- 前言:

癌症是國人十大死因的第一名，其中又以肺癌在癌症死亡排名中一直名列前茅，對於國民健康是一大威脅。肺癌不易早期診斷，大部分在診斷時已是晚期，所以治療成績不佳，死亡率高。儘管近年來健檢風氣盛行，然而定期胸部X光檢查或是電腦斷層檢查，是否就能提高早期診斷的比例而減少肺癌的死亡率，目前仍未有定論，如何早期診斷以提高治癒率，是目前重要的課題。

以治療的方式區分，肺癌可分為「小細胞肺癌」及「非小細胞肺癌」；小細胞肺癌以化學治療為主，較少見；非小細胞肺癌則以手術切除為主，大部分的肺癌屬此類。近年來，在手術、放射線及藥物治療的進步之下，肺癌的治療成績有長足的進展，尤其是在非小細胞肺癌部分，經由標靶治療的問世，在東亞地區，顯著的提升了肺癌的治療成績，也大大的改變了治療風貌，更進一步使得醫師及科學家們，對於肺癌的腫瘤生物學及不同人種之間腫瘤表現及治療上的差異，有更深切的了解。

以肺癌當中佔大多數的非小細胞肺癌來說，手術仍是治療的首選，在手術技術以及術後照顧的進步之下，開刀不再令人望而生畏，年齡也不再是開刀的障礙，高齡患者經由開刀而治癒的比例逐漸增加；對於局部晚期，無法以手術切除的非小細胞肺癌，放射線則是治療的主力，近年來由於放射線治療技術的進步，藉由「強度調控放射線治療」或是「導航螺旋刀」等新技術，使得放射線能量能夠更精準的給予，提升療效、減少併發症，嘉惠了更多的患者。

藥物治療方面，不但化學治療的效果提高、副作用降低，標靶治療的加入，更是改變治療的風貌。對於已經手術可完整切除的非小細胞肺癌，術後的輔助性化療已證實能提高治癒率；對局部晚期無法切除的腫瘤，強而有力的藥物治療也提高了手術完整切除的機會；對於轉移性疾病，雖然仍無法治癒，但是生活品質的提升及時間的大幅延長，都是很大的進步。

儘管肺癌的治療在多年來得到很大的進步，然而肺癌的死亡率仍居高不下，有賴臨床醫師及研究團隊持續的努力，提早診斷、有效治療，期能得到更好的結果。

本共識依下列參考資料修改版本：

•NCCN Clinical Practice Guidelines in Oncology- Non- Small cell Lung cancer. Version 2.2013.

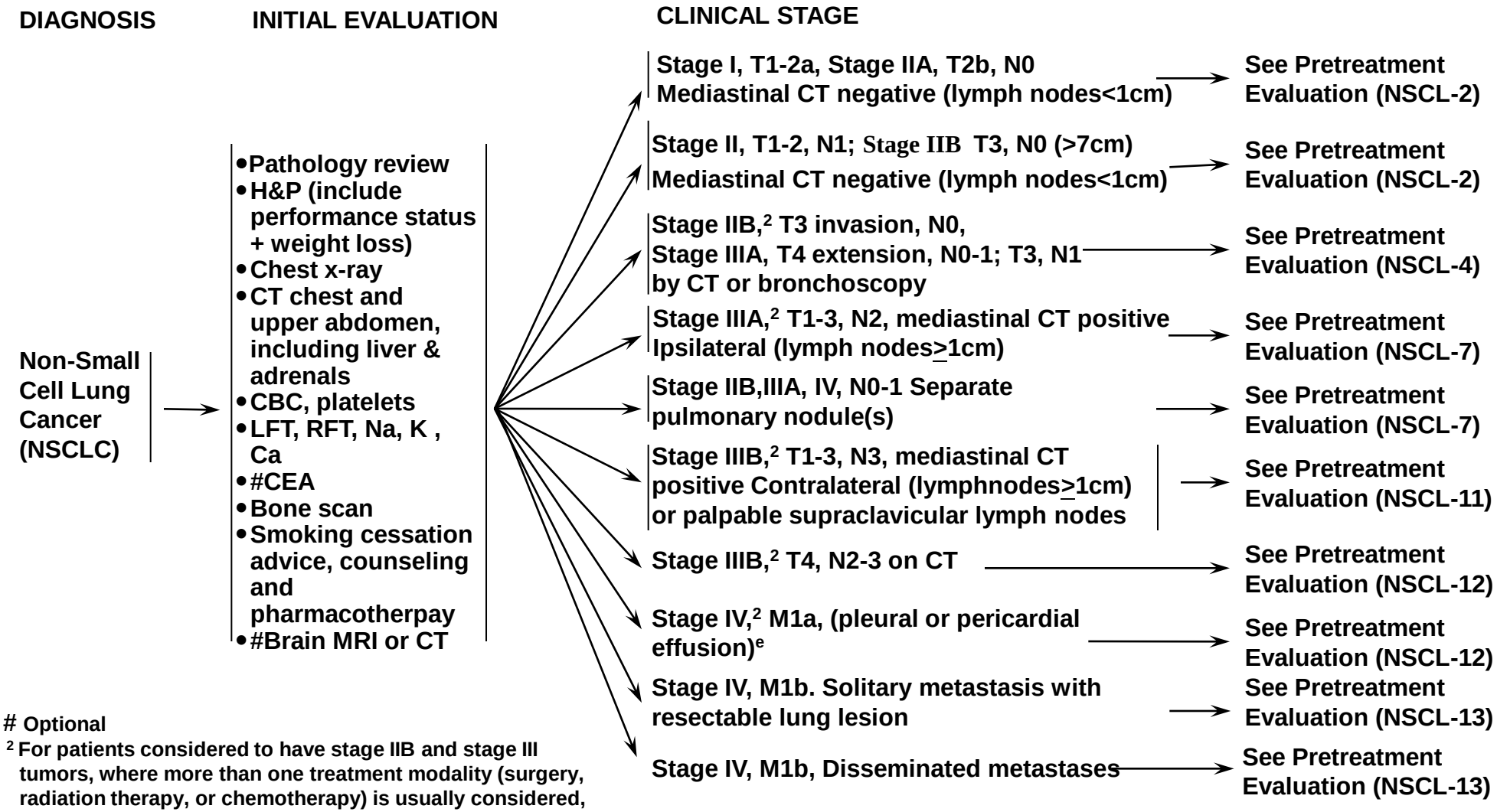
•Evidence to Clinical Practice: 2011 Guidelines and Recommendations for Advance NSCLC.

Moderater Howard (Jack) West, MD
Medical Director
Thoracic Oncology Program
Swedish Cancer Center
Seattle, Washington

制訂人員：

腫瘤科暨血液科：蕭吉晃主任
胸腔外科： 梁嘉儀醫師、劉昭宇醫師
胸腔內科： 鄭世隆主任、張厚台主任、許永隆醫師、張晟瑜醫師、林倬漢醫師
放射腫瘤科:吳樂榮醫師
組織病理科:張閔翔醫師
影像醫學科:張永強醫師
核子醫學科:汪姍瑩醫師

非小細胞肺癌臨床指引



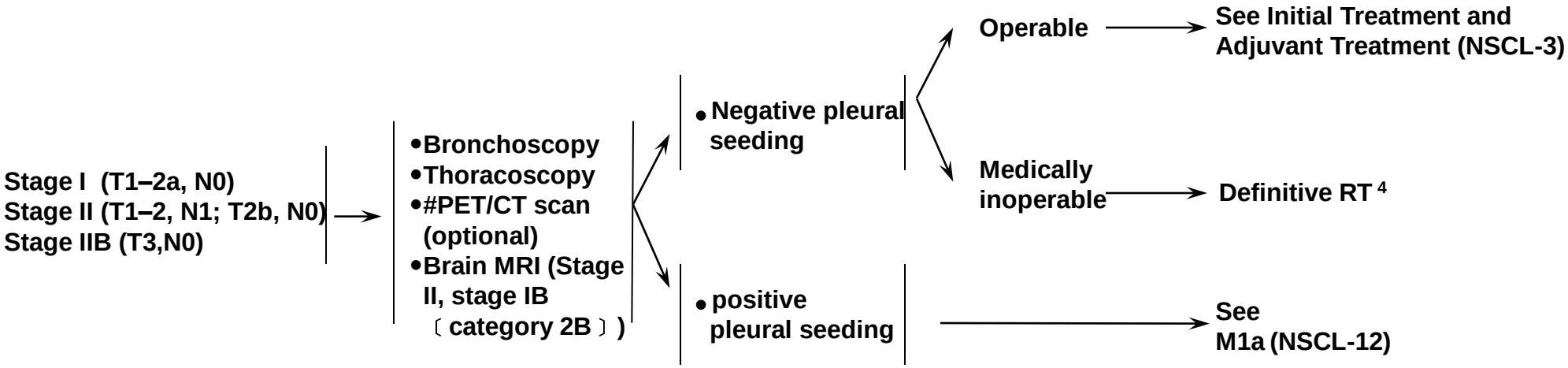
Optional

[2] For patients considered to have stage IIB and stage III tumors, where more than one treatment modality (surgery, radiation therapy, or chemotherapy) is usually considered, a multidisciplinary evaluation should be performed.

