National Comprehensive Cancer Network®

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)

非小细胞肺癌

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NCCN Guidelines Panel Disclosures

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临床试验: NCCN认为任何癌症患者的最佳治疗是在一项临床试验中。特别鼓励参与临床试验。

在线寻找NCCN成员机构的临床试验，点击此处 nccn.org/clinical_trials/physician.html.

NCCN证据与共识等级： 所有的推荐均是2A级除非另作说明。

见 NCCN Categories of Evidence and Consensus.

非小细胞肺癌NCCN指南2017第7版较2017第6版的更新包括：

NSCL-20
- ***在一线化疗前发现ALK重排：增加 阿雷替尼（艾乐替尼）作为一个1类治疗选择和首选。***
- **在一线化疗期间发现ALK重排：完成计划的化疗，包括维持治疗；或中断，然后 阿雷替尼*（艾乐替尼）*或 克唑替尼 或 色瑞替尼**

NSCL-21
- **无症状的脑及全身孤立性病变：增加“继续阿雷替尼*（艾乐替尼）*”为一个治疗选择。**

MS-1
- **基于指南的最新变化更新了讨论部分。**

非小细胞肺癌NCCN指南2017第6版较2017第5版的更新包括：

NSCL-21
- **无症状进展；症状性进展——脑或多发的全身性病变：增加了布加替尼作为一个治疗选择。**
- **脚注“rr”修改为：无法耐受克唑替尼的患者可转换至色瑞替尼、alectinib阿雷替尼（艾乐替尼）或*brigatinib布加替尼*。**
- **脚注“tt”增加了：阿雷替尼（艾乐替尼）或布加替尼作为克唑替尼已经进展的、ALK阳性的转移性非小细胞肺癌患者的治疗选择。**

MS-1
- **基于指南的最新变化更新了讨论部分。**

非小细胞肺癌NCCN指南2017第5版较2017第4版的更新包括：

NSCL-20
- **在一线化疗前发现ALK重排：增加色瑞替尼为一个1类治疗选择。**
- **在一线化疗期间发现ALK重排：完成计划的化疗，包括维持治疗；或中断，然后克唑替尼*或色瑞替尼***

NSCL-21
- **无症状的脑及全身孤立性病变：增加“继续色瑞替尼”为一个治疗选择。**
- **脚注“ss”增加了：如果未曾给予。**

MS-1
- **基于指南的最新变化更新了讨论部分。**

非小细胞肺癌NCCN指南2017第4版较2017第3版的更新包括：

NSCL-9
- **分散肺结节;术后N2、R0：辅助治疗推荐明确为化疗（1类）或序贯化疗+放疗。既往所述为序贯化疗（1类）+放疗。**

NSCL-19
- **奥希替尼从2A类改为1类推荐。**
- **脚注“nn”补充修改为：如果血浆T790M突变检测阴性，考虑可反过来进行基于组织的检测。**
- **删除了脚注：对于经过FDA批准的或其他实验室验证过的由CLIA批准的实验室开发的检测方法测定的EGFR T790M突变阳性的转移性肿瘤患者，奥希替尼是一个选择。**

~~**NSCL-24**~~
- **阿特珠单抗从2A类更改为1类推荐。（也适用于NSCL-25）**

非小细胞肺癌NCCN指南2017第3版较2017第2版的更新包括：

MS-1
- **讨论部分已经更新为反映出工作步骤方面的变化。**

非小细胞肺癌NCCN指南2017第2版较2017第1版的更新包括：

NSCL-17
- **检测结果修改为：“PD-L1阳性和EGFR、ALK、ROS1阴性或未知。”**

NSCL-24
- **后续治疗；PS 0-2：增加了Atezolizumab阿特珠单抗作为一个治疗选择。增加了参考文献：Barlesi F, Park K, Ciardiello F, et al. Primary analysis from OAK, a randomized phase III study comparing atezolizumab with docetaxel in 2L/3L NSCLC [abstract]. ESMO Congress; Copenhagen. ESMO 2016: LBA44.（也适用于NSCL-25）**
- **删除了厄洛替尼作为后续和维持治疗的一个选择。**
- **脚注“ww”修改为：FDA已批准派姆单抗用于经FDA批准的检验测定的肿瘤PD-L1表达水平≥1%的非小细胞肺癌患者的治疗。~~对于PD-L1使用派姆单抗~~。（也适用于NSCL-25）**
- **脚注“aaa”修改为：如果未曾给予，对于PS 0-2患者的选择包括（尼鲁单抗、派姆单抗或阿特珠单抗）、~~厄洛替尼、~~多西他赛（2B类）、培美曲塞（2B类）、吉西他滨（2B类）或雷莫芦单抗+多西他赛（2B类）；PS 3-4患者的选择包括最佳支持治疗。进一步进展患者的选择是最佳支持治疗或临床试验。**

NSCL-25
- **脚注“bbb”修改为：如果未曾给予，对于PS 0-2患者的选择包括（尼鲁单抗、派姆单抗*或阿特珠单抗*）、多西他赛（2B类）、吉西他滨（2B类）或雷莫芦单抗+多西他赛（2B类）；PS 3-4患者的选择包括最佳支持治疗。进一步进展患者的选择是最佳支持治疗或临床试验。**

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非小细胞肺癌NCCN指南2017第1版较2016第4版的更新包括：

PREV-1

- **增加了至NCCN戒烟指南的链接。**

DIAG-2 和 DIAG-3

- **修订了这些页，改编自Fleischner协会指南。**

NSCL-2

- **IA期: “考虑”增加到“纵隔淋巴结病理评估。”**
- **IB期; 脑MRI：删除了2B类，列为“可选”。**
- **因内科因素不能手术；N0：对于高危IB-ⅢA期澄清为IB-ⅡB期考虑辅助化疗。**
- **脚注“j”修改并加入了第一句：颅底到膝关节或全身PET/CT检查。（同样适用于NSCL-4、NSCL-7、NSCL-9、NSCL-11至NSCL-13）**

- **脚注“p”修改为：典型的高危因素包括低分化肿瘤（包括肺神经内分泌肿瘤[不包括分化良好的神经内分泌肿瘤]）、血管侵犯、楔形切除、肿瘤>4cm、脏层胸膜受累和~~淋巴结取样不彻底~~*淋巴结状态不明*（Nx）。单独这些因素可能不是一个指征，但当确定辅助化疗治疗时可以考虑。（也适用于NSCL-3）**

NSCL-5

- **明确了手术重新评估：包括胸部强化或平扫CT±PET/CT**

NSCL-8

- **T1-3, N0-1: 手术切除，如同在初始治疗中指出的。**
  - **对于N0-1与N2的辅助治疗链接回NSCL-3。**
- **T1-2、T3（除外侵袭性）N2阳性和T3（侵袭性）N2阳性更改为包括M0。**
  - **删除了脑MRI及FDG PET/CT，因为已在上一页提到。**
  - **删除了转移性病变，因为已经在上一页提到。**
- **脚注“w”对于该页是新的：“胸部强化CT和/或PET/CT以评估进展。”**

NSCL-10

- **不可能根治性局部治疗：从“姑息化疗±局部姑息治疗”中去除了“考虑”并增加了“观察”。**
- **F脚注“aa”修改为：“首选保留肺切除术，但应该使用肿瘤分类和学会专家的意见指导个体化的治疗计划。*应该对患者进行多学科（即外科、放射肿瘤学、内科肿瘤学）评估。*”**

NSCL-13

- **对局限转移的管理进行了重大修改。目前包括NSCL-13和NSCL-14页。**

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非小细胞肺癌NCCN指南2017第1版较2016第4版的更新包括：

NSCL-15

- 修改了监测标题："根治性治疗结束后监测"
- 推荐随初始治疗不同而异。
  - *I-II*期（初始治疗包括手术±化疗）
    病史与体格检查和胸部CT±强化，最初2-3年每6个月1次，之后每年1次病史与体格检查和胸部低剂量非强化CT
  - *I-II*期（初始治疗包括放疗）或III期或IV期（所有部位的寡转移灶均给予根治性治疗）
    病史与体格检查和胸部CT±强化，最初3年每3-6个月1次，之后病史与体格检查和胸部CT±强化，最初2年每6个月1次，之后每年1次病史与体格检查和胸部低剂量非强化CT
    - ◊ 残存或新的影像学异常可能需要更频繁的影像学检查"
- 不包括IV期的推荐。
- "不常规要求PET/CT或脑部核磁共振造影"

NSCL-16

- 治疗后局部复发：增加了下列影像以评估疾病播散："胸部强化CT；脑强化磁共振成像；PET/CT。"

- 远处转移；骨转移；重新整理了推荐："如有骨折风险，骨科固定+姑息性外放疗。"

NSCL-17

- 增加了ROS1和PD-L1检测。
- 鳞状细胞癌："~~尤其是~~在从不吸烟者中或小活检标本或混合型组织学，考虑EGFR基因突变检测和ALK检测。"

- 脚注"f"增加了："如果重复活检不可行，应考虑血浆活检。"
- 脚注"gg"修改为："NCCN NSCLC指南小组强烈~~认同~~*建议*更广泛的分子分析…"
- 脚注"kk"增加了："PD-L1表达水平≥50%为阳性检测结果，一线派姆单抗治疗。"
- 由于将内容加入到工作步骤中，因此删除了脚注：考虑ROS1检测；如果阳性，可以用克唑替尼治疗。

NSCL-18

- 在一线化疗期间发现表皮生长因子受体突变："中断或完成计划的化疗，然后…"更改为"完成计划的化疗，包括维持治疗，或中断，然后…"（也适用于NSCL-20）

NSCL-19

- T790M检测"增加了脚注"nn"："如果组织活检不可行，应考虑血浆活检。"
- 无症状："考虑局部治疗"增加为一个治疗选择。
- 脑：增加"奥希替尼"为一个治疗选择。
- 脑部病变无症状或有症状及孤立的全身性病变：对于多发性病变，针对进展病变治疗。
- 全身孤立性或多发性病变：
  - T790M+ 增加了奥希替尼治疗推荐。
  - 对于腺癌、鳞状细胞癌或PD-L1表达阳性（≥50%）的T790M-者，增加了推荐转至一线治疗方案。
- 脚注"pp"修改为："奥希替尼是被批准…患者的一个选择"
- 脚注"qq"增加了："对于影像学快速进展或威胁器官功能者，应开始替代治疗。"

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非小细胞肺癌NCCN指南2017第1版较2016第4版的更新包括：

NSCL-21
- 无症状：增加“考虑局部治疗”为一个选择。
- 脑及全身孤立性病变：“继续ALK抑制剂”澄清为“继续克唑替尼。”
- 在局部治疗和/或切换到色瑞替尼或阿雷替尼后症状性全身进展更改为“进展”。

NSCL-22
- 为ROS1重排阳性添加了新页面。克唑替尼注明为2A类推荐。

NSCL-23
- 为PD-L1表达阳性添加了新页面。派姆单抗注明为1类推荐。

NSCL-24
- 一线治疗：二联化疗与贝伐单抗+化疗更改为“全身治疗”，作为具体推荐在NSCL-F中注明。相关脚注移至NSCL-F。

- 后续治疗；PS 3-4：删除了厄洛替尼、阿法替尼、吉非替尼、克唑替尼的治疗选择。删除了相关脚注。
- 脚注“v”增加了：“如果未曾给予派姆单抗。”（也适用于NSCL-25）
- 脚注“xx”增加了：“如果未曾给予”（也适用于NSCL-25）

NSCL-A (1 of 5)
- 病理学评价，第3项修改为：“在切除标本或小活检中病理诊断报告应包括WHO对肺恶性肿瘤描述的组织学分类。~~在切除标本和小活检中对于这一肿瘤亚型应该使用最近公布的腺癌分类。~~”

- 病理学评价，第6项修改为：“在单独基于常规组织学不能可靠分类的标本中，强烈建议在小组织标本中限制使用免疫组化研究，从而保留关键的肿瘤组织用于分子研究，尤其是在晚期疾病患者中。对于大多数诊断问题，一个鳞状细胞癌标记（如p63、p40）和一个腺癌标记（如甲状腺转录因子-1、新天冬氨酸蛋白酶A）的有限组合应该足够。”

NSCL-A (3 of 5)
- ALK; 第1项：“阿雷替尼"添加到第三句。
- ALK; 第2项：“易位”改为“重排”。
- ALK; 第3项修改为：用于检测ALK NSCLC现行的标准方法是荧光原位杂交（FISH）~~，尽管目前正在评估其他方法，包括聚合酶链反应（PCR）和免疫组化~~。

NSCL-A (4 of 5)
- 为ROS-1和PD-L1增加了新章节。

NSCL-A (5 of 5)
- 更新了以下参考资料：6, 7. 增加了下列参考资料：33–38.

NSCL-B 1 of 4
- 第6项增加了：应对主动吸烟者提供戒烟指导和教育（戒烟NCCN指南）。尽管主动吸烟者略微增加术后肺部并发症的发生率，但这不应视为手术的一个禁止性危险因素。外科医生不应该单纯由于吸烟状态拒绝为患者手术，因为对于延长早期肺癌患者的生存期，手术占主导地位。

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非小细胞肺癌NCCN指南2017第1版较2016第4版的更新包括：

NSCL-C (1 of 10)

• 一般原则；第5项修改为："有用的参考包括ACR~~-ASTRO放射肿瘤学实践指南~~*实践参数与技术标准*.."

• 一般原则；第4项修改为另外一句话：在一项根治性化/放疗治疗Ⅲ期非小细胞肺癌的前瞻性试验（RTOG 0617）中，与三维适形放疗相比，尽管调强放疗组Ⅲ B期比例较高且治疗体积较大，但是，调强放疗降低高级别放射性肺炎近60%而生存和肿瘤控制结果相似；因此，在这种情况下，适形调强放疗优于三维适形放疗。

NSCL-C (3 of 10)

• 早期淋巴结阴性的立体定向消融放疗；第2项修改为："在美国，只有分割≤5的方案才能符合立体定向放疗任意计费代码的定义，但是，更持久的方案同样略微更合适。~~对于中心型肿瘤（定义为距近端支气管树2cm内），4-10分割风险调整的立体定向消融方案似乎是有效且安全的，而54-60Gy/3f是不安全的，应该避免。前瞻性RTOG 0813正在研究5分割剂量方案。~~*对于中心型肿瘤（定义变为近端支气管树和/或邻接纵隔胸膜2cm内）甚至超中心型肿瘤（定义为紧邻支气管树），4-10分割风险调整的立体定向消融方案似乎是安全有效的，而54-60Gy/3f是不安全的，应该避免。RTOG 0813前瞻性研究了5分割方案的最大耐受剂量，初步显示50 Gy/5f没有高级别的毒性，等待最终结果。*"

NSCL-C (4 of 10)

• 局部晚期/常规分割放疗；第2项修改为："在非随机对照试验中，单纯增加放疗剂量、序贯化/放疗或同步化/放疗与更好的生存相关。~~当遵守正常组织剂量限制时，尽管剂量高达74Gy同步化疗可以安全实施，但是，RTOG 0617比较60Gy对74Gy同步化疗的结果，发现74Gy不能改善总生存，且可能有害。~~*尽管最佳的放疗剂量强度仍然是一个悬而未决的问题，但是，目前不建议常规使用74Gy的更高剂量。*

• 晚期/姑息性放疗；最后一句修改为："当使用更高剂量（> 30 Gy）可行时，应该使用技术减少正常组织的照射（至少3D-CRT以及包括IMRT或酌情使用质子治疗）。"

NSCL-C (7 of 10)

• "请注意-表2-5提供的通常或在过去临床试验中的剂量和使用限制为有用的参考，而不是具体的推荐。"（也适用于NSCL-C 8/10）

NSCL-C (8 of 10)

• 表5：脚注"*"增加了："RTOG 0617数据表明，在胸部放疗后，即使比以前更低的心脏照射剂量也可能不利于生存，因此，更严格的限制可能是合适的。"

NSCL-C (9 of 10)

• 添加了以下参考文献： 5, 17.

