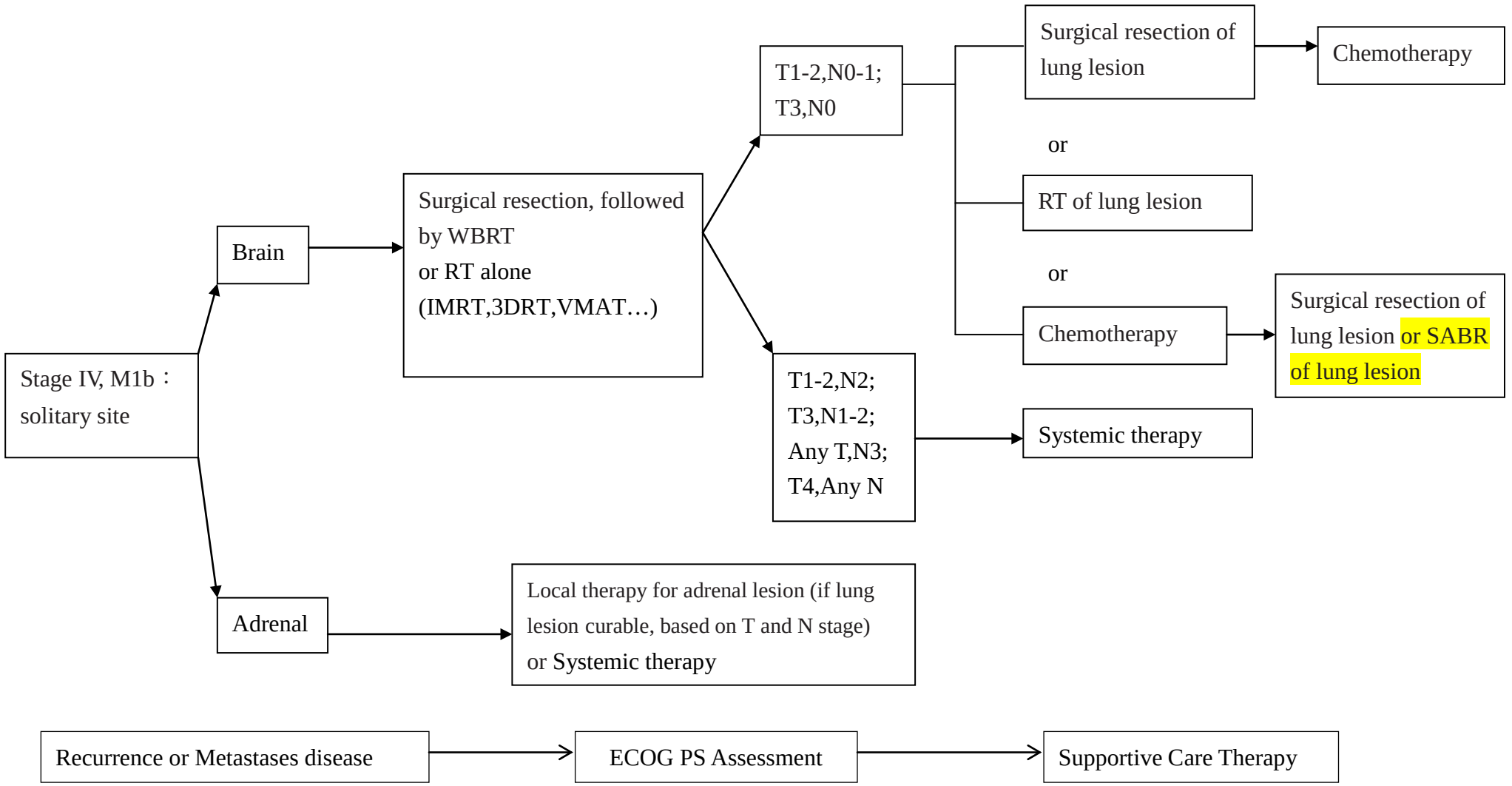
Stage IIIA (T1–3, N2)




Stage IIIB
(T1–3, N3)
N3 negative
Initial treatment for stage I–IIIA
N3 positive
Concurrent chemoradiation
Chemotherapy
Metastatic disease
Treatment for Metastasis