[e] Most pleural effusions associated with lung cancer are due to tumor. There are few patients in whom multiple cytopathologic examinations of pleura fluid are negative for tumor and fluid is non-bloody and not an exudate. When these elements and clinical judgment dictate the effusion is not related to the tumor, the effusion should be excluded as a staging element. Pericardial effusion is classified using the same criteria.

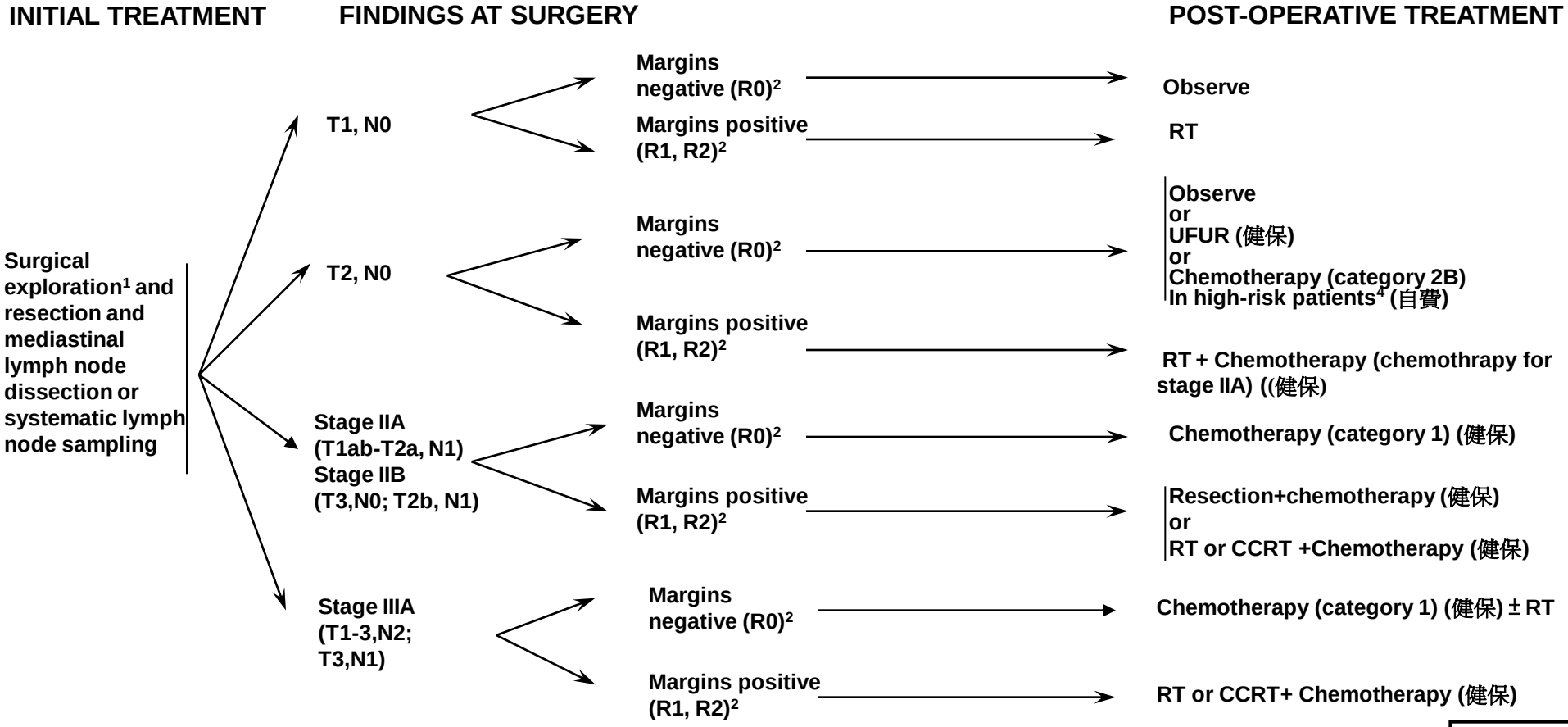
CLINICAL ASSESSMENT

PRETREATMENT EVALUATION



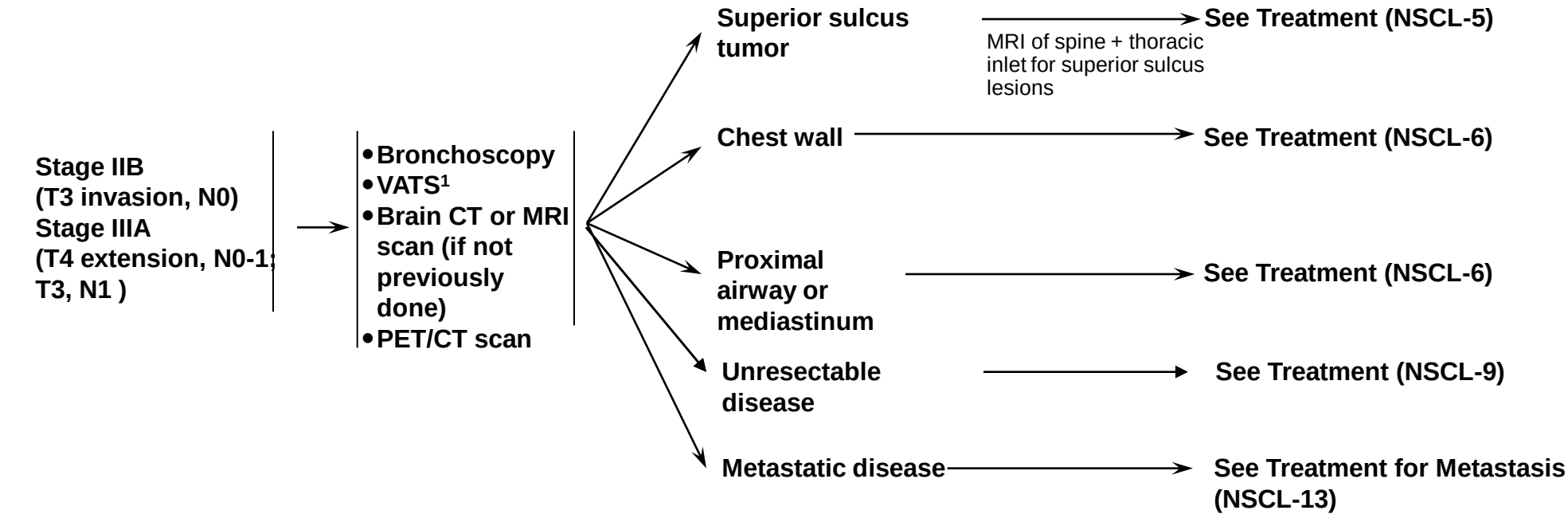
[#][#]**Optional choice**
PET scan findings need pathologic or other radiologic confirmation. If PET scan positive in the mediastinum, lymph node status needs pathologic confirmation.