NSCL-C (10 of 10)

• 添加了以下参考文献： 52, 53, 55, 89.

非小细胞肺癌NCCN指南2017第1版较2016第4版的更新包括：

NSCL-E

- **同步化/放疗方案**
  - **第4项修改为："顺铂75mg/㎡ d1，培美曲塞500mg/㎡ d1，每21天重复共3周期；同期胸部放疗（非鳞癌）±*追加4周期的培美曲塞500mg/㎡*"**
  - **第5项修改为："紫杉醇45-50mg/㎡每周1次；卡铂AUC 2，同期胸部放疗±*追加2周期紫杉醇200mg/㎡加卡铂AUC 6*"**
- **删除了"同步化/放疗序贯化疗"。**
  - **删除了顺铂/依托泊苷同步放疗序贯顺铂/依托泊苷。**

NSCL-F (1 of 4)

- **一线治疗；第4项修改为："1-2周期后疗效评估，然后每2-4周期1次*或有临床指征时对已知部位强化或平扫CT检查。*"**
- **后续治疗；删除了下列药物项目：尼鲁单抗、派姆单抗、多西他赛、培美曲塞、雷莫芦单抗+多西他赛、厄洛替尼。此信息在讨论中详述。**
- **后续治疗；增加了项目："每6-12周对已知部位强化或平扫CT检查评估疗效。"**

NSCL-F (2 of 4)

- **一线全身治疗方案；腺癌、大细胞肺癌、非特指的NSCLC（PS 0-1）；删除了下列方案：卡铂/长春瑞滨、顺铂/长春瑞滨。**
- **一线全身治疗方案；腺癌、大细胞肺癌、非特指的NSCLC（PS 2）；删除了下列方案：卡铂/长春瑞滨、依托泊苷、伊立替康、长春瑞滨。**

NSCL-F (3 of 4)

- **一线全身治疗方案；鳞状细胞癌（PS 0-1）；删除了下列方案：卡铂/依托泊苷，卡铂/长春瑞滨、顺铂/吉西他滨/奈昔妥珠单抗、顺铂/长春瑞滨。**
- **一线全身治疗方案；鳞状细胞癌（PS 2）；删除了下列方案：卡铂/长春瑞滨、顺铂/吉西他滨/奈昔妥珠单抗、依托泊苷、伊立替康、长春瑞滨。**
- **增加了脚注："在NCCN机构中对于这些适应症，基于这些药物的疗效与安全性和其他可用药物的疗效与安全性相比较，顺铂/吉西他滨/奈昔妥珠单抗不用于一线、厄洛替尼或阿法替尼不用于二线。"**

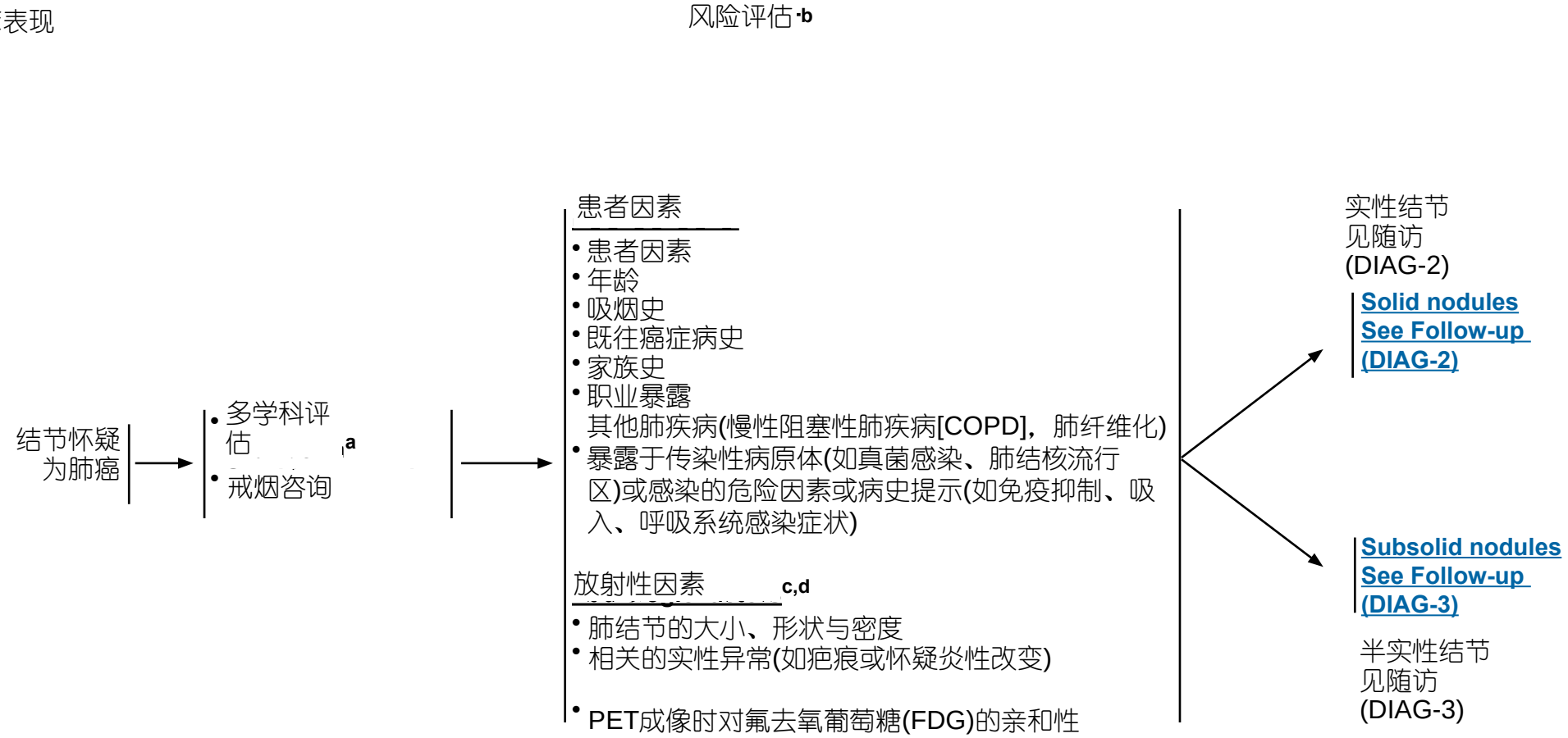
NSCL-H

- **具有遗传学改变患者的新兴靶向药物**
  - **RET重排：增加了凡德他尼作为一个选择。**
  - **删除了ROS1重排，因为该信息已增加到工作步骤中。**
  - **更新了脚注参考资料：3, 4. 增加了脚注参考资料：9, 12.**

肺癌的预防与筛查

- 肺癌是一种独特疾病，主要病因是一种某个行业生产和推销的成瘾性产品。
  大约85%-90%的病例是由主动吸烟或被动吸烟（二手烟）所致。降低肺癌死亡率需要有效的公共卫生政策以阻止开始吸烟，美国食品和药物管理局（FDA）监管烟草产品及其他控烟措施。
- 持续吸烟与第二原发癌、治疗并发症、药物相互作用、其他烟草相关疾病、生活质量降低以及生存期缩短有关。
- 美国外科医生总会报告 (http://www.cdc.gov/tobacco/data_statistics/sgr/2004/pdfs/executivesummary.pdf) 主动吸烟和吸二手烟都可以导致肺癌。证据显示，与吸烟者生活在一起从而吸二手烟者，罹患肺癌的风险增加20%-30% (http://www.ncbi.nlm.nih.gov/books/NBK44324/).
  每个公民都应该被告知烟草消费和暴露于烟草烟雾可对健康产生危害、导致成瘾并威胁生命，应考虑在合适的政府级别通过有效的立法、执法、管理或其他措施来保护所有公民避免暴露于烟草烟雾 (www.who.int/tobacco/framework/final_text/en/).
- 肺癌的致癌物中还含有高度成瘾性物质尼古丁，使该问题进一步复杂化。降低肺癌死亡率需要广泛贯彻医疗保健研究与质量局（AHRQ）指南 (http://www.ahrq.gov/professionals/clinicians-providers/guidelines-recommendations/tobacco/index.html) 以发现、劝告及治疗尼古丁成瘾患者。
- 当前吸烟或有吸烟史者患肺癌的风险明显增高；对于这些患者，尚未确定化学预防药物。如果可能，应鼓励这些患者参加化学预防试验。
- 推荐对选择性高危吸烟者和有吸烟史者使用低剂量CT（LDCT）进行肺癌筛查 (见 NCCN 肺癌筛查指南).
- 见 NCCN 戒烟指南。

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.



[a]包括胸外科医生、胸部放射学家和肺科专家的多学科评估共同确定癌症诊断的可能性和最的佳诊断或随访策略。
[b]风险计算器可用于量化具体患者和放射因素，但不能代替在肺癌诊断方面有丰富经验的多学科诊断小组的评估。.
[c]见诊断评估原则 (DIAG-A 1 of 2).
[d]最重要的影像因素是与既往影像学检查相比是发生变化还是稳定。

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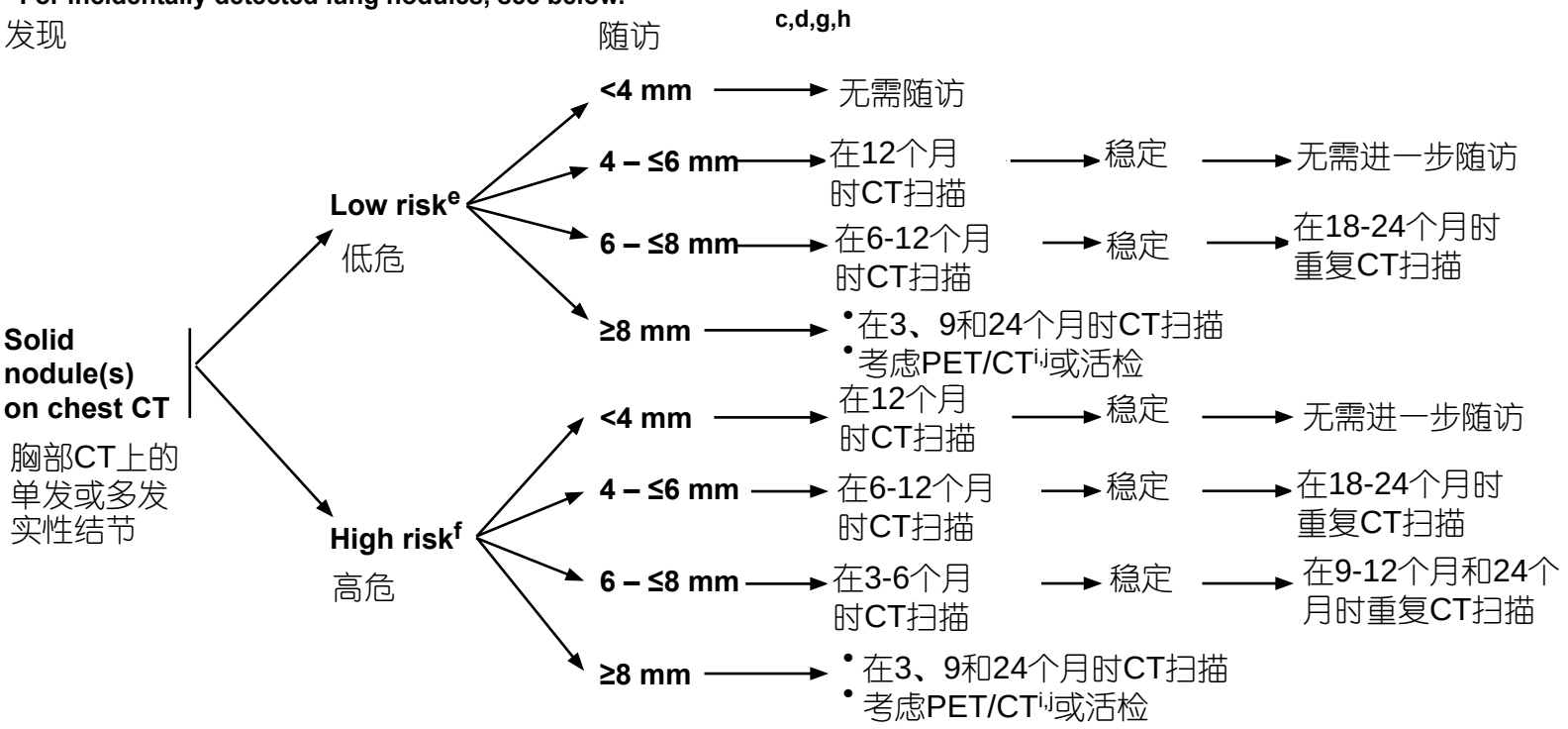
• Lung nodules in asymptomatic, high-risk patients detected during lung cancer screening with LDCT, see the NCCN Guidelines for Lung Cancer Screening.
• For incidentally detected lung nodules, see below.