Separate pulmonary nodule(s) (Stage IIB, IIIA, IV)
Separate pulmonary nodule(s), same lobe (T3, N0) or ipsilateral
Surgery
Margins negative (R0)
Chemotherapy
Margins positive (R1, R2)
Concurrent chemoradiation(if tolerated)
Stage IV (N0, M1a): Contralateral lung (solitary nodule)
Treat as two primary lung tumors if both curable
Stage IV (N0, M1a): Contralateral lung (multiple nodules)
Therapy for Recurrence or Metastasis
Stage IIIA (T3, N1; T4, N0-1) Unresectable
Concurrent chemoradiation
Chemotherapy
Extrathoracic metastatic disease

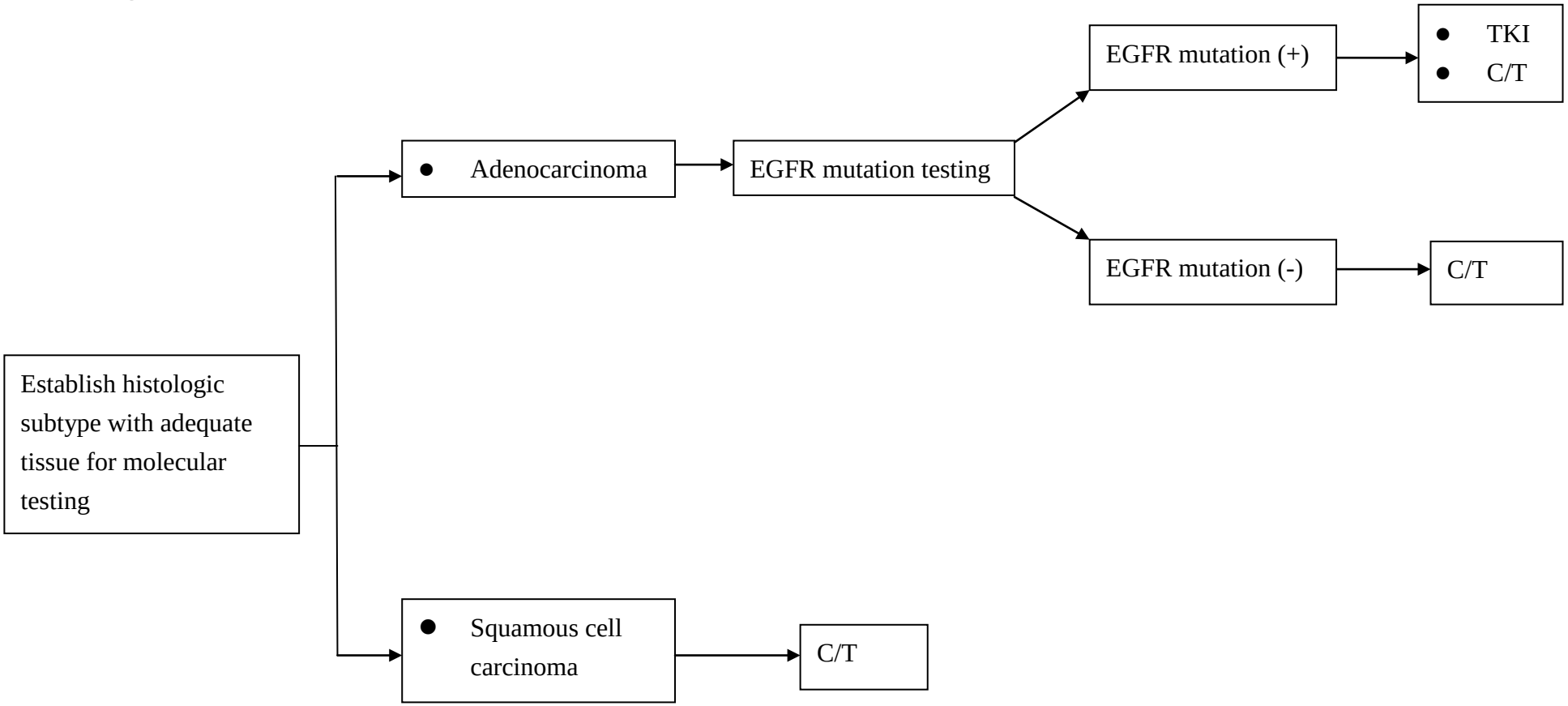

Stage IV, M1a：
pleural or
pericardial effusion
Thoracentesis or
pericardiocentesis ±
thoracoscopy if
thoracentesis
indeterminate
Negative
Treatment according to T, N, M stage
Positive
Local therapy if necessary (eg,
pleurodesis, ambulatory small catheter
drainage, pericardial window) + treatment
as for stage IV disease