[4] **See Principles of Radiation Therapy (NSCL-B).**



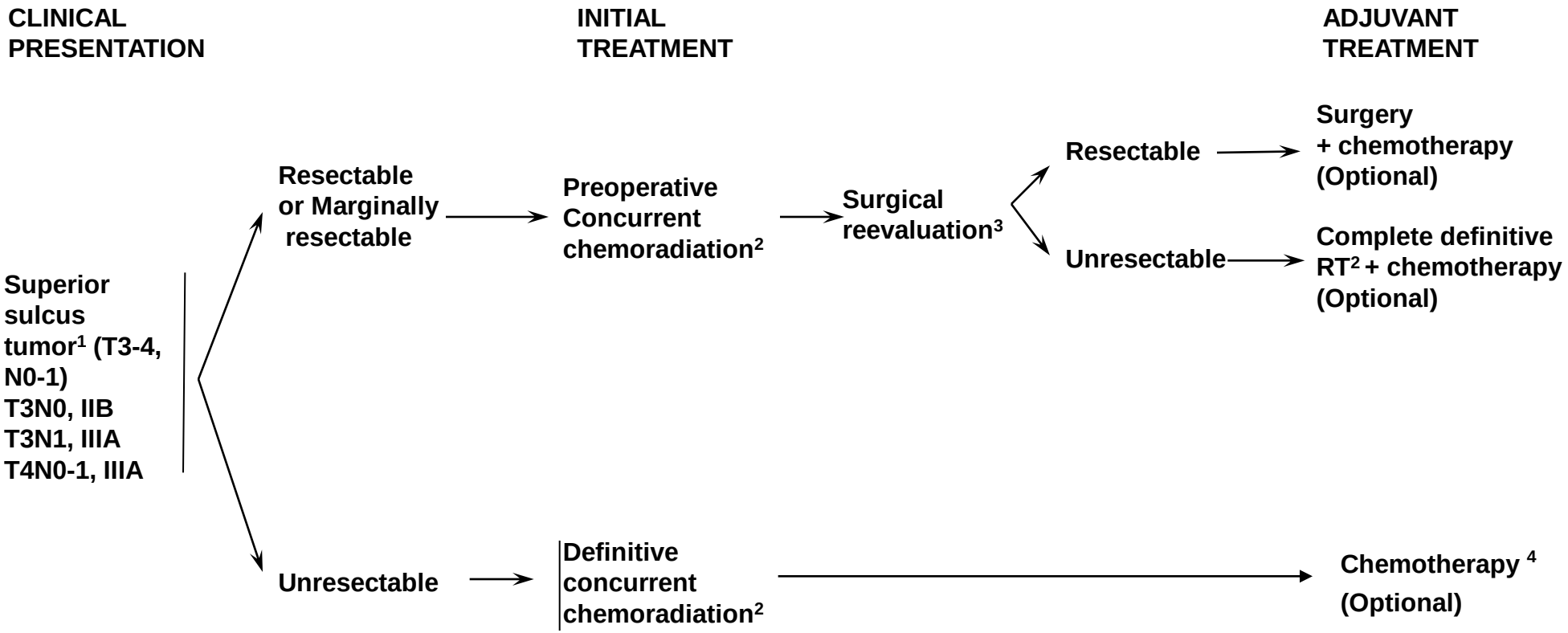
Surveillance
NSCL-14

[1] See Principles of Surgical Resection (NSCL-A).
[2] R0 = no residual tumor, R1 = microscopic residual tumor, R2 = macroscopic residual tumor.
[3] Adverse factors include: inadequate mediastinal lymph node dissection, extracapsular spread, multiple positive hilar nodes, close margins.
4 High- risk patients are defined by poorly differentiated tumors (including lung neuroendocrine tumors), vascular invasion, wedge resection, tumor>4cm, visceral pleural involvement, Nx.
[5] Cisplatin-based doublet therapy for selected patients. Carboplatin/paclitaxel is an alternate regimen.
The cost is not covered by Bureau of National Health Insurance (BNHI).



[1] VATS: Video-assisted Thorascopic Surgery

[2] Positive PET scan findings need pathologic or other radiologic confirmation. If PET scan positive in the mediastinum, lymph node status needs pathologic confirmation.



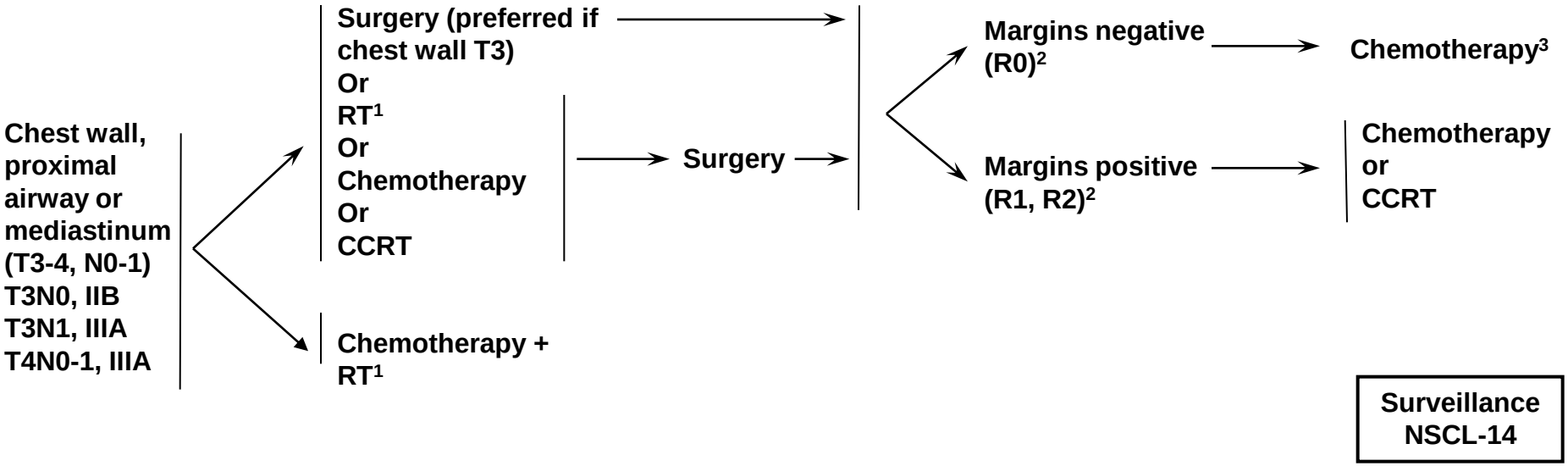
[1] It is difficult to distinguish between T3 and T4 superior sulcus tumors.
[2] See Principles of Radiation Therapy (NSCL-B).
3 RT should continue to definitive dose without interruption if patient is not a surgical candidate.
4 If full- dose chemotherapy not given concurrently with RT as initial treatment.