[c]见诊断评估原则 (DIAG-A 1 of 2).
[d]最重要的影像因素是与既往影像学检查相比是发生变化还是稳定。

[e]低危=几乎不吸烟或无吸烟史或其他已知的危险因素。
[f]高危=吸烟史或其他已知的危险因素。已知的危险因素包括一级亲属的肺癌史；暴露于石棉、氡或铀。

[g]非实性、部分实性或磨玻璃结节可能需要较长时间的随访以排除进展缓慢的（惰性）腺癌。

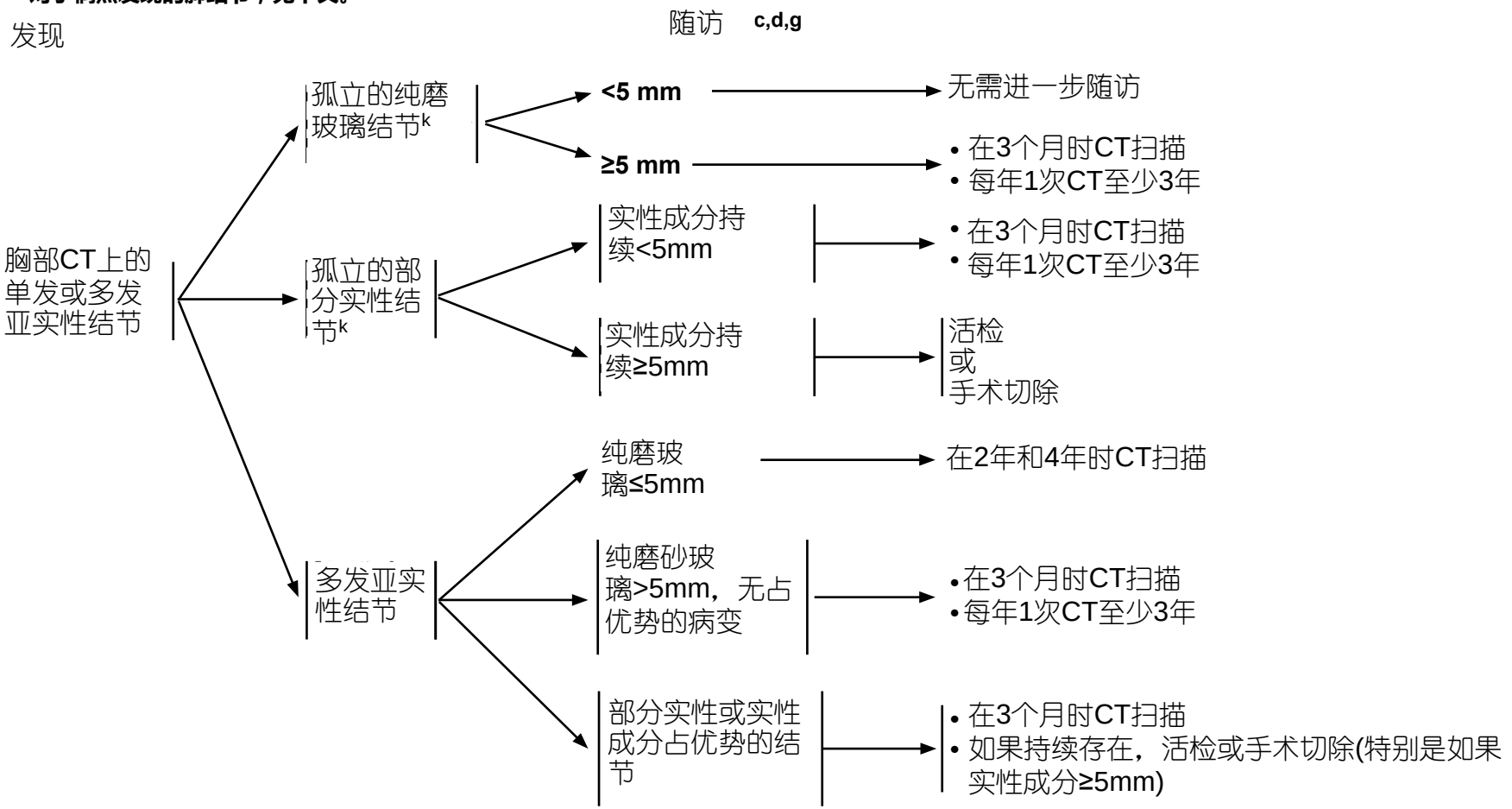
[h]根据美国弗莱施纳学会指南改编： MacMahon H, Austin JH, Gamsu G, et al. Guidelines for management of small pulmonary nodules detected on CT scans: a statement from the Fleischner Society. Radiology 2005;237:395-400. © Radiological Society of North America. 美国弗莱施纳学会指南并未规定是否有必要强化或LDCT是合适的。首选LDCT，除非有为了更好的诊断分辨率而进行对比剂增强的理由。

[i]颅底到膝关节或全身PET/CT检查。阳性PET结果定义为肺结节的标准摄取值（SUV）大于基线纵隔血池。PET扫描阳性发现可以是由感染或炎症所致，包括无肺癌的局部感染、肺癌合并相关的（如阻塞性）感染以及存在肺癌合并相关的炎症（如淋巴结、肺组织、胸膜）。PET扫描假阴性可以是由小结节、低细胞密度（非实性结节或磨玻璃影[GGO]）或肿瘤的FDG亲和力低（如原位腺癌[以前称为细支气管肺泡癌]、类癌）所引起的。

[j]经PET-CT检查后怀疑肺癌的患者，在任何非手术治疗前均需要组织学证实。当不可能活检时，应开展包括放射肿瘤学、外科和肺病介入科的多学科评估。

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

- **肺癌筛查期间LDCT发现的无症状、高危患者的肺结节，见 NCCN Guidelines for Lung Cancer Screening.**
- **对于偶然发现的肺结节，见下文。**



[c] 见诊断评估原则 (DIAG-A 1 of 2).
[d] 最重要的影像因素是与既往影像学检查相比是发生变化还是稳定。
[g] 非实性、部分实性或磨玻璃结节可能需要较长时间的随访以排除进展缓慢的（惰性）腺癌。
[k] Naidich DP, Bankier AA, MacMahon H, et al. Recommendations for the management of subsolid pulmonary nodules detected on CT: A statement from the Fleischner Society. Radiology 2013;266:304-317. 指南并未规定是否有必要强化或LDCT是合适的。首选LDCT，除非有为了更好的诊断分辨率而进行对比剂增强的理由。

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诊断评估原则

- 临床高度怀疑I或II期肺癌的患者（根据危险因素和影像学表现）术前不需要活检。
  - 活检增加时间成本、费用和程序风险，对于治疗决策可能不需要。
  - 如果强烈怀疑不是肺癌，术前活检可能是恰当的，可经空芯针活检或细针穿刺抽吸（FNA）确诊。
  - 如果术中诊断好像困难或非常危险，术前活检可能是合理的。
  - 如果术前未获得组织诊断，则在肺叶切除、双肺叶切除或全肺切除术之前必须术中诊断（即楔形切除、针吸活检）。
- 支气管镜检查最好在计划好的切除术中进行，而不是作为一个单独的步骤。
  - 支气管镜检查应该在术前进行 (见 NSCL-2).
  - 术前可能不需要单独的支气管镜检查来确定治疗决策，因增加时间成本、费用和程序风险。
  - 如果中心型肿瘤切除前需要评估活检、手术计划（如有可能袖状切除）或术前气道准备（如阻塞性病变的取芯），那么术前支气管镜检查可能是合适的。
- 对于大多数临床I或II期肺癌患者，在术前推荐侵袭性纵隔分期 (见 NSCL-2).
  - 在计划的切除术前患者最好接受侵袭性纵隔分期作为最初的步骤（同一麻醉过程），而不是作为一个单独的步骤。
  - 单独的分期步骤增加时间成本、费用、照护协调、不便以及额外的麻醉风险。
  - 对于临床高度怀疑淋巴结为N2或N3或无法获得术中细胞学或冰冻切片分析时，术前侵袭性纵隔分期可能是合理的。
- 在怀疑非小细胞肺癌（NSCLC）的患者，许多技术可获得组织学诊断。
  - 应常规使用的诊断工具包括：
    - ◊ 痰细胞学检查
    - ◊ 支气管镜活检和经支气管针吸活检（TBNA）
    - ◊ 影像引导下经皮肺穿刺活检（首选）或细针穿刺活检
    - ◊ 胸腔穿刺术
    - ◊ 纵隔镜检查
    - ◊ 电视胸腔镜手术（VATS）和开放手术活检
  - 为活检提供重要辅助策略的诊断工具包括：
    - ◊ 支气管内超声（EBUS）引导下活检
    - ◊ 内镜超声（EUS）引导下活检
    - ◊ 导航支气管镜

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诊断评估原则

- 对于个体患者首选的诊断策略取决于肿瘤的大小和位置、病变位于纵隔还是远处、患者特征（如肺的病理学和/或其他重要的合并症）以及本地医生的经验和专业知识。
  - 选择最佳诊断步骤应考虑的因素包括：
    - ◊ 预期的诊断阳性率（敏感性）
    - ◊ 诊断准确性包括特异性，特别是阴性诊断的可靠性（即真阴性）
    - ◊ 用于诊断和分子检测的组织标本足够大
    - ◊ 操作的侵袭性与风险
    - ◊ 评估的效能
      - – 操作的路径与时机
      - – 同步分期是有益的，因为这避免了额外的活检或程序。活检最好可以得到最高分期的病理组织（即，对可疑转移灶或纵隔淋巴结而非肺部病变进行活检）。因此，在临床高度怀疑侵袭性、晚期肿瘤的情况下，在选择诊断活检部位之前，通常最好进行PET成像。
    - ◊ 现有的技术和专业知识
    - ◊ PET成像提议的活检部位的肿瘤活性。
  - 可疑I-Ⅲ期肺癌的最佳诊断步骤应该由胸部放射学家、介入放射学家以及将胸部肿瘤作为其实践的重要部分、通过职业认证的胸外科医生决定。多学科评估还应包括具有高级支气管镜诊断专业技巧的肺脏专家或胸外科医生。
  - 首次诊断检查首选效率最高、侵袭性最小的活检。
    - ◊ 中心性肿块以及怀疑支气管受累的患者应行支气管镜检查。
    - ◊ 周围性（外1/3）结节患者可能受益于导航支气管镜、径向探头支气管内超声或经胸针吸活检（TTNA）。
    - ◊ 具有可疑淋巴结病变的患者应通过支气管内超声（EBUS）、超声内镜（EUS）、导航支气管镜或纵隔镜活检。
      - – 如有必要，支气管内超声（EBUS）可进入2R/2L、4R/4L、7、10R/10L和肺门淋巴结区。
      - – 超声内镜（EUS）引导的穿刺活检可进一步进入5、7、8和9淋巴结区，如果这些区域临床可疑。
      - – 经皮经胸针吸活检（TTNA）和前纵隔切开术（即Chamberlain术式，左前纵隔切开术）可进一步进入前纵隔（5和6区）淋巴结，如果这些临床可疑。
    - ◊ 超声内镜（EUS）同样可以可靠地进入左侧肾上腺。
    - ◊ 合并胸腔积液的肺癌患者应进行胸腔穿刺细胞学检查。初始穿刺细胞学阴性并不能排除胸膜受累。在开始根治性治疗前，应该考虑追加胸腔穿刺和/或胸腔镜评估胸膜情况。
    - ◊ 怀疑有孤立性转移灶的患者，如果可行的话，该病灶应该有组织学证实。
    - ◊ 怀疑有转移性疾病的患者，如果可行的话，应该确认其中的一个转移灶。
    - ◊ 可能有多发转移灶的患者——根据临床强烈怀疑——如果对这些转移灶活检在技术上有困难或者有很大风险，应该行肺原发灶或纵隔淋巴结活检。

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Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

非小细胞肺癌的病理诊断

NSCLC

初步评估

- 复阅病理[a]
- 病史与体格检查(包括一般情况+体重减轻)[b]
- 胸部和上腹部强化CT，包括肾上腺
- CBC，血小板
- 化学检查
- 戒烟咨询、辅导和药物治疗
- 使用5A准则：询问、建议、评估、协助、协商

http://www.ahrq.gov/clinic/tobacco/5steps.htm

- **Integrate palliative care[c]** (See NCCN Guidelines for Palliative Care)

一体化姑息治疗[c](见姑息治疗NCCN指南)

临床分期

IA期，周围型 [d] **(T1ab, N0)**	See Pretreatment Evaluation (NSCL-2)
I期，周围型[d](T2aN0)；中心型[d](T1ab-T2aN0)；ⅡA期(T1ab-T2abN1；T2bN0)；ⅡB期(T3N0)[e] ⅢA期(T3N1)	See Pretreatment Evaluation (NSCL-2)
ⅡB期[f](T3浸润，N0) ⅢA期[f](T4扩散，N0-1；T3N1)	See Pretreatment Evaluation (NSCL-4)
ⅢA期[f](T1-3、N2)	See Pretreatment Evaluation (NSCL-7)
孤立或分散的肺结节；(ⅡB、ⅢA、Ⅳ期)	See Pretreatment Evaluation (NSCL-7)
多发性肺癌	See Treatment (NSCL-9)
ⅢB期[f](T1-3N3)纵隔CT阳性 对侧(淋巴结≥1cm)或可触及锁骨上淋巴结	See Pretreatment Evaluation (NSCL-11)
CT扫描ⅢB期[f](T4N2-3)	See Pretreatment Evaluation (NSCL-12)
Ⅳ期(M1a)[c](胸腔或心包积液)	See Pretreatment Evaluation (NSCL-12)
Ⅳ期(M1b)[c] 局限部位可切除的肺部病灶	See Pretreatment Evaluation (NSCL-13)
Ⅳ期(M1b)[c]广泛转移	See Systemic Therapy (NSCL-16)

[a] 见病理学评估原则 (NSCL-A).

[b] 加强虚弱或老年患者的评估可以更好地预测各种治疗模式（特别是手术）后的并发症。首选的虚弱评估体系尚未建立。

[c] Temel JS, Greer JA, Muzikansky A, et al. Early palliative care for patients with metastatic non-small cell lung cancer. N Engl J Med 2010;363:733-742.

[d] 根据胸部CT：周围型=肺的外1/3；中心型=肺的内2/3。

[e] T3, N0 与大小或卫星结节有关。

[f] 对于ⅡB和Ⅲ期患者，通常考虑一种以上的治疗模式（手术、放疗或化疗），应进行多学科评估。

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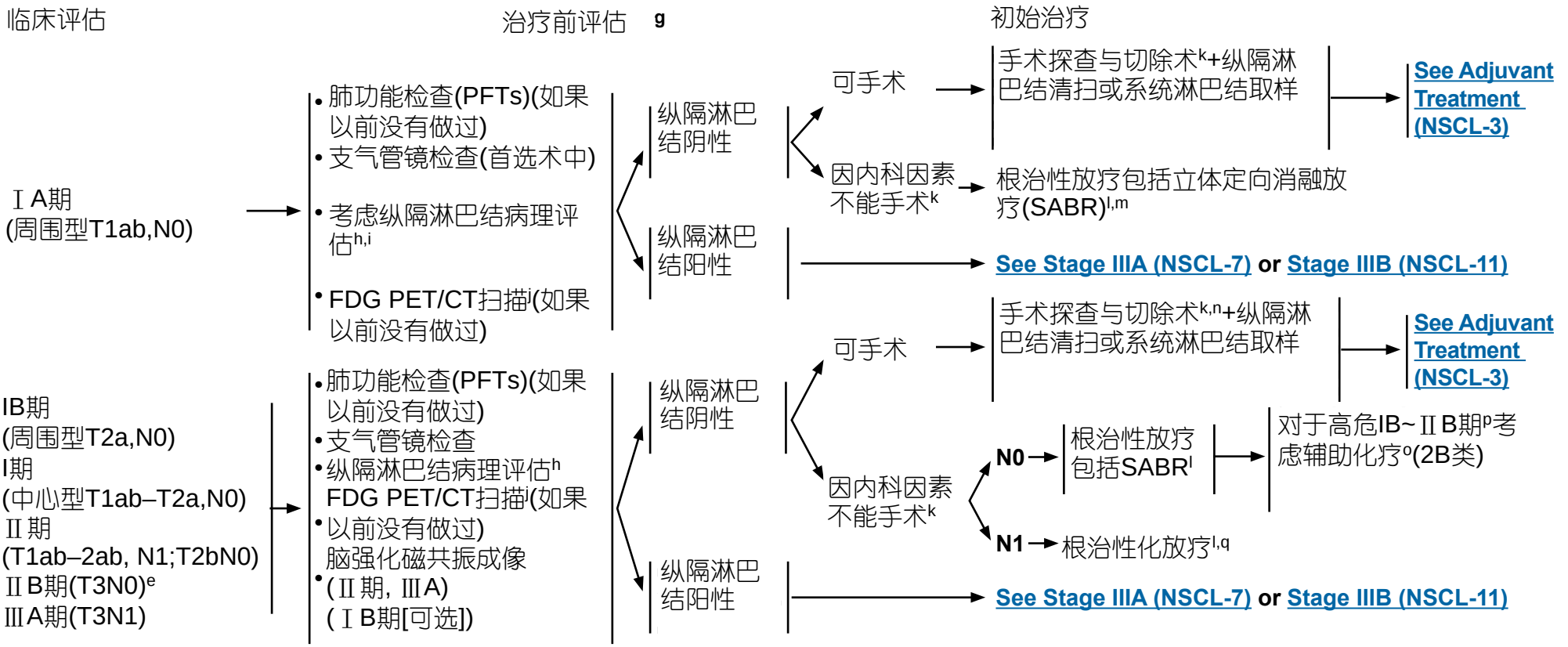

[e] T3, N0与大小或卫星结节有关。

[g] 检查不是按照优先级顺序列表，而是根据临床情况、工作流程以及资源的明智地使用而定。

[h] 评估方法包括纵隔镜检查、纵隔切开术、超声支气管镜、超声内镜以及CT引导下穿刺活检。

[i] 实性肿瘤<1cm和纯的非实性肿瘤<3cm，CT和PET阴性，纵隔淋巴结阳性的可能性小，因此，切除术前纵隔病理评估不是必须的。

[j] 颅底到膝关节或全身PET/CT检查。PET/CT扫描发现的阳性远隔病变需要病理或其他影像学确认。如果PET/CT扫描纵隔淋巴结阳性，需要病理学确认淋巴结状态。

[k] 见外科治疗原则 (NSCL-B).