Stage IV, M1b：
solitary site
Brain
Surgical resection, followed by WBRT
or RT alone
(IMRT,3DRT,VMAT…)
T1-2,N0-1;
T3,N0
Surgical resection of lung lesion
Chemotherapy
or
RT of lung lesion
or
Chemotherapy
Surgical resection of lung lesion or SABR of lung lesion
T1-2,N2;
T3,N1-2;
Any T,N3;
T4,Any N
Systemic therapy
Adrenal
Local therapy for adrenal lesion (if lung lesion curable, based on T and N stage)
or Systemic therapy
Recurrence or Metastases disease
ECOG PS Assessment
Supportive Care Therapy

Surgical exploration and resection + mediastinal lymph node dissection or systematic lymph node sampling

Stage IA		Stage IB	Stage IIA	Stage IIA	Stage IIB	Stage IIIA	
T1ab, N0		T2a, N0	T2b, N0	T1ab-T2a, N1	T3, N0; T2b, N1	T1-3, N2; T3 [>7 cm], N1	
Margins(-) R0	Margins(+) R1.R2	Margins(-) R0	Margins(+) R1.R2	Margins(-) R0	Margins(+) R1.R2	Margins(-) R0	Margins(+) R1.R2 or nodal ECE
Observe	Reresection(preferred) or RT	Observe	Reresection(preferred) ± C/T or RT±C/T (C/T for stage IIA)	C/T	Reresection + C/T or CCRT +C/T	C/T or RT(N2 only)	CCRT+C/T

Stage ⅢB or Ⅳ


Establish histologic subtype with adequate tissue for molecular testing
Adenocarcinoma
EGFR mutation testing
EGFR mutation (+)
TKI
C/T
EGFR mutation (-)
C/T
Squamous cell carcinoma
C/T

CHEMOTHERAPY REGIMENS FORNEOADJUVANT AND ADJUVANT THERAPY

(Non-Small Cell Carcinoma)

- Cisplatin 50 mg/m^2 days 1 and 8; vinorelbine 25 mg/m^2 days 1, 8, 15, 22, every 28 days for 4 cycles*
- Cisplatin 75 mg/m^2 on day 1; gemcitabine 1250 mg/m^2 on days 1, 8 every 21 days for 4 cycles *
- Cisplatin 75 mg/m^2; docetaxel 75 mg/m^2 every 21 days for 4 cycles *

Chemotherapy Regimens for patients with comorbidities or patients not able to tolerate cisplatin Paclitaxel 200 mg/m^2 on day 1, carboplatin AUC 6 on day 1, every 21 days*

*These regimens can be used as neoadjuvant chemotherapy. They are to be given for 3 cycles prior to localized therapy. See Discussion for further information and references.

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CHEMOTHERAPY REGIMENS USED WITH RADIATION THERAPY (Non-small cell carcinoma)

Concurrent Chemotherapy/RT Regimens

- Cisplatin 50 mg/m^2 on day 1, 8, 29, and 36; etoposide 50 mg/m^2 days 1-5, 29-33; concurrent thoracic RT (preferred)**
- Cisplatin 75mg/m2 on day1, Pemetrexed 500mg/m2 on day 1 every 21 days for 4 cycles; concurrent thoracic RT (nonsquamous) (Option)
- Carboplatin AUC 5 on day1, Pemetrexed 500mg/m2 on day 1 every 21 days for 4 cycles; concurrent thoracic RT (nonsquamous) (Option)

*There are data that support full-dose cisplatin over carboplatin-based regimens. Carboplatin regimens have not been adequately tested.