Surveillance
NSCL-14

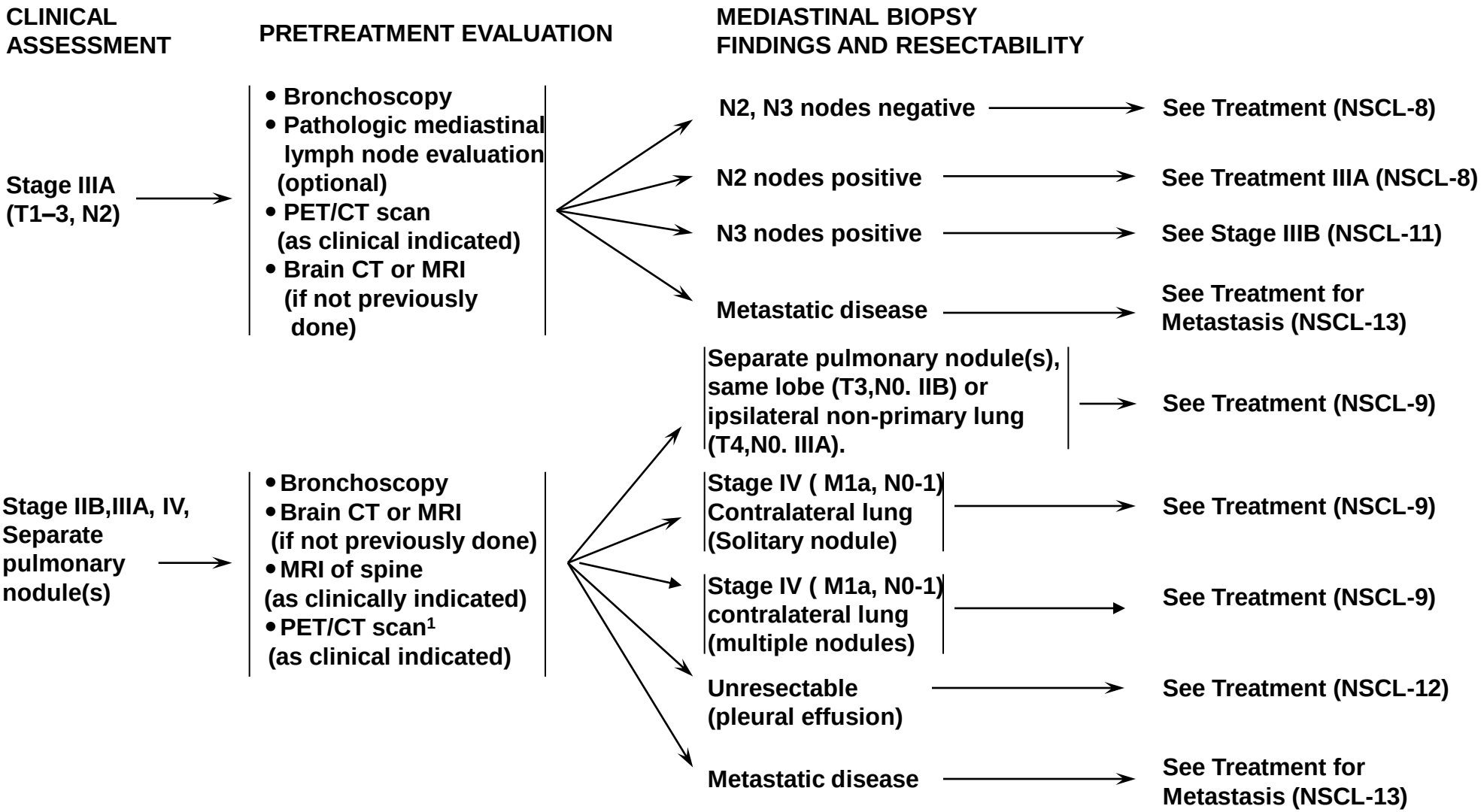
CLINICAL PRESENTATION

INITIAL TREATMENT

ADJUVANT TREATMENT

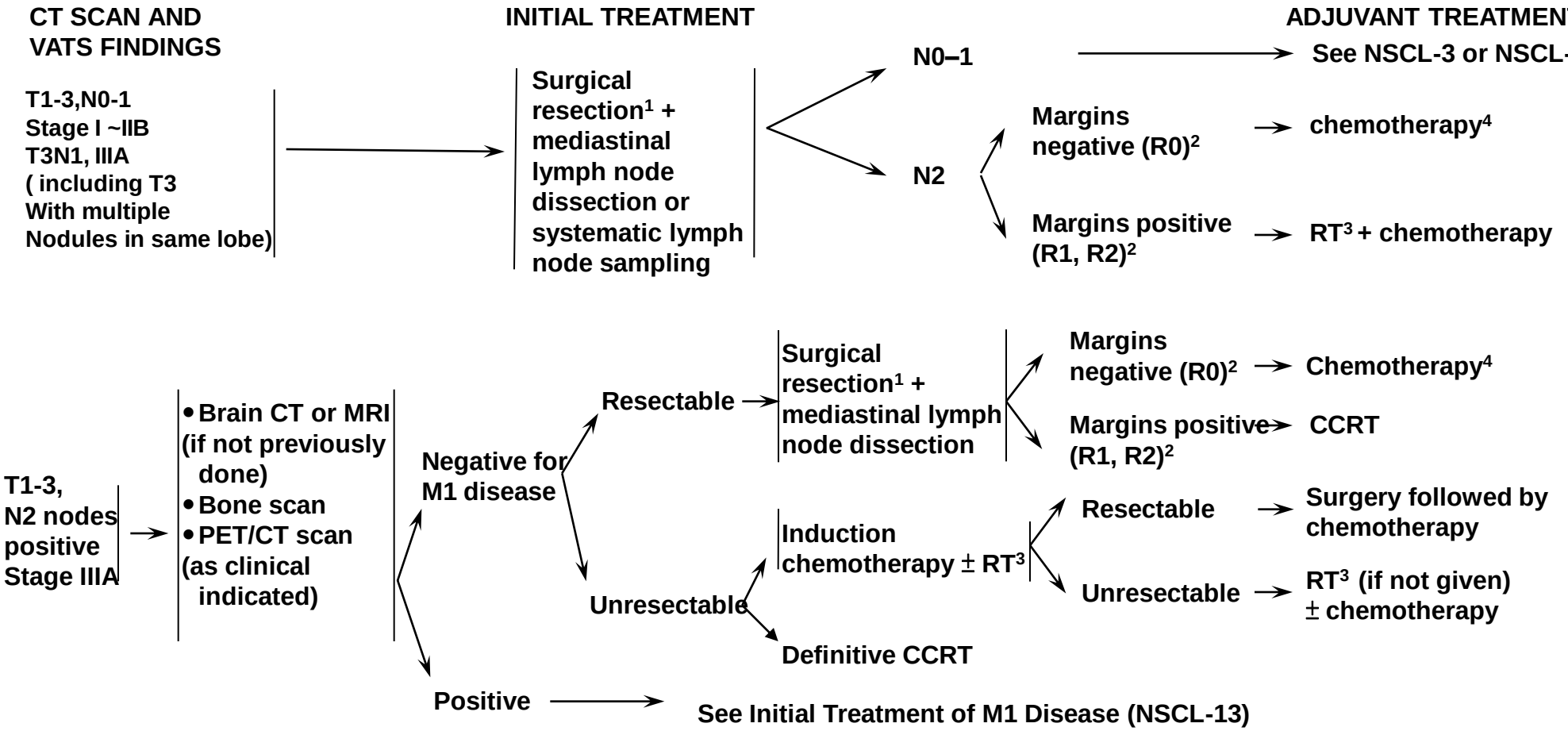


[1] See Principles of Radiation Therapy (NSCL-B).
[2] R0 = no residual tumor, R1 = microscopic residual tumor, R2 = macroscopic residual tumor.
[3] Cisplatin-based doublet therapy for selected patients. Carboplatin/paclitaxel is an alternate regimen.



[1] Positive PET scan findings need pathologic or other radiologic confirmation. If PET scan findings are positive for mediastinal lymphadenopathy, lymph node status needs pathologic confirmation.

非小細胞肺癌臨床指引



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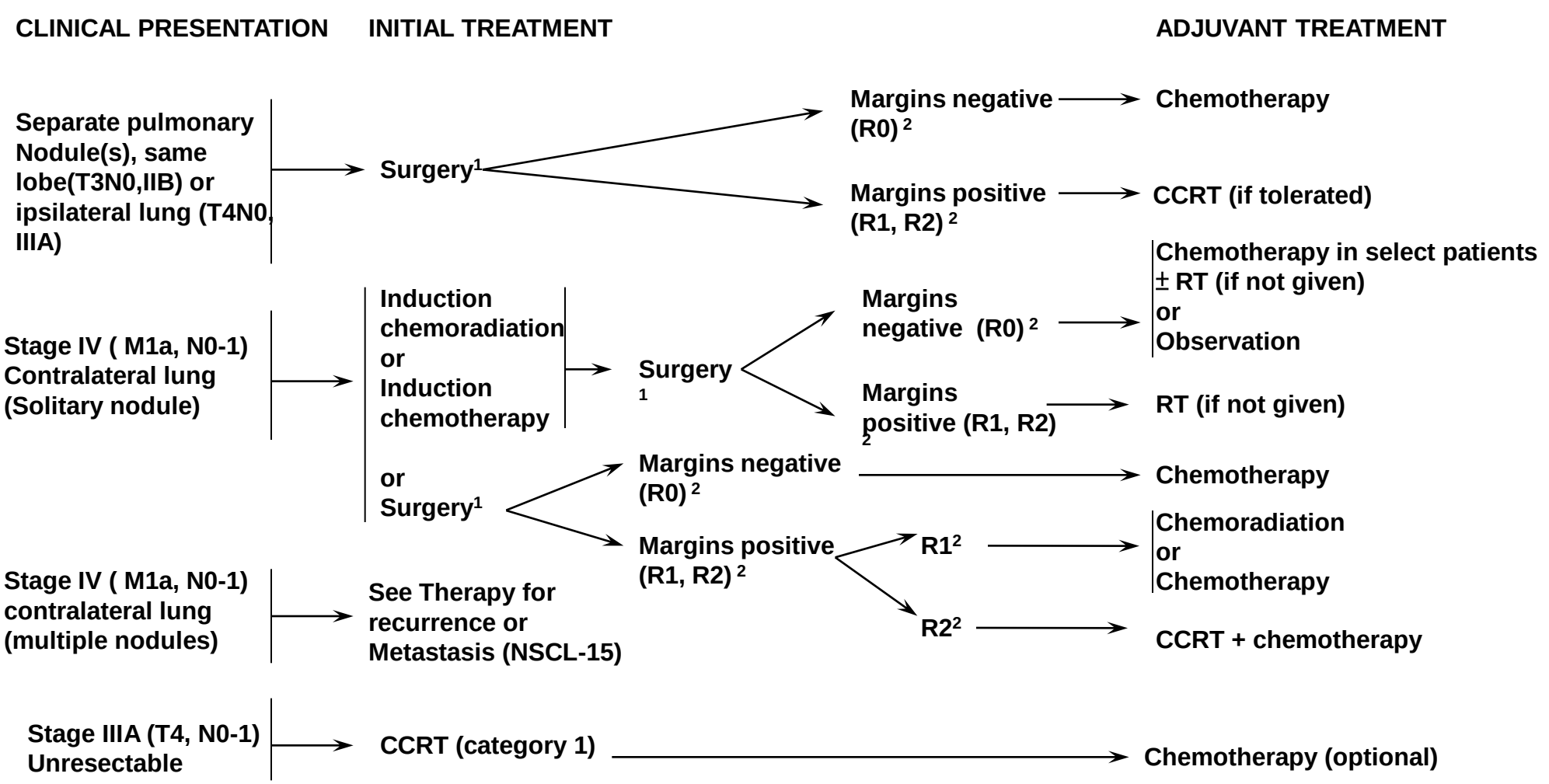
Surveillance
NSCL-14