[l] 见放射治疗原则 (NSCL-C).

[m] 对于选择的患者介入放射消融治疗是一种选择。

[n] 在手术评估后，有可能接受辅助化疗的患者可用诱导化疗代替。

[o] 见新辅助和辅助治疗的化疗方案 (NSCL-D).

[p] 典型的高危因素包括低分化肿瘤（包括肺神经内分泌肿瘤[不包括分化良好的神经内分泌肿瘤]）、血管侵犯、楔形切除、肿瘤>4cm、脏层胸膜受累和淋巴结状态不明（Nx）。单独这些因素可能不是一个指征，但当确定辅助化疗治疗时可以考虑。

[q] 见联合放射治疗使用的化疗方案 (NSCL-E).

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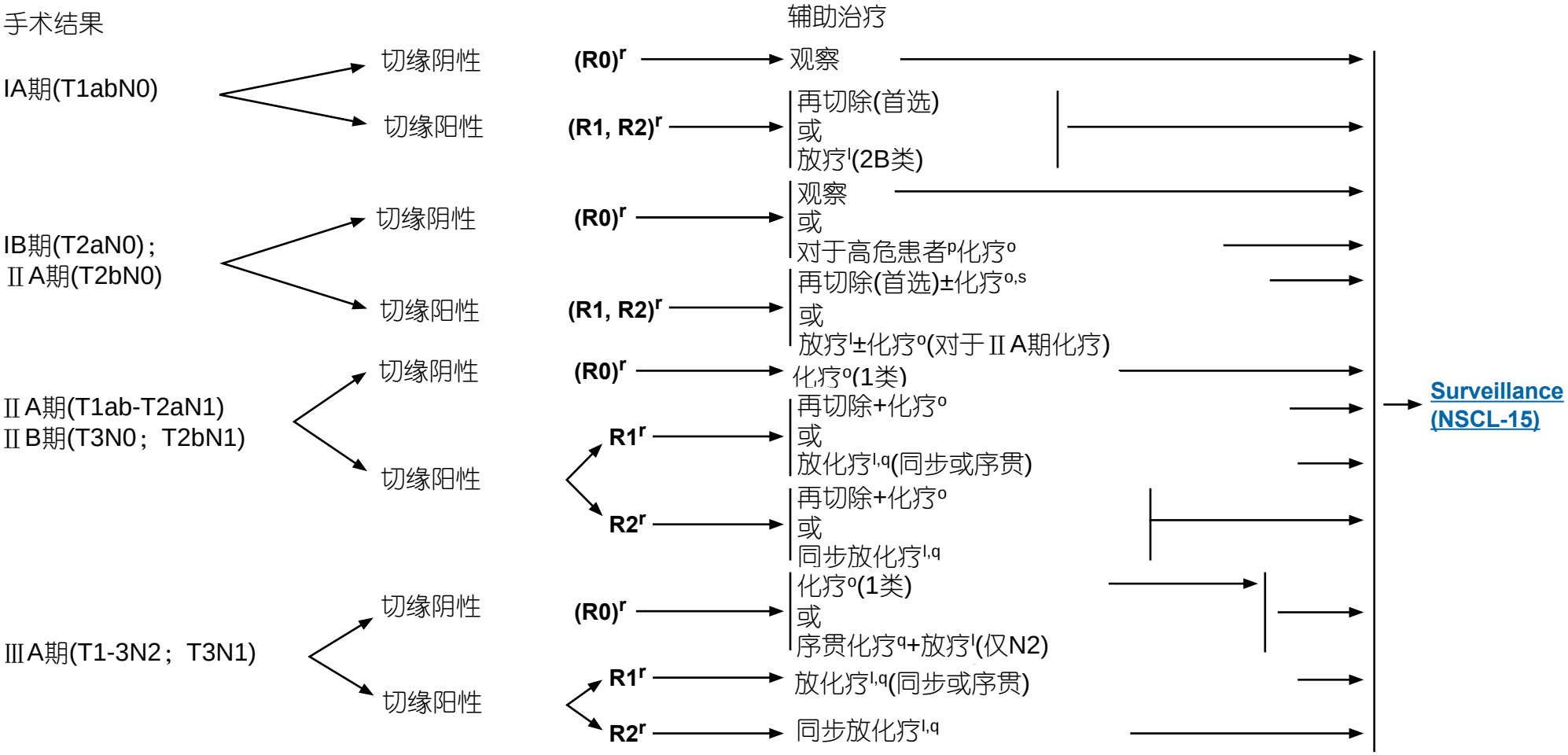

l见放射治疗原则 (NSCL-C).

o见新辅助和辅助治疗的化疗方案 (NSCL-D).

p典型的高危因素包括低分化肿瘤（包括肺神经内分泌肿瘤[不包括分化良好的神经内分泌肿瘤]）、血管侵犯、楔形切除、肿瘤>4cm、脏层胸膜受累和淋巴结状态不明（Nx）。单独这些因素可能不是一个指征，但当确定辅助化疗治疗时可以考虑。

q见联合放射治疗使用的化疗方案 (NSCL-E).

r R0 =无肿瘤残留，R1 =镜下肿瘤残留，R2 =肉眼肿瘤残留。

s在评估辅助化疗的必要性时，肿瘤增大是一个重要变量。

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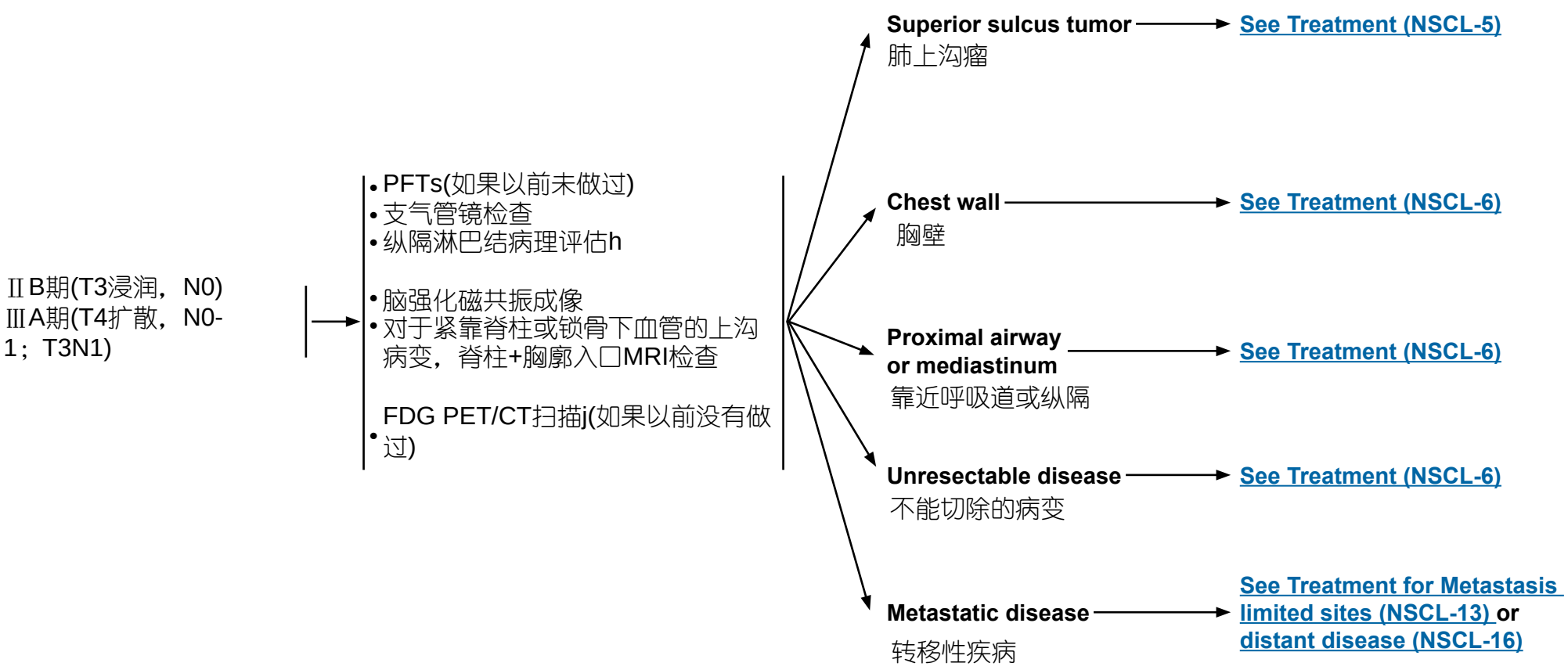

h评估方法包括纵隔镜检查、纵隔切开术、超声支气管镜、超声内镜以及CT引导下穿刺活检。
j颅底到膝关节或全身PET/CT检查。PET/CT扫描发现的阳性远隔病变需要病理或其他影像学确认。如果PET/CT扫描纵隔淋巴结阳性，需要病理学确认淋巴结状态。

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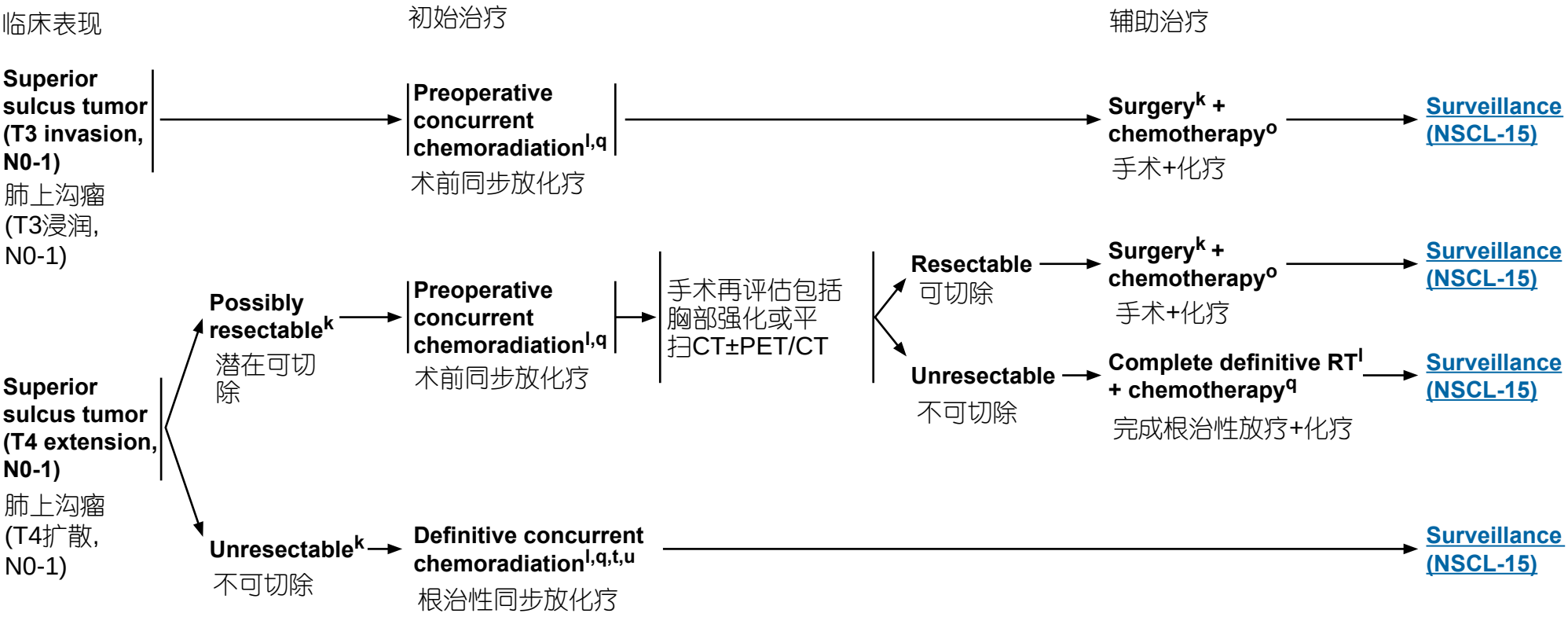

[k] 见外科治疗原则 (NSCL-B).
[l] 见放射治疗原则 (NSCL-C).
[o] 见新辅助和辅助治疗的化疗方案 (NSCL-D).
[q] 见联合放射治疗使用的化疗方案 (NSCL-E).

[t] 如果患者不适于手术，放疗应持续不间断直至根治量。
[u] 如果初始同步放疗时未给予足量化疗，则追加2周期的足量化疗。

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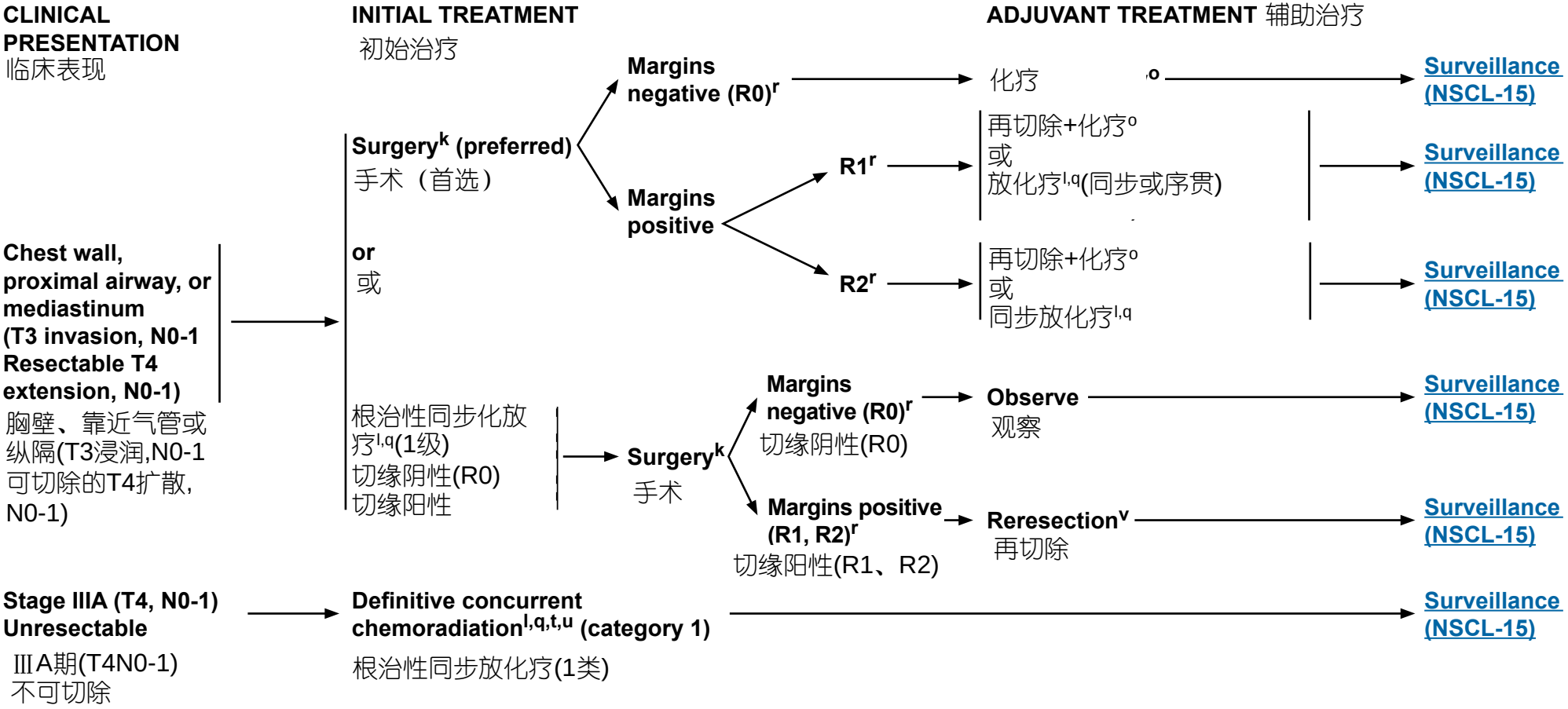