**These regimens can be used as neoadjuvant chemoradiotherapy. Cisplatin and etoposide is the preferred regimen. If weekly carboplatin and paclitaxel is used because the patient is not able to tolerate concurrent full-dose cisplatin and radiotherapy, the treating physician should consider 3 cycles of full-dose platinum therapy after local treatment is completed.

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.非小細胞肺癌健保化療藥物適用細胞型態一覽表

	Adenocarcinoma	Squamous Cell Ca	Adjuvant C/T
Taxotere (Docetaxel)	V	V	
Gemzar	V	V	
Paclitaxel (Taxol)	V (+ cis)	V	
Vinorelbine	V	V	V (+cis x 4 courses)
U-Fur	V	V	V (T2,>3cm x 2yrs)
Alimta	V		
Iressa (Gefitinib)	V		
Tarceva (Erlotinib)	V	V (第三線)	
Afatinib(Giotrif)	V		

（底線部分需事先申請）

CHEMOTHERAPY REGIMENS FOR ADJUVANT THERAPY (Small cell carcinoma)

Limited stage (maximum of 4-6 cycles)

- Cisplatin 60 mg/m^2 day 1 and etoposide 120 mg/m^2 days 1, 2, 3
- Cisplatin 80 mg/m^2 day 1 and etoposide 100 mg/m^2 days 1, 2, 3
- Carboplatin AUC 5-6 day 1 and etoposide 100 mg/m^2 days 1, 2, 3
- During chemotherapy + RT, cisplatin/etoposide is recommended
- The use of myeloid growth factors is not recommended during concurrent chemotherapy plus radiotherapy.

Extensive stage (maximum of 4-6 cycles)

- Cisplatin 75 mg/m^2 day 1 and etoposide 100 mg/m^2 days 1, 2, 3
- Cisplatin 80 mg/m^2 day 1 and etoposide 80 mg/m^2 days 1, 2, 3
- Cisplatin 25 mg/m^2 days 1, 2, 3 and etoposide 100 mg/m^2 days 1, 2, 3
- Carboplatin AUC 5-6 day 1 and etoposide 100 mg/m^2 days 1, 2, 3
- Cisplatin 60 mg/m^2 day 1 and irinotecan 60 mg/m^2 days 1, 8, 15
- Cisplatin 30 mg/m^2 and irinotecan 65 mg/m^2 days 1, 8
- Carboplatin AUC 5 day 1 and Irinotecan 50 mg/m^2 days 1, 8, and 15

Subsequent chemotherapy:

- Clinical trial preferred.
- Relapse < 2-3 mo, PS 0-2：paclitaxel、docetaxel、topotecan PO or IV、irinotecan、temozolomide 75mg/m^2/day x 21 days、ifosfamide、gemcitabine
- Relapse > 2-3 mo up to 6 mo topotecan ：PO or IV (category 1)、paclitaxel、docetaxel、irinotecan、gemcitabine、vinorelbine、oral etoposide、temozolomide mg/m2 day x 21 days 75cyclophosphamide/doxorubicin/vincristine (CAV)
- Relapse > 6 mo：original regimen

Consider dose reductions versus growth factors in the poor performance status patient.

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肺癌放射線治療政策

Non-Small Cell Lung Cancer

I-II Operable: Adjuvant RT is not indicated except for + margin (PORT meta-analysis Level I)

I-II Inoperable:

Definitive RT .

C/T, if patient can tolerate, maybe added as induction, adjuvant , or concurrent.

IIIA Operable

Post-OP C/T , (+, -) RT indicated for close/+ margin, nodal ECE (SEER, Level IV)

Alterantively, neoadjuvant CCRT followed by re-staging and surgery (SWOG 8805, Level III). Pre-OP RT alone is not recommended for resectable disease (GradeA)

III Inoperable

Combined C/T and RT(prefer)

Radiation Technique

- **Adjuvant**

CTV: Involved LN region ± ipsilateral hilum ± subcarinal LN region to 50.4 Gy depending on the extent of node dissection, number, bulk, and location of mediastinal disease and primary tumor. 10–16 Gy boost if extranodal extension with gross residual disease, at least 66Gy, concurrent C/T should be considered (Level II)

- **Definitive Radiation**

At least 66GY with conventional fractionation, concurrent C/T should be considered

GTV is visible tumor on imaging including all nodes on CT >= 1 cm, or PET/CT (+)

CTV is the region of microscopic disease spread. It expands the GTV by 10-15 mm

PTV: add 0.5–1.5 cm margin on CTV to account for set-up uncertainties and respiratory motion.