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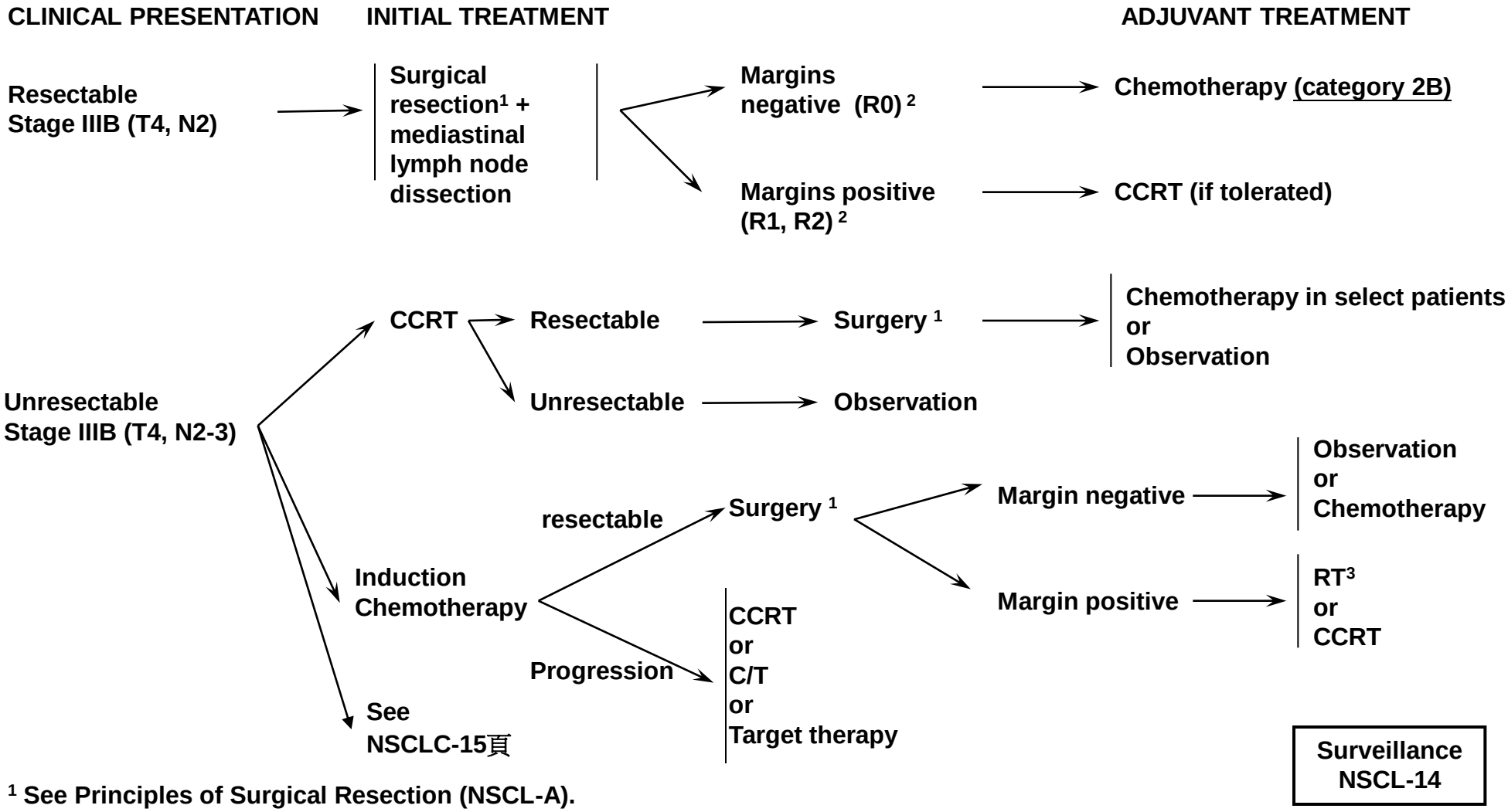
Surveillance NSCL-14



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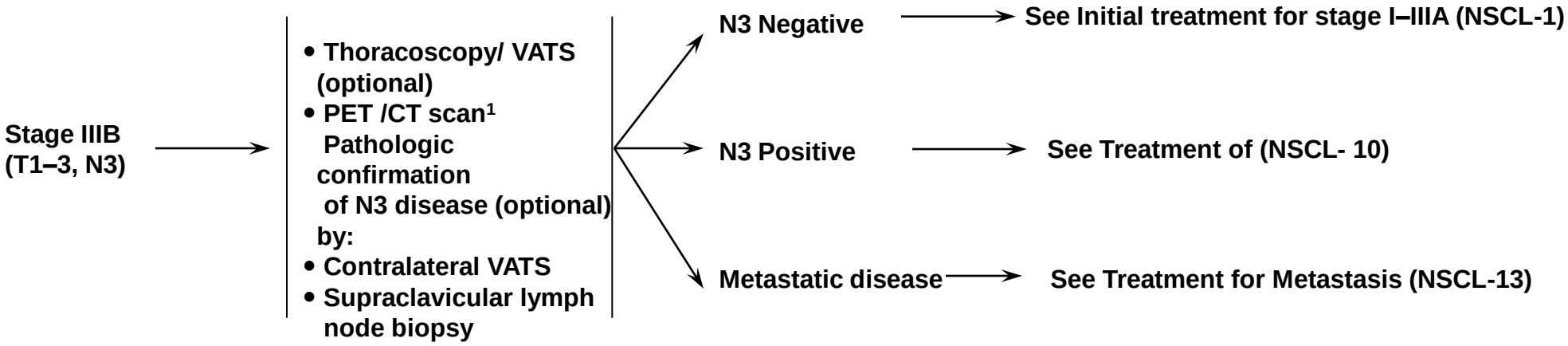
CLINICAL ASSESSMENT

PRETREATMENT EVALUATION

INITIAL TREATMENT



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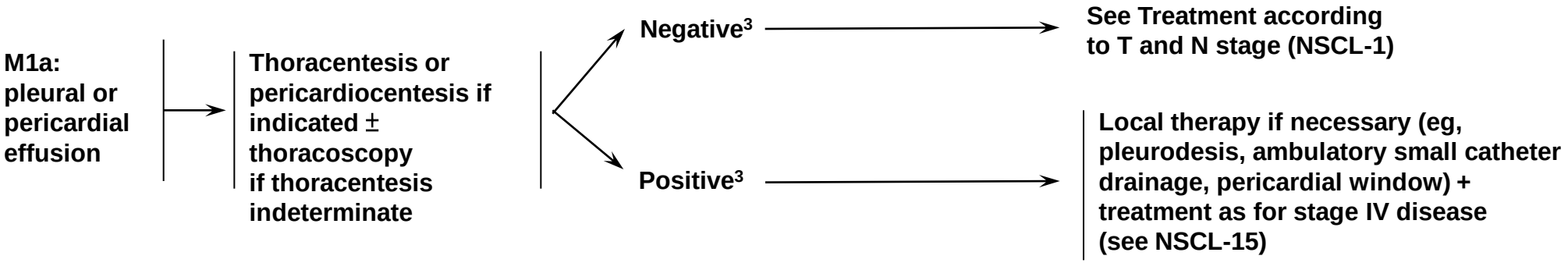
[2] See Principles of Radiation Therapy (NSCL-B).