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[l] 见放射治疗原则 (NSCL-C).
[o] 见新辅助和辅助治疗的化疗方案 (NSCL-D).
[q] 见联合放射治疗使用的化疗方案 (NSCL-E).
[r] R0 =无肿瘤残留，R1 =镜下肿瘤残留，R2 =肉眼肿瘤残留。

[t] 如果患者不适于手术，放疗应持续不间断直至根治量。
[u] 如果初始同步放疗时未给予足量化疗，则追加2周期的足量化疗。
[v] 如果放化疗作为初始治疗，则考虑追量放疗。

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CLINICAL ASSESSMENT
临床评估

PRETREATMENT EVALUATION
治疗前评估

MEDIASTINAL BIOPSY FINDINGS AND RESECTABILITY 纵隔活检结果与可切除性

Stage IIIA (T1-3, N2)
ⅢA期(T1-3、N2)

- **PFTs (if not previously done)**
- **Bronchoscopy**
- **Pathologic mediastinal lymph node evaluation[h]**
- **FDG PET/CT scan[j] (if not previously done)**
- **Brain MRI with contrast**

肺功能检查(PFTs)(如果以前没有做过)
支气管镜检查
纵隔淋巴结病理评估
FDG PET/CT扫描(如果以前没有做过)
脑强化磁共振成像

- **N2, N3 nodes negative** → **See Treatment T 1-3, N0-1 (NSCL-8)**
  N2、N3淋巴结阴性
- **N2 nodes positive, M0** → **See Treatment (NSCL-8)**
  N2+、M0
- **N3 nodes positive, M0** → **See Stage IIIB (NSCL-11)**
  N3+、M0
- **Metastatic disease** → **See Treatment for Metastasis limited sites (NSCL-13) or distant disease (NSCL-16)**
  转移性疾病

Separate pulmonary nodule(s) (Stage IIB, IIIA, IV)
孤立或分开的肺结节(ⅡB、Ⅲ、Ⅳ期)

- **PFTs (if not previously done)**
- **Bronchoscopy**
- **Pathologic mediastinal lymph node evaluation[h]**
- **Brain MRI with contrast**
- **FDG PET/CT scan[j] (if not previously done)**

肺功能检查(PFTs)(如果以前没有做过)
支气管镜检查
纵隔淋巴结病理评估
脑强化磁共振成像
FDG PET/CT扫描(如果以前没有做过)

- **Separate pulmonary nodule(s), same lobe (T3, N0-1) or ipsilateral non-primary lobe (T4, N0-1)** → **See Treatment (NSCL-9)**
  分开的肺结节、同叶(T3,N0-1)或同侧非原发叶(T4,N0-1)
- **Stage IV (N0, M1a): Contralateral lung (solitary nodule)** → **See Treatment (NSCL-9)**
  Ⅳ期(N0、M1a)对侧肺(孤立结节)
- **Extrathoracic metastatic disease** → **See Treatment for Metastasis limited sites (NSCL-13) or distant disease (NSCL-16)**
  胸外转移性疾病

[h]评估方法包括纵隔镜检查、纵隔切开术、超声支气管镜、超声内镜以及CT引导下穿刺活检。
[j]颅底到膝关节或全身PET/CT检查。PET/CT扫描发现的阳性远隔病变需要病理或其他影像学确认。如果PET/CT扫描纵隔淋巴结阳性，需要病理学确认淋巴结状态。

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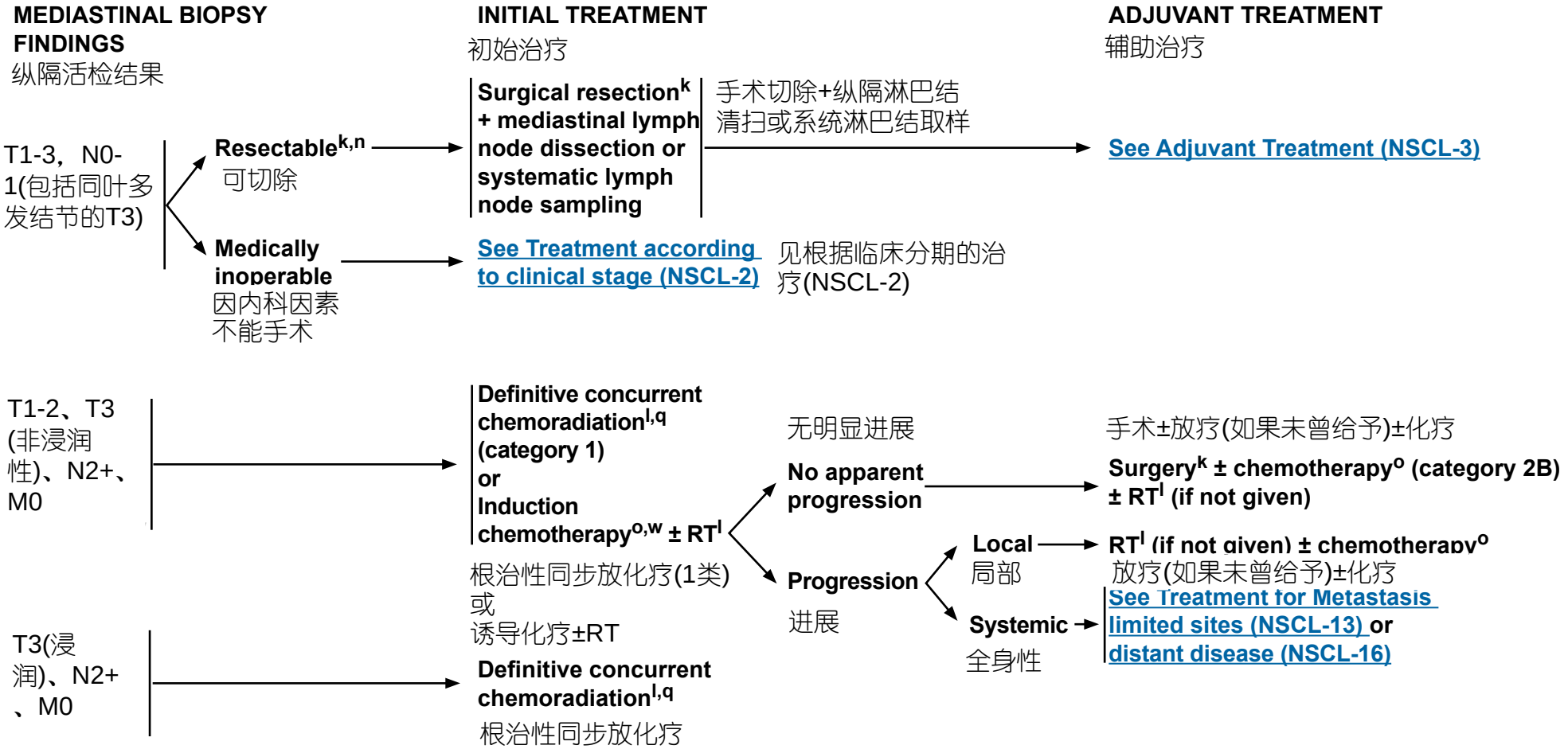

[k] 见外科治疗原则 (NSCL-B).
[l] 见放射治疗原则 (NSCL-C).
[n] 在手术评估后，有可能接受辅助化疗的患者可用诱导化疗代替。
[o] 见新辅助和辅助治疗的化疗方案 (NSCL-D).
[q] 见联合放射治疗使用的化疗方案 (NSCL-E).
[w] 胸部强化CT和/或PET/CT以评估进展。

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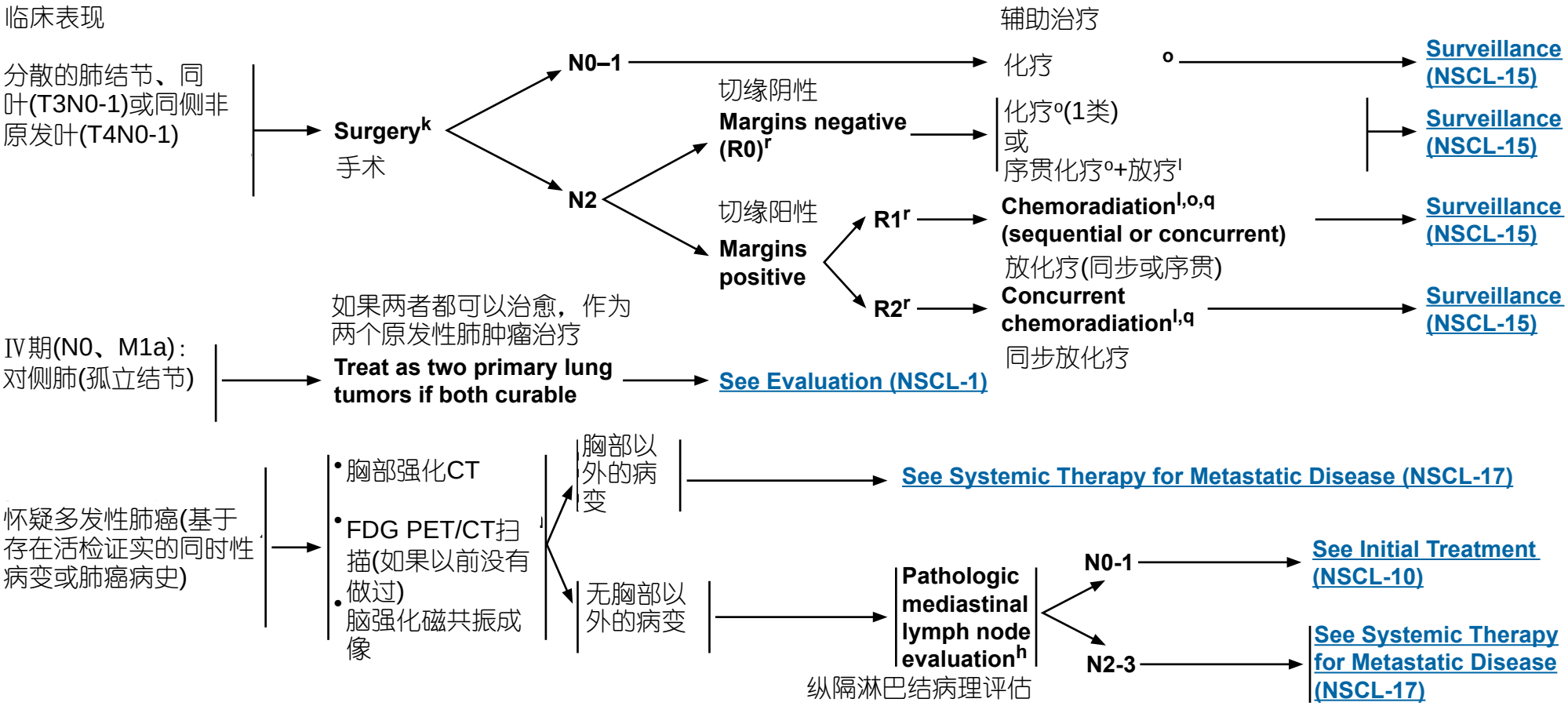

[h]评估方法包括纵隔镜检查、纵隔切开术、超声支气管镜、超声内镜以及CT引导下穿刺活检。

[j]颅底到膝关节或全身PET/CT检查。PET/CT扫描发现的阳性远隔病变需要病理或其他影像学确认。如果PET/CT扫描纵隔淋巴结阳性，需要病理学确认淋巴结状态。

[k]见外科治疗原则 (NSCL-B).

[l]见放射治疗原则 (NSCL-C).

[o]见新辅助和辅助治疗的化疗方案 (NSCL-D).

[q]见联合放射治疗使用的化疗方案 (NSCL-E).

[r]R0 =无肿瘤残留，R1 =镜下肿瘤残留，R2 =肉眼肿瘤残留。

[x]不同细胞类型（如鳞状细胞癌、腺癌）的病变可能是不同的原发性肿瘤。这种分析可能受到小活检标本的制约。不过，细胞类型相同的病变不一定是转移。

[y]关于半实性肺结节的评估、检查和管理指南，请见可疑肺癌结节的诊断评估（DIAG-1）。(DIAG-1).

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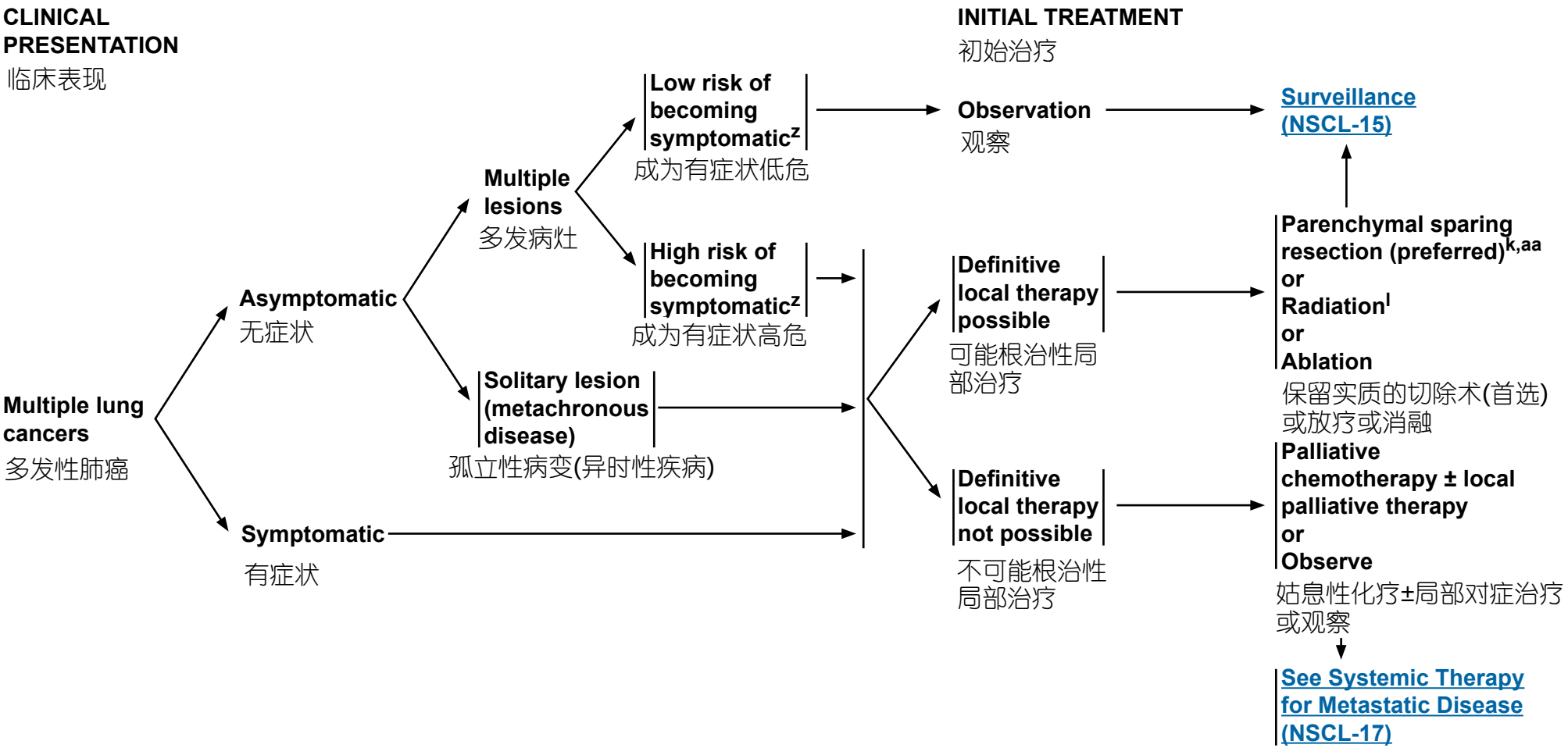