IMRT may be advantageous as it better limits dose to normal lung as compared to conventional delivery.

Small Cell Lung Cancer

- **Limited Stage**

ECOG 0-2 CCRT (prefer)

Prophylactic Cranial Irradiation (PCI) is part of the standard treatment for SCLC with complete response after treatment (Grande A)

PCI is also recommended for SCLC with partial response after treatment. (Grade B)

- **Extensive Stage**

Chemotherapy is the mainstay treatment of extensive stage SCLC (Grade A)

Radiotherapy is usually reserved for palliation.

PCI should be considered in all SCLC patients who achieve response to C/T (Grade A, EORTC, Level I)

- **Radiation Technique**

GTV is visible tumor on imaging including all nodes on CT >= 1 cm, or PET/CT (+)

CTV is the region of microscopic disease spread. It expands the GTV by 10-15 mm

PTV: add 0.5–1.5 cm margin on CTV to account for set-up uncertainties and respiratory motion.

Dose: With conventional fractionation, 54Gy or higher should be considered (Grade B)

執行程序(procedures)

Simulation for Lung Cancer

Immobilize with a with customized immobilization device (with arms up). 4D planning is preferred.

Dose Limiting Structures

Spinal Cord:
Dose of radiation to the spinal cord should be limited to 45 Gy (1.8–2.0 Gy daily) (Level I)

Esophagus: Dose to the esophagus should be limited to 60 Gy for 1/3 of the esophagus, or 55 Gy for the 2/3 of the esophagus. 45Gy for the entire esophagus

Heart: V40 of the heart should be limited to 50% or less.
Lung: V20 of bilateral lung should be limited to < =30% as probability of pneumonitis increases rapidly when more than V20 >30% (Level III).

References

1.Decision Making in Radiation Oncology, V1-2, L.W. Brady, H.-P. et al, 2011

2.Handbook of Evidence-Based Radiation Oncology, Eric K. Hansen et al, 2010

PRIMARY TUMOR (T)	
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Tis	Tis Carcinoma in situ
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)*
T1a	Tumor≦ 2 cm in greatest dimension
T1b	Tumor > 2 cm but ≦3 cm in greatest dimension
T2	Tumor > 3 cm but ≦7 cm or tumor with any of the following features (T2 tumors with these features are classified T2a if ≦ 5 cm) Involves main bronchus, ≧2 cm distal to the carina Invades visceral pleura (PL1 or PL2) Associated with atelectasis or obstructive pneumonitis that extends to the hilar region but does not involve the entire lung
T2a	Tumor > 3 cm but ≦5 cm in greatest dimension
T2b	Tumor > 5 cm but ≦7 cm in greatest dimension
T3	Tumor > 7 cm or one that directly invades any of the following: parietal pleural (PL3) chest wall (including superior sulcus tumors), diaphragm, phrenic nerve, mediastinal pleura, parietal pericardium; or tumor in the main bronchus (< 2 cm distal to the carina* but without involvement of the carina; or associated atelectasis or obstructive pneumonitis of the entire lung or separate tumor nodule(s) in the same lobe
T4	Tumor of any size that invades any of the following: mediastinum, heart, great vessels, trachea, recurrent laryngeal nerve, esophagus, vertebral body, carina, separate tumor nodule(s) in a different ipsilateral lobe
* The uncommon superficial spreading tumor of any size with its invasi vecomponent limited to the bronchial wall, which may extend proximally to the main bronchus, is also classified as T1a.	