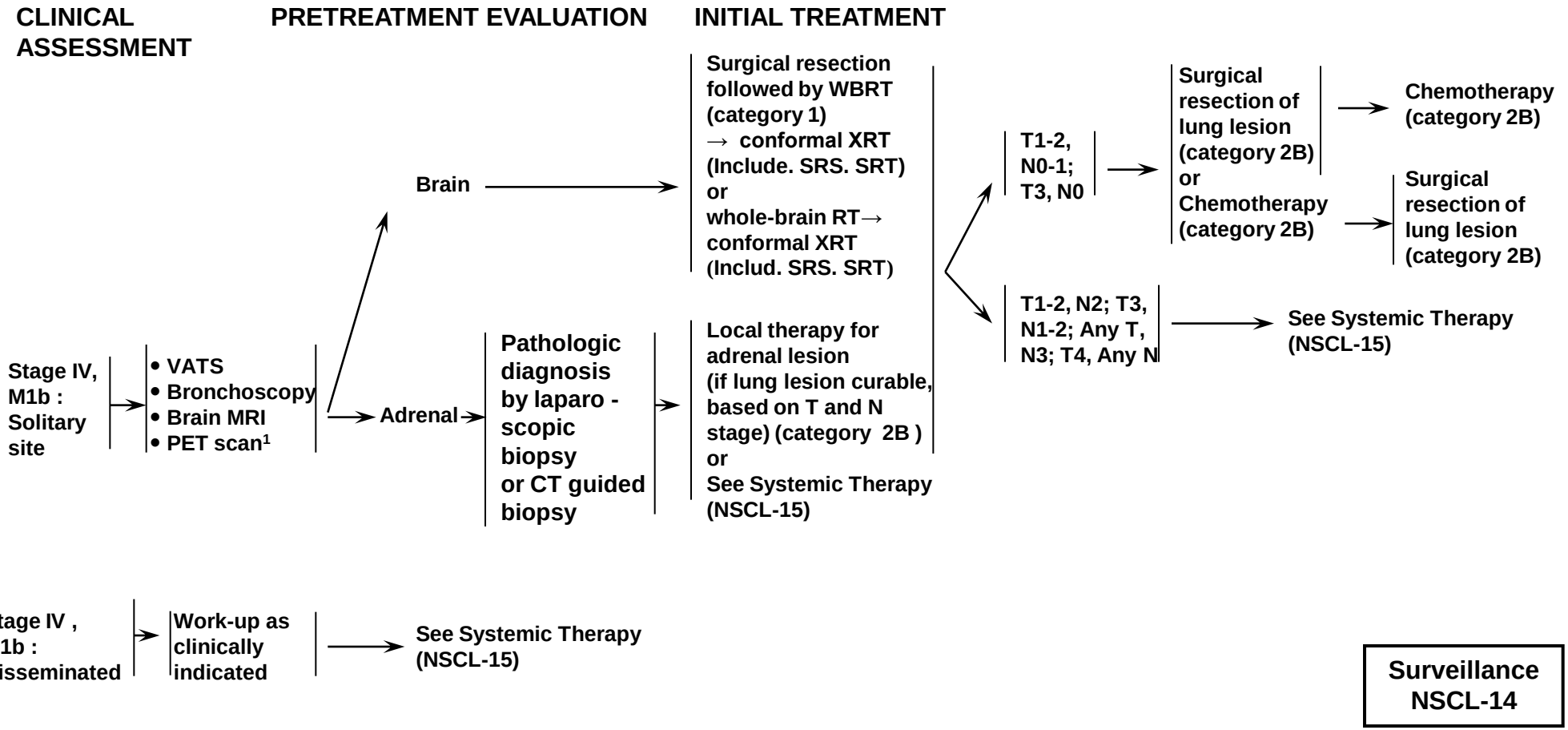
CLINICAL ASSESSMENT | **PRETREATMENT EVALUATION** | **INITIAL TREATMENT**



[2] See Principles of Radiation Therapy (NSCL-B).

[3] Most pleural effusions associated with lung cancer are due to tumor. There are few patients in whom multiple cytopathologic examinations of pleural fluid are negative for tumor. Fluid is non-bloody and not an exudate. When these elements and clinical judgement dictate the effusion is not related to the tumor, the effusion should be excluded as a staging element and the patient should be staged T1, T2, or T3. Pericardial effusion is classified using the same criteria.

非小細胞肺癌臨床指引



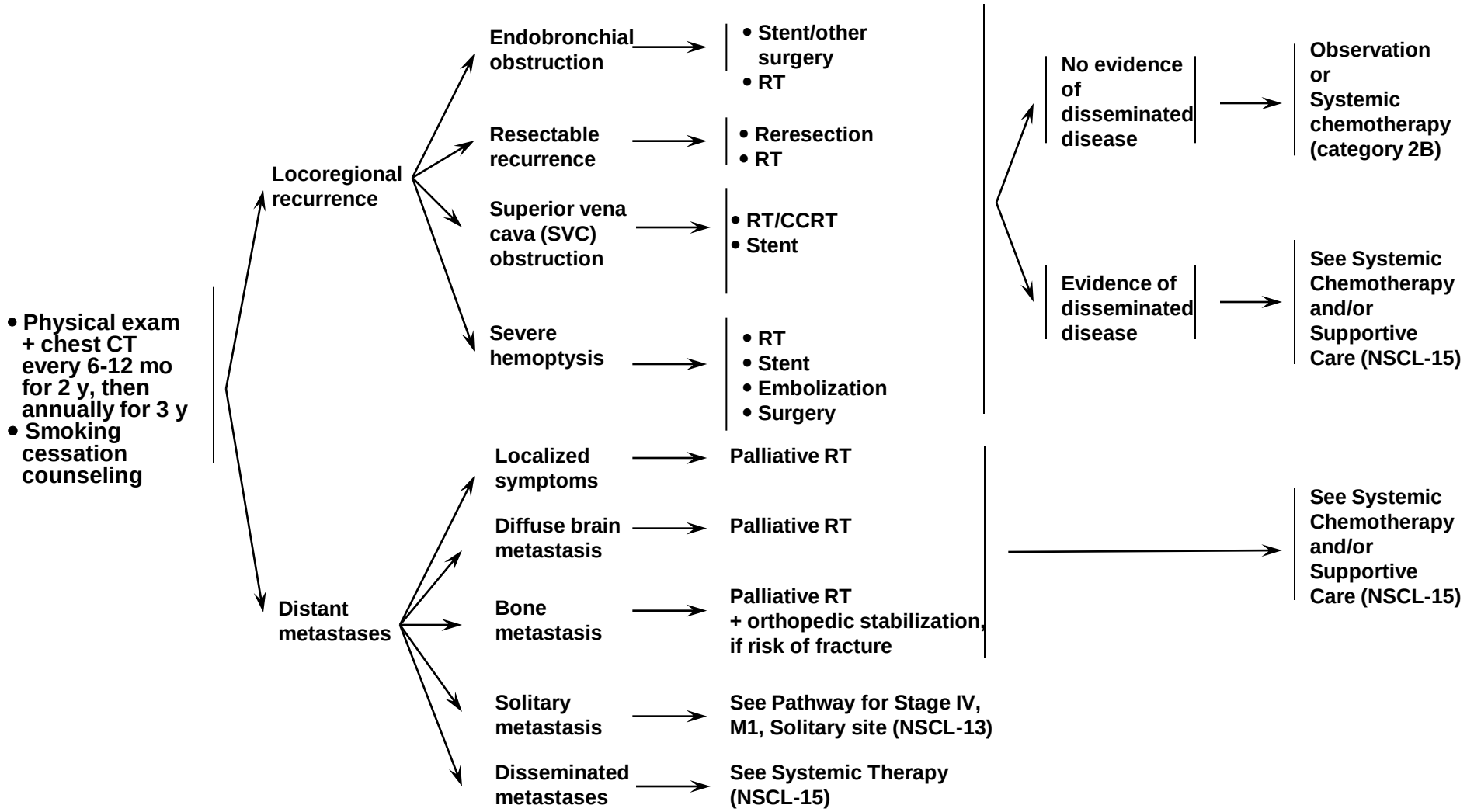
Surveillance NSCL-14

[1] Positive PET scan findings need pathologic or other radiologic confirmation. If PET scan findings are positive for mediastinal lymphadenopathy, lymph node status needs pathologic confirmation.