[k] 见外科治疗原则 (NSCL-B).
[l] 见放射治疗原则 (NSCL-C).
[z] 发展成有症状的低危病变可以观察（如生长缓慢的小的亚实性结节）。然而，如果病灶发展到有症状或出现症状高危（如亚实性结节加速生长或实性成分增加或氟脱氧葡萄糖摄取增加，即便小），则应考虑治疗。
[aa] 首选保留肺切除术，但应该使用肿瘤分类和学会专家的意见指导个体化的治疗计划。应该对患者进行多学科（即外科、放射肿瘤学、肿瘤内科）评估。

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CLINICAL ASSESSMENT
临床评估

PRETREATMENT EVALUATION
治疗前评估

INITIAL TREATMENT
初始治疗

Stage IIIB (T1–3, N3) →

- 肺功能检查(PFTs)(如果以前没有做过)
- FDG PET/CT扫描[j](如果以前没有做过)
- 脑强化磁共振成像
- 经病理学证实的N3病变：
  - 纵隔镜检查
  - 锁骨上淋巴结活检
  - 胸腔镜
  - 针吸活检
  - 纵隔切开术
  - 内镜超声活检
  - 支气管内超声活检

→ **N3 negative** N3阴性 → **See Initial treatment for stage I–IIIA (NSCL-8)**

→ **N3 positive** N3+ → **Definitive concurrent chemoradiation[l,q,u] (category 1)** 根治性同步放化疗(1类)

→ **Metastatic disease** 转移性疾病 → **See Treatment for Metastasis limited sites (NSCL-13) or distant disease (NSCL-16)**

[j]颅底到膝关节或全身PET/CT检查。PET/CT扫描发现的阳性远隔病变需要病理或其他影像学确认。如果PET/CT扫描纵隔淋巴结阳性，需要病理学确认淋巴结状态。
[l]见放射治疗原则 (NSCL-C).
[q]见联合放射治疗使用的化疗方案 (NSCL-E).
[u]如果初始同步放疗时未给予足量化疗，则追加2周期的足量化疗。

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CLINICAL ASSESSMENT
临床评估

PRETREATMENT EVALUATION
治疗前评估

INITIAL TREATMENT
初始治疗

ⅢB期
(T4, N2–3)

- FDG PET/CT扫描(如果以前没有做过)
- 脑强化磁共振成像
- 经病理学证实的N3病变：
  - 纵隔镜检查
  - 锁骨上淋巴结活检
    胸腔镜
  - 针吸活检
  - 纵隔切开术
  - 内镜超声活检
  - 支气管内超声活检

对侧纵隔淋巴结阴性

Contralateral mediastinal node negative

同侧纵隔淋巴结阴性(T4N0-1) → See Treatment for Stage IIIA (NSCL-6)

同侧纵隔淋巴结阳性(T4N2) → **Definitive concurrent chemoradiation[l,q,u] (category 1)** 根治性同步放化疗(1类)

Contralateral mediastinal node positive (T4, N3) → **Definitive concurrent chemoradiation[l,q,u] (category 1)** 根治性同步放化疗(1类)

对侧纵隔淋巴结阳性(T4N3)

Metastatic disease
转移性疾病 → See Treatment for Metastasis limited sites (NSCL-13) or distant disease (NSCL-16) 见局限部位转移(NSCL-13)或远处转移(NSCL-16)的治疗

Ⅳ期，M1a：胸腔或心包积液

Stage IV, M1a: pleural or pericardial effusion → **Thoracentesis or pericardiocentesis ± thoracoscopy if thoracentesis indeterminate**
胸腔或心包穿刺±胸腔镜检查，如果胸腔穿刺术不能确定

Negative[bb]
阴性 → **See Treatment according to TNM stage (NSCL-8)** 见根据临床分期的治疗

Positive[bb]
阳性 → **Local therapy if necessary (eg, pleurodesis, ambulatory small catheter drainage, pericardial window) + treatment for stage IV disease solitary site or distant disease (NSCL-17)**
如有必要局部治疗(如胸膜固定术，不卧床小导管引流、心包开窗)+治疗Ⅳ期孤立病变或远处转移性病变(NSCL-17)

[j]颅底到膝关节或全身PET/CT检查。PET/CT扫描发现的阳性远隔病变需要病理或其他影像学确认。如果PET/CT扫描纵隔淋巴结阳性，需要病理学确认淋巴结状态。

[l]见放射治疗原则 (NSCL-C).

[q]见联合放射治疗使用的化疗方案 (NSCL-E).

[u]如果初始同步放疗时未给予足量化疗，则追加2周期的足量化疗。

[bb]尽管肺癌患者的胸腔积液大多数是肿瘤引起的，仍有少数患者多次胸腔积液细胞病理学检查未发现肿瘤，且积液是非血性、非渗出性。当这些因素及临床判断确定积液与肿瘤无关时，积液应不作为分期因素。心包积液使用同样的标准分类。

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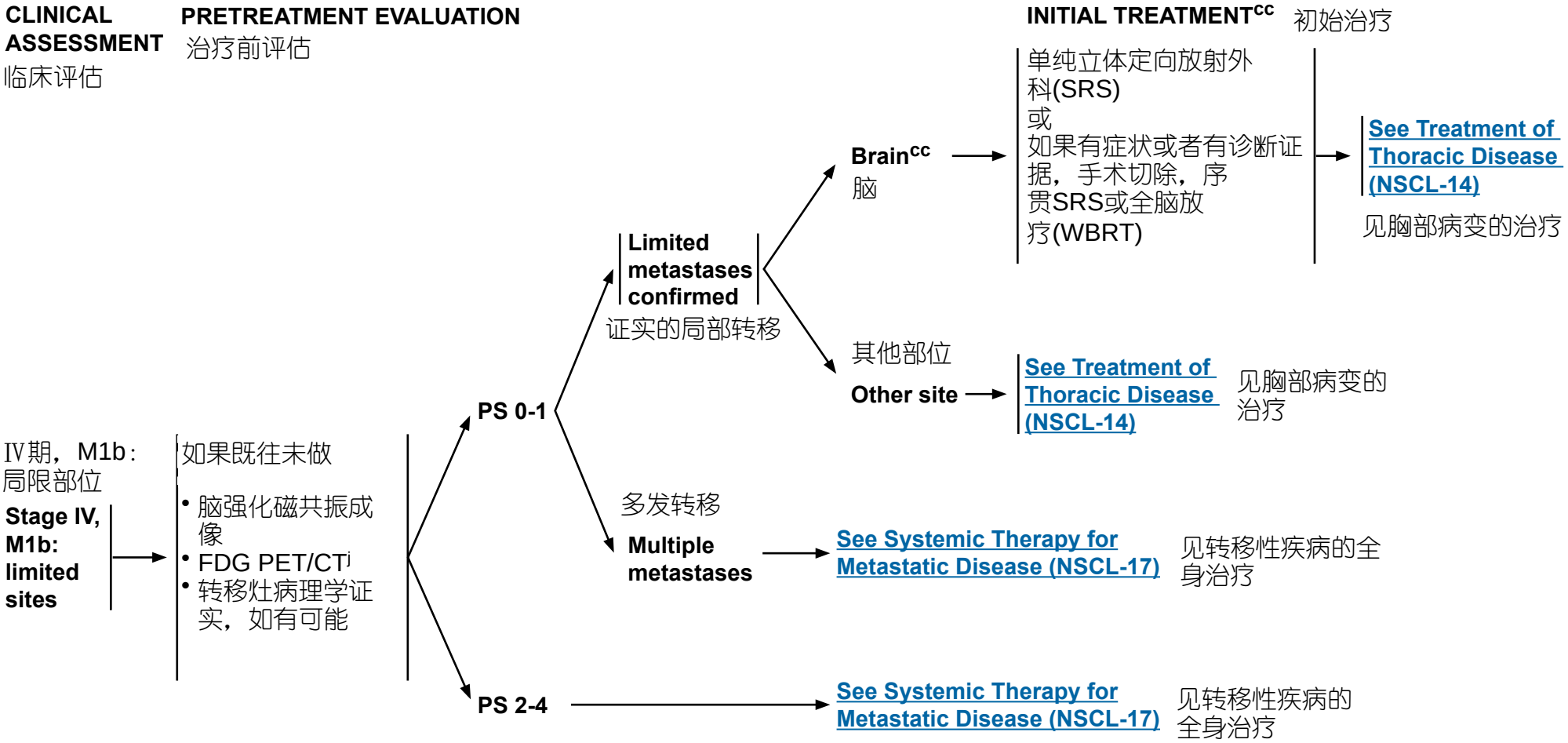

j颅底到膝关节或全身PET/CT检查。PET/CT扫描发现的阳性远隔病变需要病理或其他影像学确认。

cc见中枢神经系统肿瘤NCCN指南

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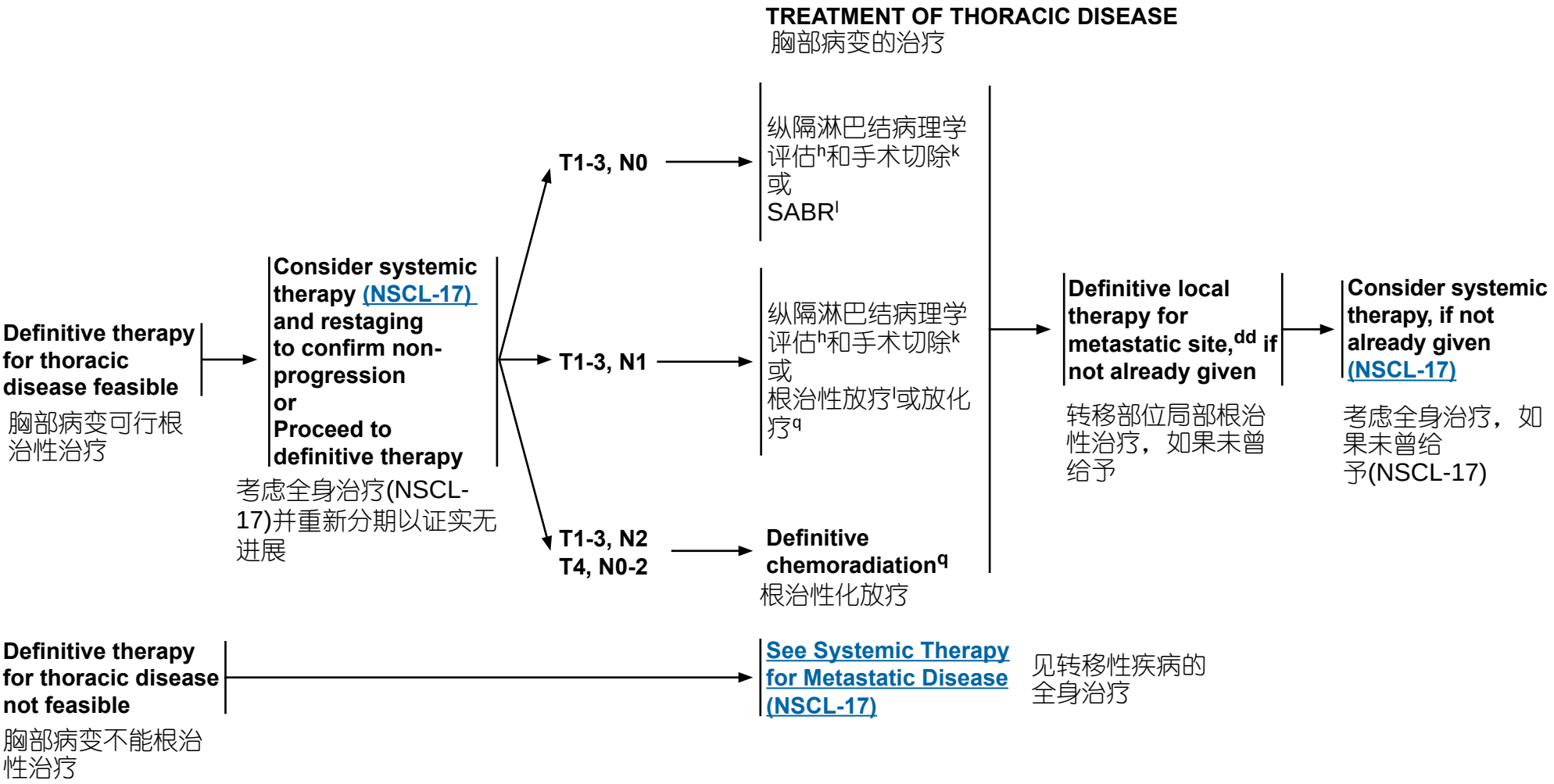


[h]评估方法包括纵隔镜检查、纵隔切开术、超声支气管镜、超声内镜以及CT引导下穿刺活检。
[k]见外科治疗原则 (NSCL-B).
[l]见放射治疗原则 (NSCL-C).
[q]见联合放射治疗使用的化疗方案 (NSCL-E).
[dd]通常放疗（包括体部立体定向放射治疗）或手术切除。

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

SURVEILLANCE AFTER COMPLETION OF DEFINITIVE THERAPY
根治性治疗结束后监测

无临床/影像学疾病证据

- I-Ⅱ期(初始治疗包括手术±化疗)
  - 病史与体格检查和胸部CT±强化，最初2-3年每6个月1次，之后每年1次病史与体格检查和胸部低剂量非强化CT
- I-Ⅱ期(初始治疗包括放疗)或Ⅲ期或Ⅳ期(所有部位的寡转移灶均给予根治性治疗)
  - 病史与体格检查和胸部CT±强化，最初3年每3-6个月1次，之后病史与体格检查和胸部CT±强化，最初2年每6个月1次，之后每年1次病史与体格检查和胸部低剂量非强化CT
    - ◊ 残存或新的影像学异常可能需要更频繁的影像学检查
- 戒烟咨询、辅导和药物治疗
- 不常规要求PET/CTee或脑部核磁共振造影
- See Cancer Survivorship Care (NSCL-G)