REGIONAL LYMPH NODES (N)	
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)

DISTANT METASTASIS (M)	
M0	No distant metastasis (no pathologic M0; use clinical M to complete stage group)
M1	Distant metastasis
M1a	Separate tumor nodule(s) in a contralateral lobe; tumor with pleural nodules or malignant pleural (or pericardial) effusion**
M1b	Distant metastasis
**Most pleural (and pericardial) effusions with lung cancer are due to tumor. In a few patients, however, multiple cytopathologic examinations of pleural (pericardial) fluid are negative for tumor, and the fluid is nonbloody and is not an exudate. Where these elements and clinical judgement dictate that the effusion is not related to the tumor, the effusion should be excluded as a staging element and the patient should be classified as M0.	

STAGE			
GROUP	T	N	M
Occult	TX	N0	M0
0	Tis	N0	M0
IA	T1a	N0	M0
	T1b	N0	M0
IB	T2a	N0	M0
IIA	T2b	N0	M0
	T1a	N1	M0
	T1b	N1	M0
	T2a	N1	M0
IIB	T2b	N1	M0
	T3	N0	M0
IIIA	T1a	N2	M0
	T1b	N2	M0
	T2a	N2	M0
	T2b	N2	M0
	T3	N1	M0
	T3	N2	M0
	T4	N0	M0
	T4	N1	M0

`STAGE			
GROUP	T	N	M
IIIB	T1a	N3	M0
	T2b	N3	M0
	T2a	N3	M0
	T2b	N3	M0
	T3	N3	M0
	T4	N2	M0
	T4	N3	M0
IV	Any T	Any N	M1a
	Any T	Any N	M1b
Stage unknown			

9.9. Vinorelbine：(91/1/1、95/6/1、96/9/1、101/3/1)

1. 限用於：

(1) 晚期或無法手術切除之非小細胞肺癌及轉移性乳癌病患。

(2) 病理分期第二期及第三期前半(stage II & stage IIIA)非小細胞肺癌於接受根治性手術後與鉑金類藥品併用之輔助治療，需事前審查後使用，最長以 4 療程為限。

2. 本成分之口服劑型與注射劑型不得併用。

9.11. Uracil-Tegafur：(如 Ufur)(100/1/1)

3. 與 cisplatin 併用治療轉移及末期肺癌。

5. 用於病理分期為 T2 且腫瘤≧3cm 之肺腺癌病人，作為手術後輔助治療，使用期限以二年為限。(100/1/1)

9.24. Gefitinib (如 Iressa):(93/11/1、96/8/1、96/11/1、100/6/1、101/5/1、101/10/1)

1. 限單獨使用於

(1)具有 EGFR-TK 基因突變之局部侵犯性或轉移性(即第ⅢB 期或第Ⅳ期)之肺腺癌病患之第一線治療。(100/6/1)

(2)先前已使用過第一線含鉑化學治療，或 70 歲(含)以上接受過第一線化學治療，但仍局部惡化或轉移之肺腺癌。(96/11/1、100/6/1)

2. 需經事前審查核准後使用：

(1)用於第一線用藥：檢具確實患有肺腺癌之病理或細胞檢查報告，及 EGFR-TK 基因突變檢測報告。(100/6/1)

(2)用於第二線以上用藥：檢具確實患有肺腺癌之病理或細胞檢查報告，並附曾經接受第一線含鉑化學治療，或 70 歲(含)以上接受過第一線化學治療之證明，及目前又有疾病惡化之影像診斷證明（如胸部 X 光、電腦斷層或其他可作為評估的影像），此影像證明以可測量（measurable）的病灶為優先，如沒有可以測量的病灶，則可評估（evaluable）的病灶亦可採用。(96/11/1、100/6/1)

(3) 每次申請事前審查之療程以三個月為限，每三個月需再次申請，再次申請時並需附上治療後相關臨床資料，如給藥四週後，需追蹤胸部 X 光或電腦斷層等影像檢查一遍，評估療效，往後每四週做胸部 X 光檢查，每隔八週需追蹤其作為評估藥效的影像（如胸部 X 光或電腦斷層）(101/5/1)。

3. 醫師每次開藥以 4 週為限。
4. 本藥品與 erlotinib（如 Tarceva）不得併用。(96/8/1)

9.29.Erlotinib（如 Tarceva）:(96/6/1、96/8/1、97/6/1、101/5/1、102/4/1)