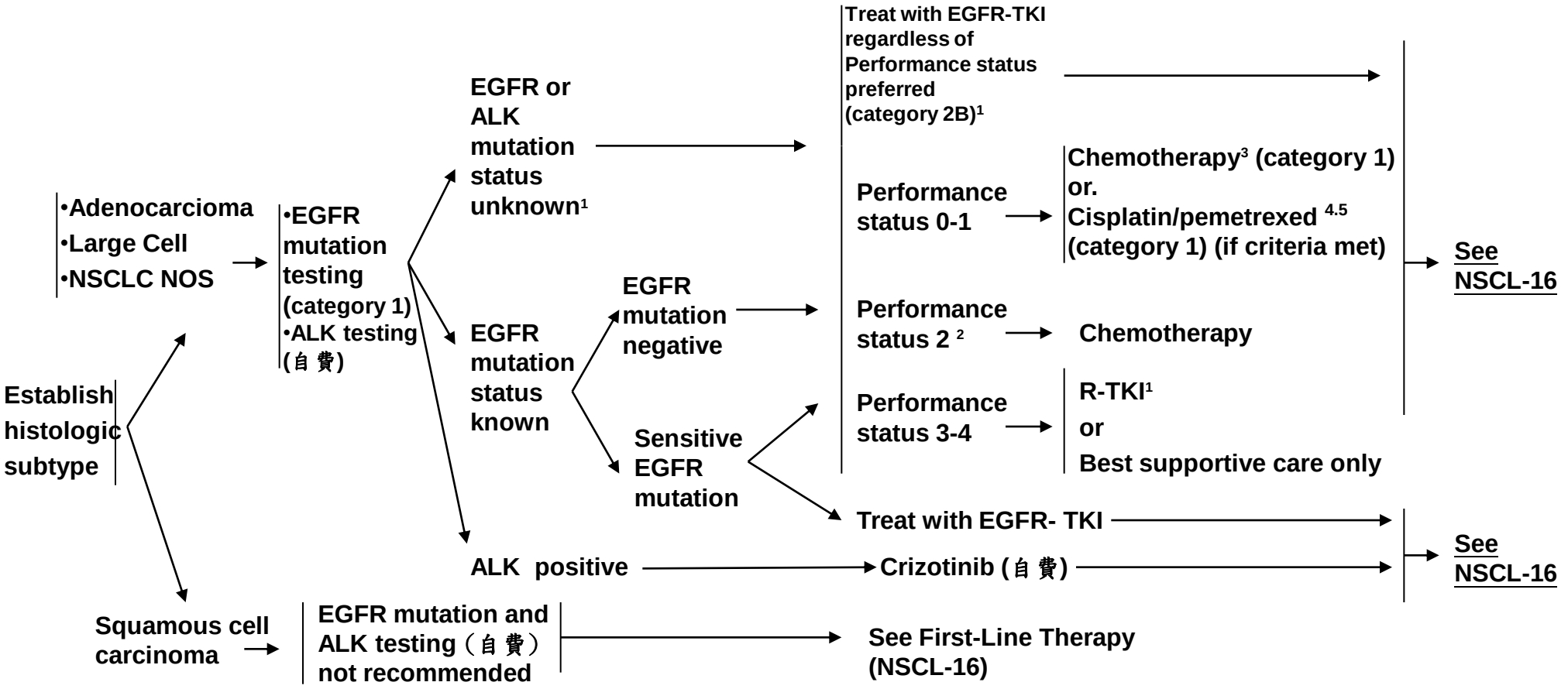
SURVEILLANCE

- Physical exam + chest CT every 6-12 mo for 2 y, then annually for 3 y
- Smoking cessation counseling

THERAPY FOR RECURRENCE AND METASTASIS

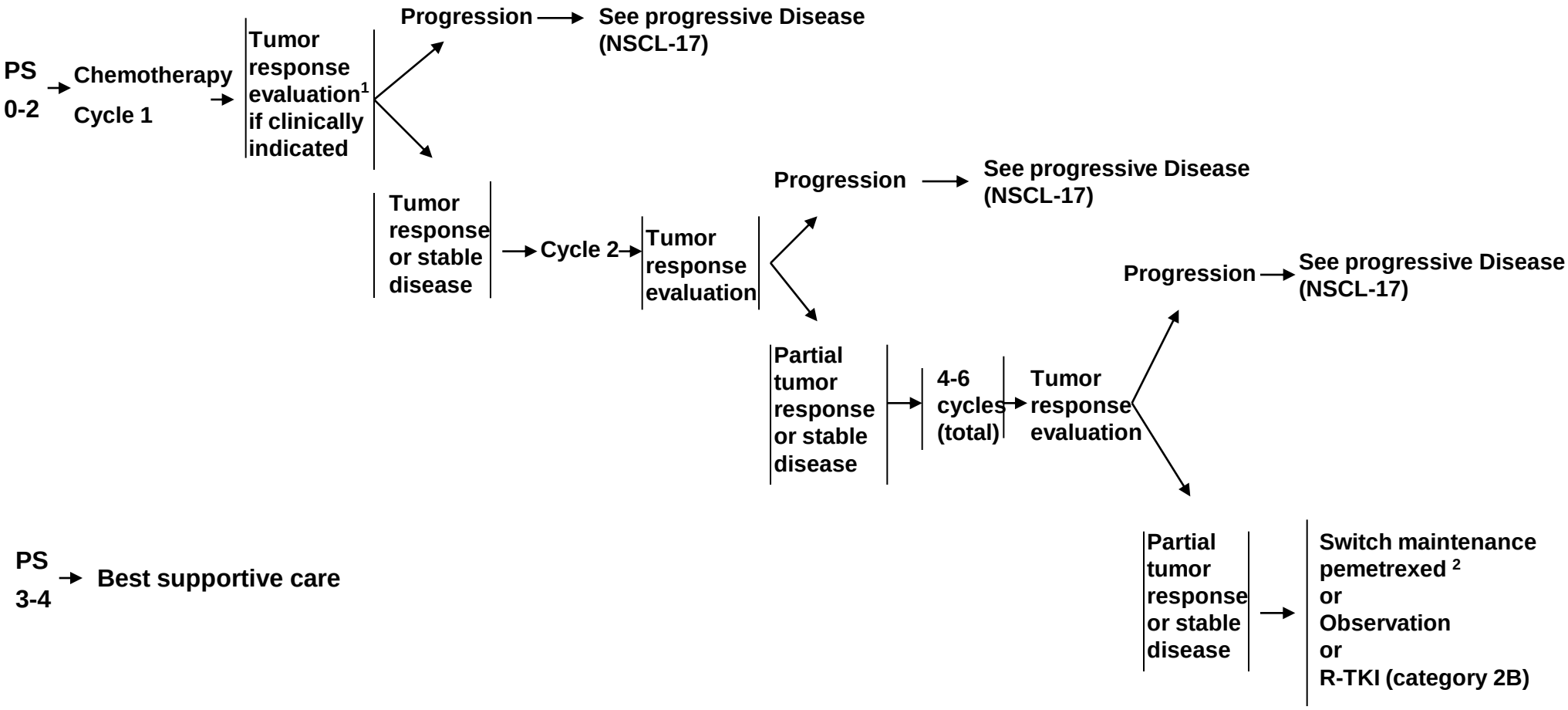


THERAPY FOR RECURRENCE AND METASTASIS



1.1st line R-TKI not reimbursed by BNHI. Detection of R-TK mutation should be conducted whenever feasible. Base on NEJM 2009; 361: 947-57.
2. Performance status (PS) 2 patients have greater toxicity and potential for lower benefit than PS 0-1 patients.
3.See Principles of Chemotherapy for Advanced Non-Small Cell Lung Cancer (NSCL-C).
4.Pemetrexed is not recommended for squamous histology:
5.There is evidence of superior efficacy and reduced toxicity for cisplatin/pemetrexed in patients who do not have squamous histology, in comparison to cisplatin/gemcitabine. Scagliotti GV, Parikh P, von Pawel J, et al. Phase III study comparing cisplatin plus gemcitabine with cisplatin plus pemetrexed in chemotherapynaive patinets with advanced-stage NSCLC. J Clin Oncol 2008;26:3543-3551.