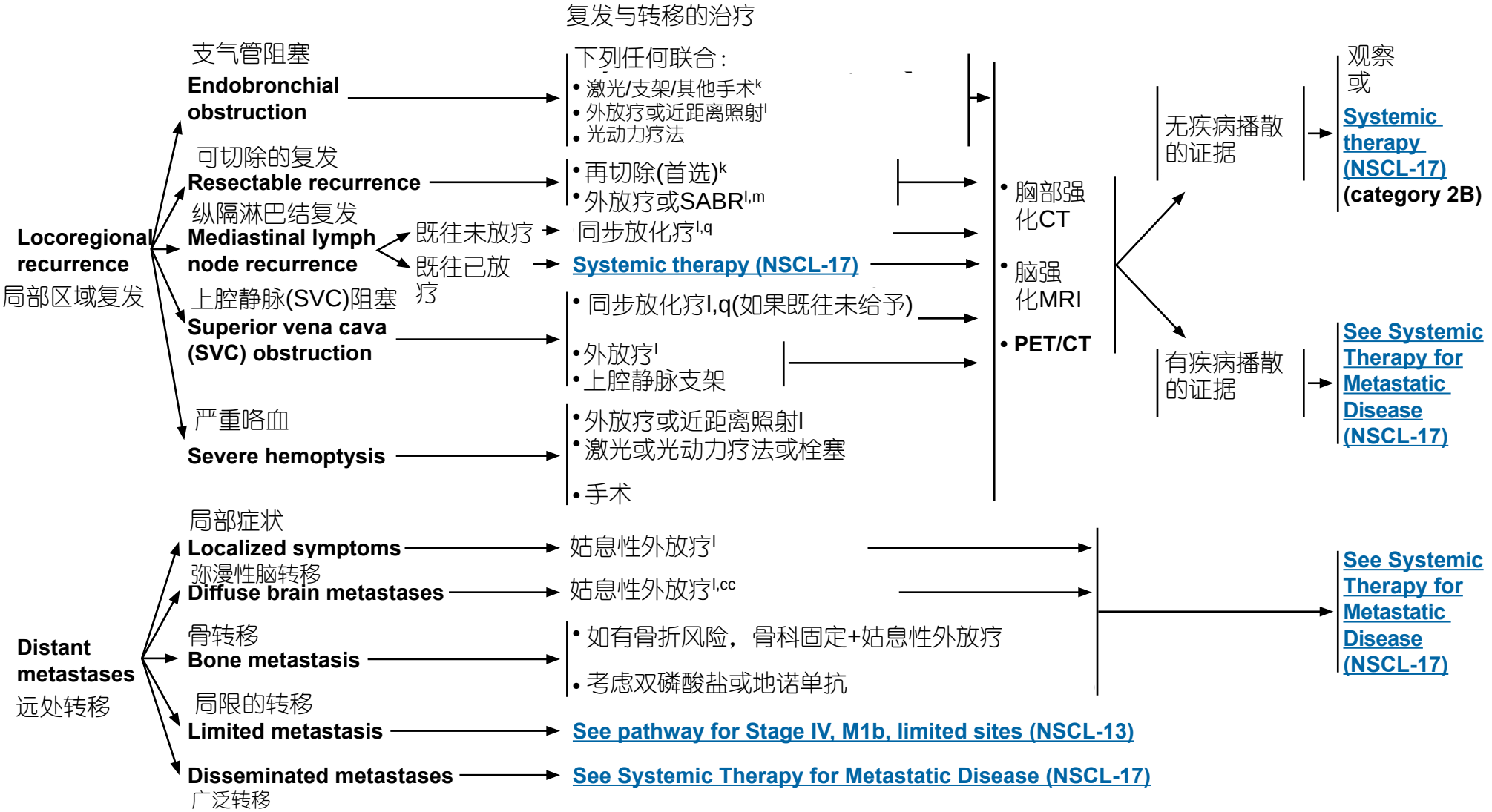
见癌症生存关怀(NSCL-G)

Locoregional recurrence
局部区域复发
→ See Therapy for Recurrence and Metastasis (NSCL-16)

Distant metastases
远处转移
→ See Therapy for Recurrence and Metastasis (NSCL-16)

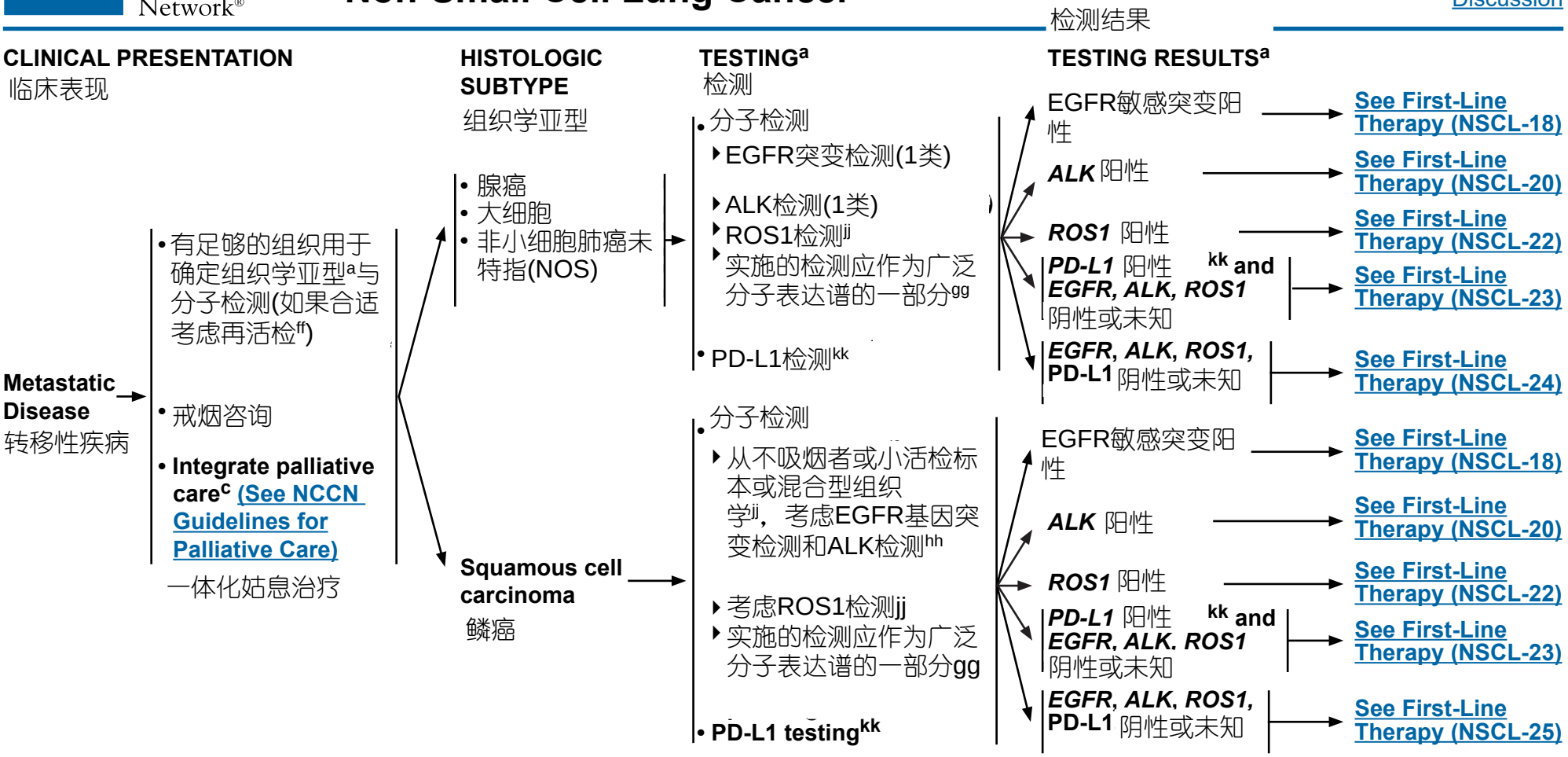
ee目前没有正当理由将FDG PET/CT用于非小细胞肺癌患者的常规监测与随访。但是，许多良性情况（如肺不张、实变和放射性纤维化）在标准的CT成像上很难与肿瘤区分，而在这些情况下FDG PET/CT可辨别真正的恶性肿瘤。不过，如果FDG PET/CT用作解决放疗后患者问题的工具，则复发病变需要组织学证实，因为既往放疗的区域FDG高摄取可长达2年。

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.



[k] 见外科治疗原则 (NSCL-B).
[l] 见放射治疗原则 (NSCL-C).
[m] 对于选择的患者介入放射消融治疗是一种选择。
[q] 见联合放射治疗使用的化疗方案 (NSCL-E).
[cc] 见中枢神经系统肿瘤NCCN指南

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.



[a] 见病理学评估原则 (NSCL-A).

[c] Temel JS, Greer JA, Muzikansky A, et al. Early palliative care for patients with metastatic non-small-cell lung cancer. N Engl J Med 2010;363:733-742.

[ff] 如果重复活检不可行，应考虑血浆活检。

[gg] NCCN非小细胞肺癌指南小组强烈建议广泛的分子表达谱检测，其目的在于发现罕见的驱动突变，因为可能已有可用的有效药物，或可以恰当建议患者参加相应的临床试验。广泛的分子表达谱检测是改善非小细胞肺癌患者治疗的关键。见 遗传学改变患者的新型靶向药物 (NSCL-H).

[hh] 在鳞癌患者中，观察到的EGFR突变率为2.7%，相信，真实的突变发生率不到3.6%。该EGFR突变率并不能在所有肿瘤标本的常规检测中证实。Forbes SA, Bharma G, Bamford S, et al. The catalogue of somatic mutations in cancer (COSMIS). Curr Protoc Hum Genet 2008;chapter 10:unit 10.11.

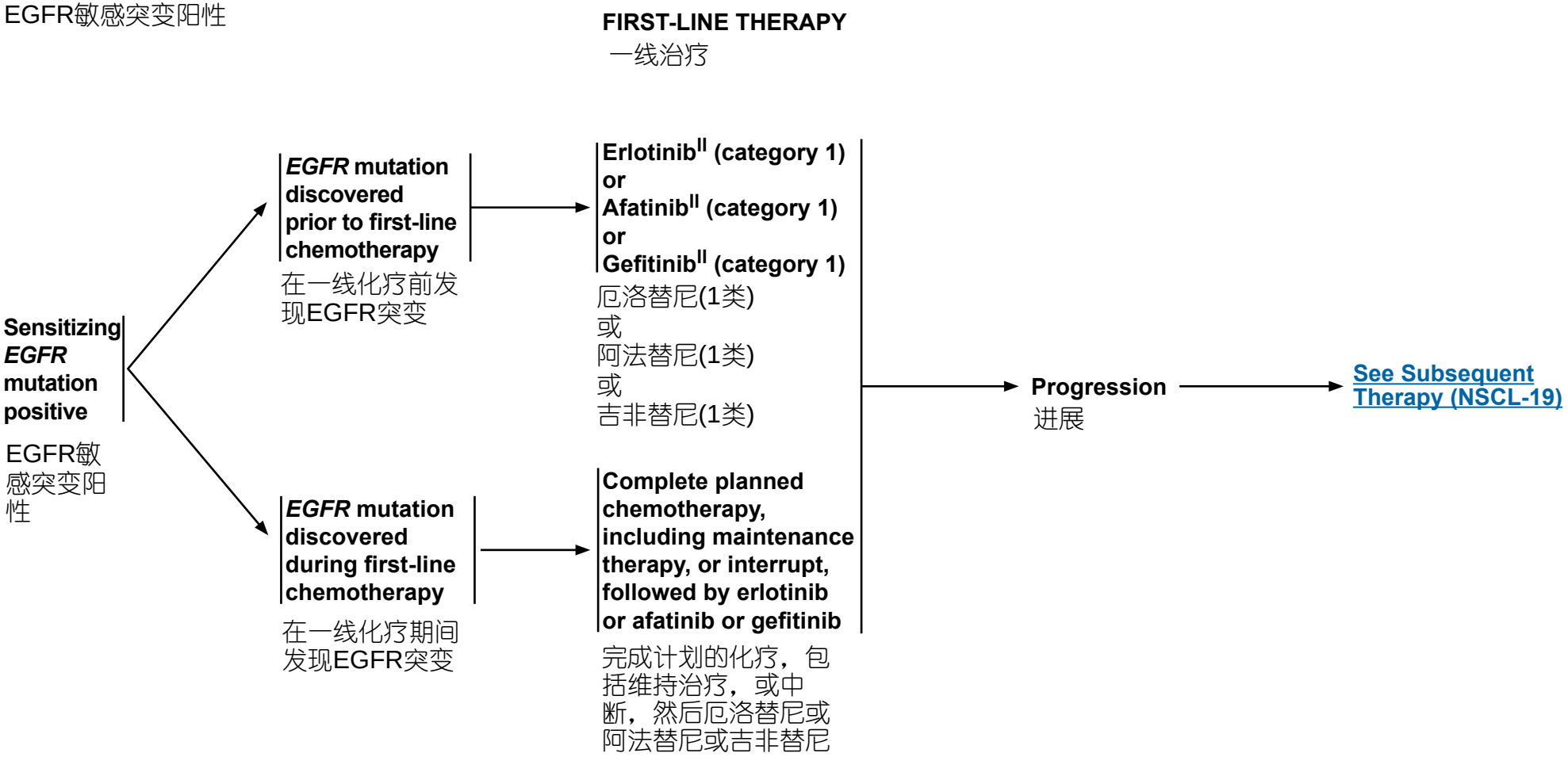
[ii] Paik PK, Varghese AM, Sima CS, et al. Response to erlotinib in patients with *EGFR* mutant advanced non-small cell lung cancers with a squamous or squamous-like component. Mol Cancer Ther 2012;11:2535-2540.

[jj] Shaw AT, Ou S-HI, Bang Y-J, et al. Crizotinib in ROS1-rearranged non-small cell lung cancer. N Engl J Med 2014;371:1963-1971.