1. 限單獨使用於
   (1) 已接受 4 個週期 platinum 類第一線化學療法後，腫瘤範圍穩定(stable disease，不含 partial response 或 complete response)之局部晚期或轉移性肺腺癌的維持療法。(102/4/1)
   (2) 先前已使用過 platinum 類第一線化學治療，或 70 歲(含)以上接受過第一線化學治療，但仍局部惡化或轉移之腺性非小細胞肺癌之第二線用藥。(97/6/1)
   (3) 先前已使用過 platinum 類及 docetaxel 或 paclitaxel 化學治療後，但仍局部惡化或轉移之非小細胞肺癌之第三線用藥。
2. 需經事前審查核准後使用，若經事前審查核准，因臨床治療需轉換同成份不同含量品項，得經報備後依臨床狀況轉換使用，惟總使用期限不得超過該次申請事前審查之療程期限。(97/6/1)
   (1) 用於已接受 platinum 類第一線化學療法後，病情穩定之維持療法：檢具確實患有肺腺癌之病理或細胞檢查報告，並附已接受 4 個週期 platinum 類第一線化學療法後，腫瘤範圍穩定(stable disease，不含 partial response 或 complete response)之影像診斷證明（如胸部 X 光、電腦斷層或其他可作為評估的影像）。(102/4/1)
   (2) 用於第二線用藥：檢具確實患有非小細胞肺癌之病理或細胞檢查報告，並附曾經接受 platinum 類第一線化學治療，或 70 歲(含)以上接受過第一線化學治療之證明，及目前又有疾病惡化之影像診斷證明（如胸部 X 光、電腦斷層或其他可作為評估的影像），此影像證明以可測量（measurable）的病灶為優先，如沒有可

以測量的病灶，則可評估（evaluable）的病灶亦可採用。（97/6/1）

(3) 用於第三線用藥：檢具確實患有非小細胞肺癌之病理或細胞檢查報告，並附曾經接受第一線及第二線化學藥物如 platinum（cisplatin 或 carboplatin）與 taxanes（paclitaxel 或 docetaxel）治療之證明，及目前又有疾病惡化之影像診斷證明（如胸部 X 光、電腦斷層或其他可作為評估的影像）， 此影像證明以可測量(measurable)的病灶為優先，如沒有可以測量的病灶，則可評估(evaluable)的病灶亦可採用。(97/6/1)

(4) 每次申請事前審查之療程以三個月為限，每三個月需再次申請，再次申請時並需附上治療後相關臨床資料，如給藥四週後，需追蹤胸部 X 光或電腦斷層等影像檢查一遍，評估療效，往後每四週做胸部 X 光檢查，每隔八週需追蹤其作為評估藥效的影像（如胸部 X 光或電腦斷層）。(101/5/1)

3. 醫師每次開藥以 4 週為限。
4. 本藥品與 erlotinib（如 Tarceva）不得併用。(96/8/1)

9.45. Afatinib（如 Giotrif）：(103/5/1)

1. 限單獨使用於具有 EGFR-TK 基因突變之局部晚期或轉移性(即第ⅢB 期或第Ⅳ期)之肺腺癌病患之第一線治療。
2. 需經事前審查核准後使用，若經事前審查核准，因臨床治療需轉換同成分不同含量品項，得經報備後依臨床狀況轉換使用，惟總使用期限不得超過該次申請事前審查之療程期限。
   (1)檢具確實患有肺腺癌之病理或細胞檢查報告，及 EGFR-TK 基因突變檢測報告。
   (2)每次申請事前審查之療程以三個月為限，每三個月需再次申請，再次申請時並需附上治療後相關臨床資料，如給藥四週後，需追蹤胸部 X 光或電腦斷層等影像檢查一遍，評估療效，往後每四週做胸部 X 光檢查，每隔八週需追蹤其作為評估藥效的影像（如胸部 X 光或電腦斷層）
3. 使用本藥品後，除因耐受性不良，否則不得轉換類似藥理機轉之其他酪胺酸激 酶阻斷劑 (tyrosine kinase inhibitor, TKI)。
4. 醫師每次開藥以 4 週為限。

5. 本藥品與 gefitinib（如 Iressa）及 erlotinib(如 Tarceva)不得併用。