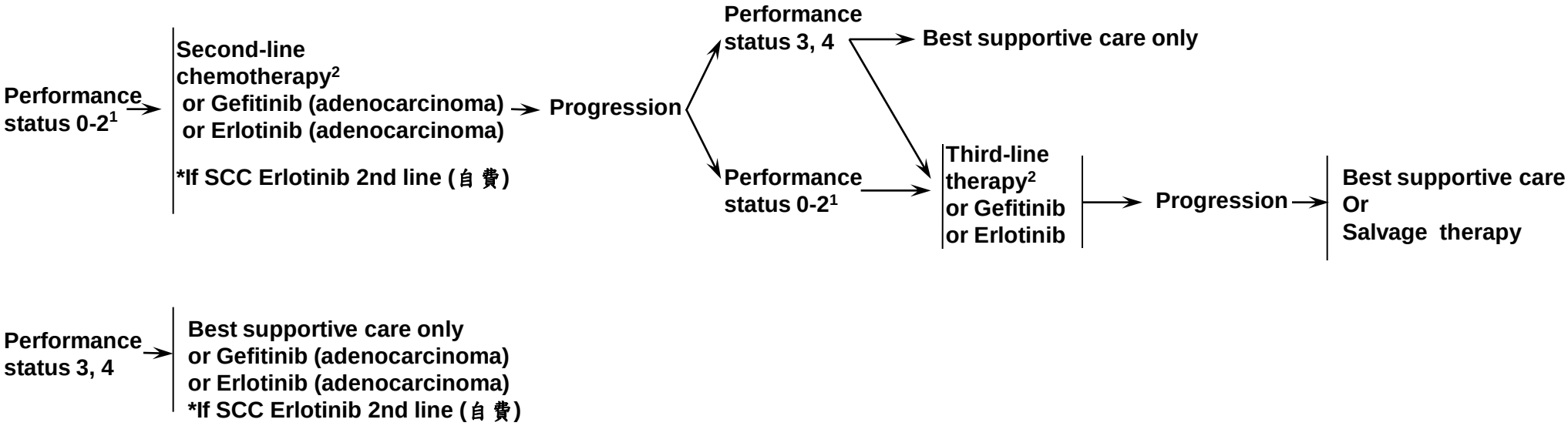
THERAPY FOR RECURRENCE AND METASTASIS



1.Some institutions advocate imaging (CT) studies to evaluate tumor response after the first course.

2.Pemetrexed is not recommended for squamous histology.

PROGRESSIVE DISEASE



[1] Performance status (PS) 2 patients have greater toxicity and potential for lower benefit than PS 0-1 patients.
[2] See Principles of Chemotherapy for Advanced Non-Small Cell Lung Cancer (NSCL-C 2 of 2). Follow rules of BNHI.

Staging

Definitions for T, N, M*

T Primary Tumor
Tx Primary tumor cannot be assessed, or tumor proven by the presence of malignant cells in sputum or bronchial washings but not visulized by imaging or bronchoscopy
T0 No evidence of primary tumor
Tis Carcinoma in situ
T1 Tumor ≦ 3cm 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)[a]
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[b]. Involves main bronchus, ≧2 cm distal to the carina
Invades visceral pleura
Associated with atelectasis or obstructive pneumonitis that extents 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: 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[a] 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 nodele(s) in a different ipsilateral lobe

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

M DistantMetastasis
MX Distant metastasis cannot be assessed
M0 No distant metastasis
M1 Distant metastasis present
M1a Separate tumor nodule(s) in a contralateral lobe; tumor with pleura nodules or maligant pleural (or pericardial) effusion[c]
M1b Distant metastasis

a The uncommon superficial spreading tumor of any size with its invasive component limited to the bronchial wall, which may extend proximally to the main bronchus, is also classified as T1.
b T2 tumors with these features are classified T2a if ≦5cm or if size cannot be determined, and if >5cm but ≦7cm
c 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 judgment 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 T1, T2, T3 or T4.

*Used with permission. Goldstraw P, Crowley J, Chansky K, et al. The IASCL Lung Cancer Staging Project: Proposals for the revision of the TNM stage groupings in the forthcoming (seventh) edition of the TNM classification of maligant tumors. J Thorac Oncol 2007;2: 706-714.

Staging

Descriptors, T and M Categories, and Stage Grouping*

Six Edition T/M Descriptor	7th Edition T/M	N0	N1	N2	N3
T1 (less than or equal to 2 cm)	T1a	IA	IIA	IIIA	IIIB
T1 (>2-3 cm)	T1b	IA	IIA	IIIA	IIIB
T2 (less than or equal to 5cm)	T2a	IB	IIA	IIIA	IIIB
T2 (>5-7 cm)	T2b	IIA	IIB	IIIA	IIIB
T2 (>7cm)	T3	IIB	IIIA	IIIA	IIIB
T3 invasion		IIB	IIIA	IIIA	IIIB
T4 (same lobe nodules)		IIB	IIIA	IIIA	IIIB
T4 (extension)	T4	IIIA	IIIA	IIIB	IIIB
M1 (ipsilateral lung)		IIIA	IIIA	IIIB	IIIB
T4 (pleural effusion)	M1a	IV	IV	IV	IV
M1 (contralateral lung)		IV	IV	IV	IV
M1 (distant)	M1b	IV	IV	IV	IV

Cells in bold indicate a change from the sixth edition for a particular TNM category.

*Used with permission. Goldstraw P, Crowley J, Chansky K, et al. The IASCL Lung Cancer Staging Project: Proposals for the revision of the TNM stage groupings in the forthcoming (seventh) edition of the TNM classification of maligant tumors. J Thorac Oncol 2007;2: 706-714.

Table 2 – Continued

HistologicGrade(G)
GX Grade cannot be assessed
G1 Well differentiated
G2 Moderately differentiated
G3 Poorly differentiated
G4 Undifferentiated

HistopathologicType
Squamous cell carcinoma
Variants: Papillary, clear cell, small cell, basaloid

Adenocarcinoma
Acinar
Papillary
Bronchioloalveolar carcinoma
Non-mucinous
Mucinous
Mixed mucinous and non-mucinous or indeterminate
Solid adenocarcinoma with mucin formation

Adenocarcinoma with mixed subtypes
Variants: Well differentiated fetal adenocarcinoma, mucinous ("colloid") adenocarcinoma, mucinous cystadenocarcinoma, signe ring adenocarcinoma, clear cell adenocarcinoma

Large cell carcinoma
Variants: Large cell neuroendocrine carcinoma, combined large cell neuroendocrine carcinoma, basaloid carcinoma, lymphoepithelioma-like carcinoma, clear cell carcinoma, large cell carcinoma with rhabdoid phenotype

†The uncommon superficial tumor of any size with its invasive component limited to the bronchial wall, which may extend proximal to the main bronchus, is also classified T1.

‡Most pleural effusions associated with lung cancer are due to tumor.
However, in a few patients, multiple cytopathologic examinations of pleural fluid are negative for tumor. In these cases, fluid is not bloody and is not an exudate. Such patients may be further evaluated by videothoracoscopy (VATS) and direct pleural biopsies. When these elements and clinical judgment dictate that the effusion is not related to the tumor, the effusion should be excluded as a staging element and the patient should be staged T1, T2, or T3.

§M1 includes separate tumor nodule(s) in a different lobe (ipsilateral or contralateral).

Chemotherapy

NSCLC，Adjuvant
【Cisplatin-Vinorelbine】
【Carboplatin-Paclitaxel】【Ccr < 60】

NSCLC，Neoadjuvant
【Cisplatin-Docetaxel】

NSCLC，Advanced
【Docetaxel + Cisplatin】
【Gemcitabine + Cisplatin】
【Paclitaxel + Cisplatin】
【Vinorelbine + Cisplatin】
【Pemetrexed + Cisplatin】

Target therapy
【 Gefitinib 】
【 Erlotinib HCl 】
【 Bevacizumab】
【 Afatinib (健保未給付) 】
【Crizotinib (健保未給付)】

NSCLC，Advanced
【Regimens of split-dose Cisplatin at FEMH】
【Docetaxel + Cisplatin】
【Gemcitabine + Cisplatin】
【Paclitaxel + Cisplatin】
【Vinorelbine + Cisplatin】

NSCLC，Advanced
【Monotherapy】
【Docetaxel】
【Pemetrexed】
【Gemcitabine】
【Paclitaxel】
【Vinorelbine】

*Details of chemotherapy regiments refer to 亞東紀念醫院化學治療處方參考集。