[kk] 对于一线派姆单抗治疗，PD-L1表达水平≥50%为阳性检测结果。

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

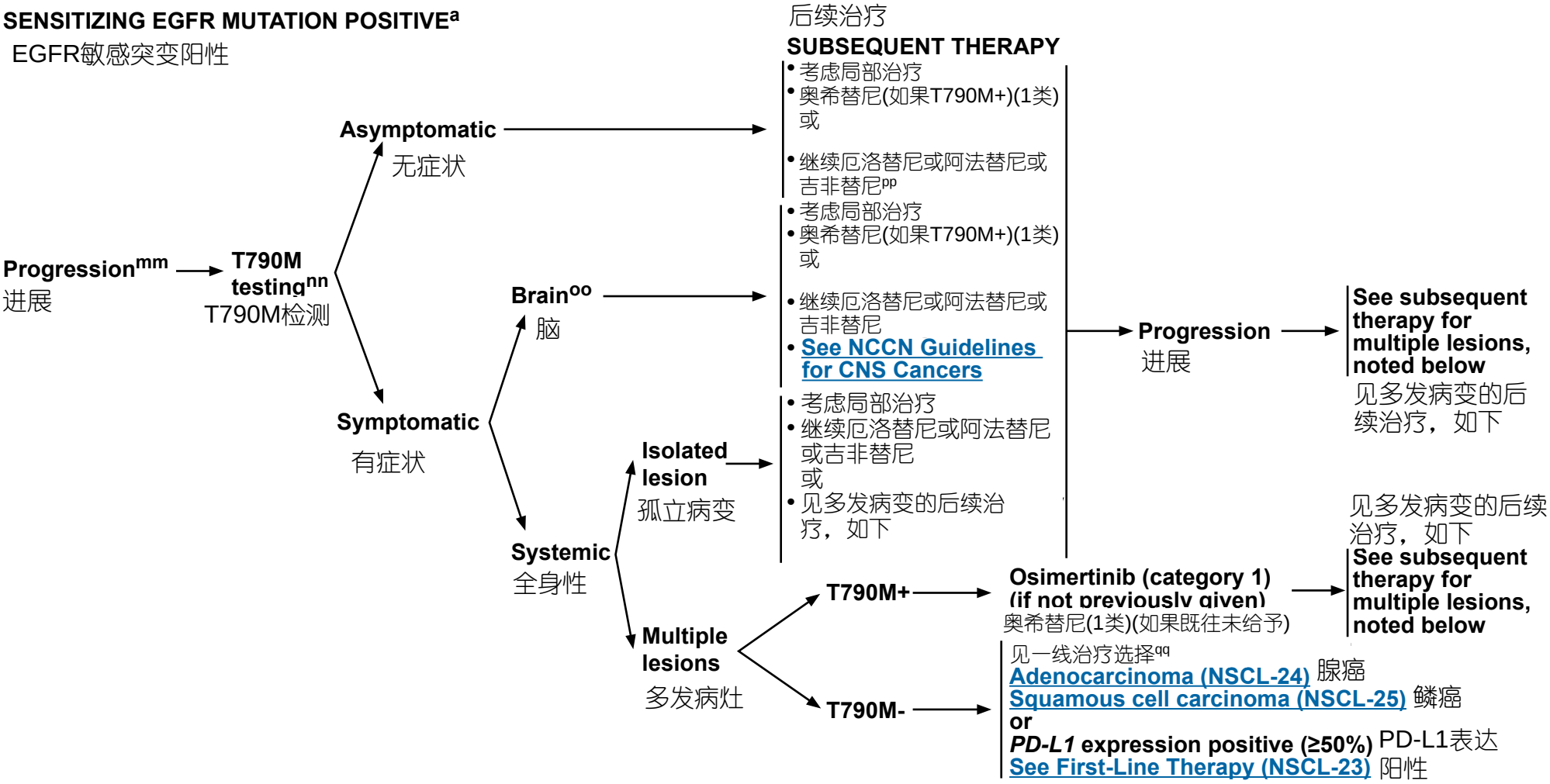
SENSITIZING EGFR MUTATION POSITIVE[a]
EGFR敏感突变阳性



[a] 见病理学评估原则 (NSCL-A).

[II] 对于PS 0-4.

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

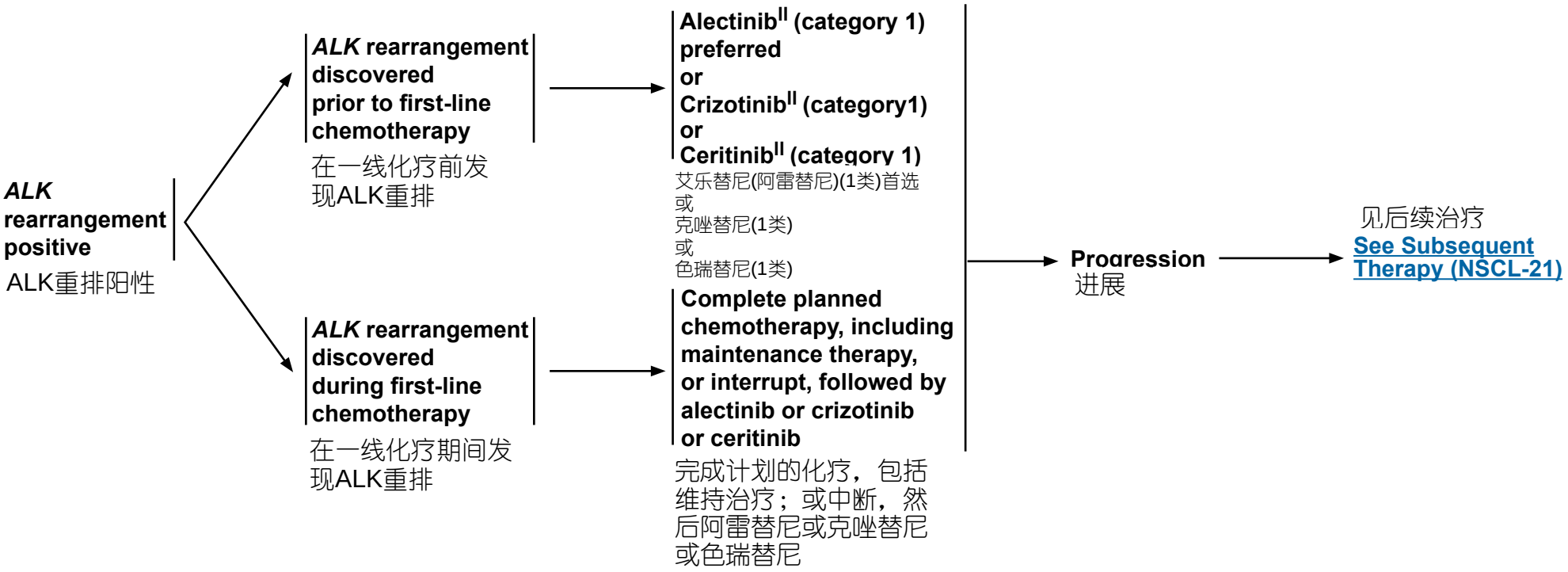


[a] 见病理学评估原则 (NSCL-A).
[mm] 注意在中断EGFR TKI的亚组患者中的恶化迹象（复燃现象）。如果发生疾病恶化迹象（复燃现象），重启EGFR TKI。
[nn] 如果重复活检不可行，应考虑血浆活检。如果血浆T790M突变检测阴性，考虑可反过来进行基于组织的检测。
[oo] 对于癌性脑膜炎，考虑厄洛替尼冲击疗法。
[pp] 对于影像学快速进展或威胁器官功能者，应开始替代治疗。
[qq] 在EGFR TKI治疗时疾病进展的患者，可以考虑阿法替尼+西妥昔单抗。

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

ALK REARRANGEMENT POSITIVE[a]
ALK重排阳性

一线治疗
FIRST-LINE THERAPY

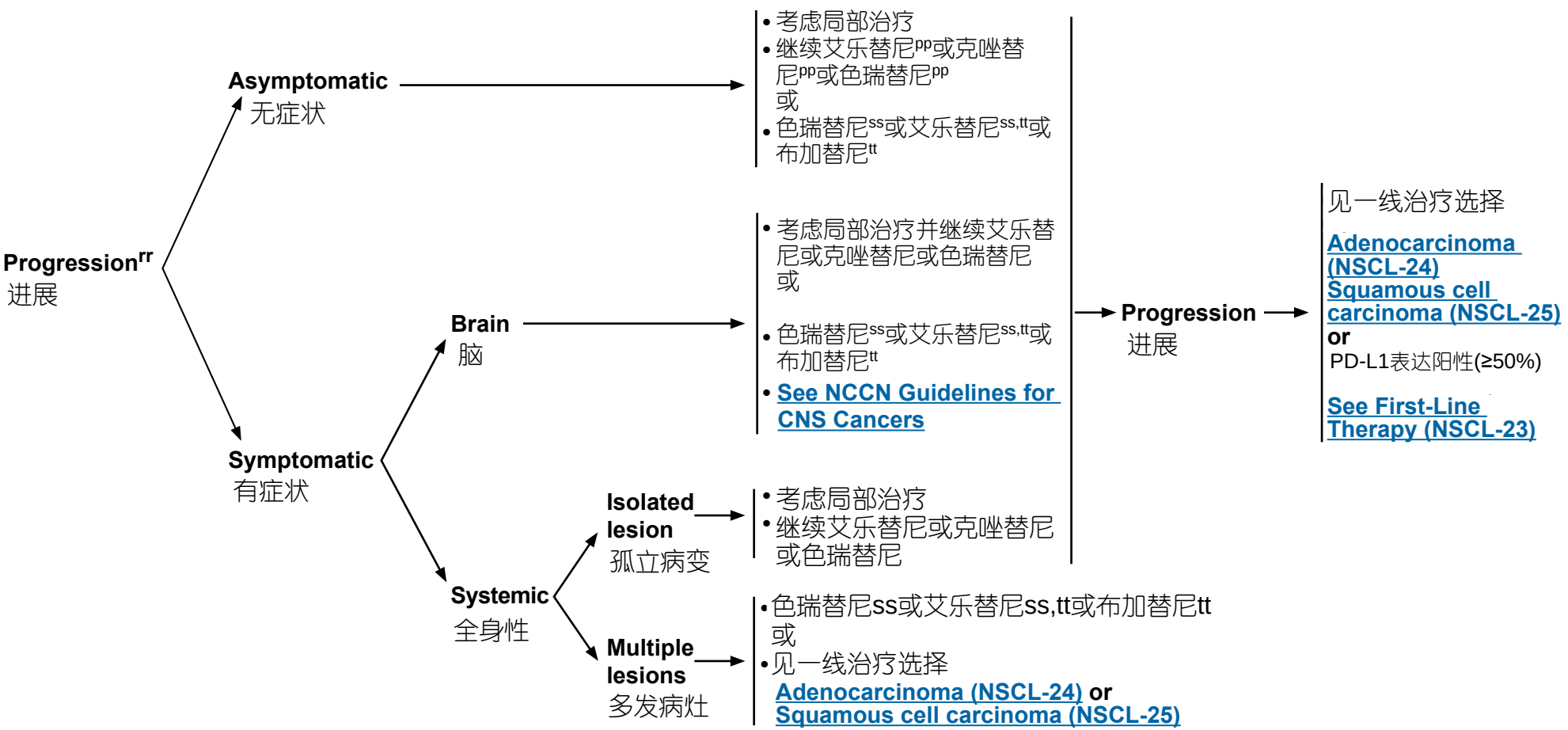


[a] 见病理学评估原则 (NSCL-A).

[II] 对于PS 0-4。

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

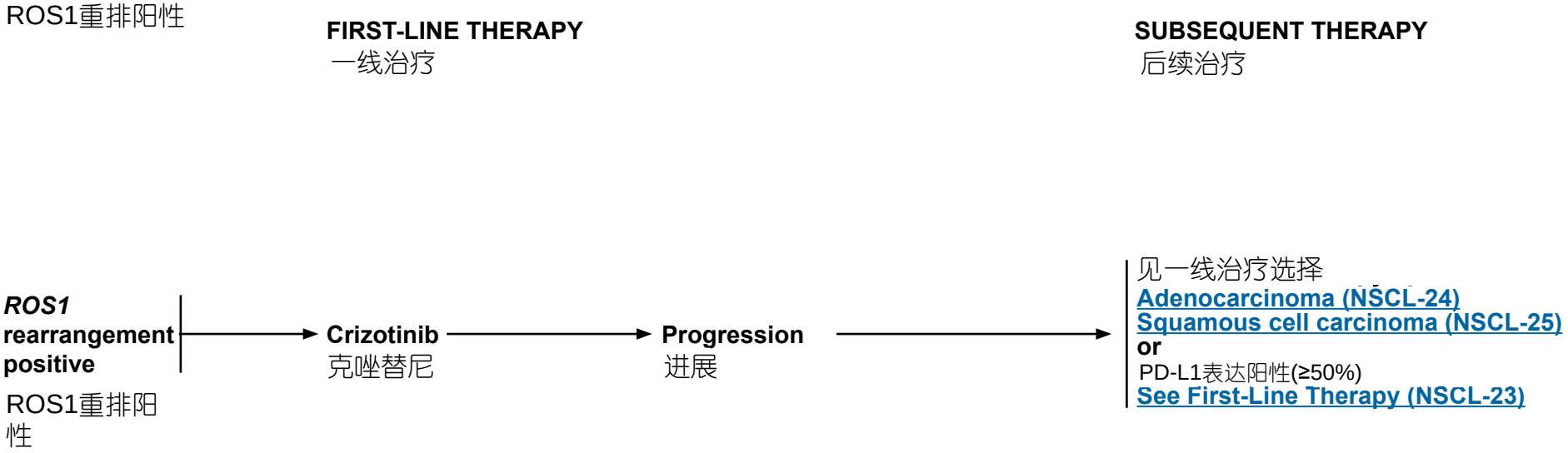
ALK REARRANGEMENT POSITIVE[a]
ALK重排阳性



[a] 见病理学评估原则 (NSCL-A).
[pp] 对于影像学快速进展或威胁器官功能者，应开始替代治疗。
[rr] 无法耐受克唑替尼的患者可转换至色瑞替尼、阿雷替尼或布加替尼。
[ss] 如果未曾给予。
[tt] 阿雷替尼或布加替尼作为克唑替尼已经进展的、ALK阳性的转移性非小细胞肺癌患者的治疗选择。

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

ROS1 REARRANGEMENT POSITIVE[a]
ROS1重排阳性



[a] 见病理学评估原则 (NSCL-A).

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

PD-L1 EXPRESSION POSITIVE[a]
PD-L1表达阳性

FIRST-LINE THERAPY
一线治疗

SUBSEQUENT THERAPY
后续治疗

***PD-L1* expression positive (≥50%) and *EGFR, ALK, ROS1* negative or unknown**
PD-L1表达阳性以及EGFR、ALK、ROS1阴性或未知

→ **Pembrolizumab[uu] (category 1)**
派姆单抗(1类)

→ **Progression**
进展

→ 见一线治疗选择
Adenocarcinoma (NSCL-24) or
Squamous cell carcinoma (NSCL-25)

[a] 见病理学评估原则 (NSCL-A).

[uu] Reck M, Rodríguez-Abreu D, Robinson AG, et al. Pembrolizumab versus chemotherapy for PD-L1–positive non–small-cell lung cancer. N Engl J Med 2016;375:1823-1833.

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

腺癌、大细胞、非小细胞肺癌非特指

ADENOCARCINOMA, LARGE CELL, NSCLC NOS

FIRST-LINE THERAPY
一线治疗

PS 0-2 → **Systemic therapy**[vv] 全身治疗 → **Tumor response evaluation**[vv] 肿瘤应答评估

- **Progression** 进展
  - PS 0-2 → 全身性免疫检查点抑制剂(首选)
    尼鲁单抗(1类)[ww]或派姆单抗(1类)[ss,xx]或阿特珠单抗(1类)[ww]
    或
    其他全身治疗[ss]：
    多西他赛或培美曲塞或吉西他滨或雷莫芦单抗+多西他赛
    → **Progression**[zz] 进展
  - PS 3-4 → 最佳支持治疗
    See NCCN Guidelines for Palliative Care
- **Response or stable disease** 有效或稳定 → **4–6 cycles (total)** 4–6周期(总) → **Tumor response evaluation**[vv] 肿瘤应答评估
  - **Progression** 进展 → 见上述的后续治疗 **See Subsequent therapy, above**
  - **Response or stable disease** 有效或稳定 →
    继续维持治疗[vv]
    - 贝伐单抗(1类)
    - 培美曲塞(1类)
    - 贝伐单抗+培美曲塞[yy]
    - 吉西他滨(2B类)

    或
    转换维持(2B类)[vv]
    - **Pemetrexed** 培美曲塞

    或
    密切观察

    → **Progression, see Subsequent therapy, above** 进展，见上述后续治疗

PS 3-4 → **Best supportive care**
See NCCN Guidelines for Palliative Care

SUBSEQUENT THERAPY[vv]
后续治疗

[ss]如果未曾给予。
[vv]见晚期或转移性疾病全身治疗 (NSCL-F).
[ww]如果未曾给予派姆单抗。
[xx]FDA已批准派姆单抗用于经FDA批准的检验测定的肿瘤PD-L1表达水平≥1%的非小细胞肺癌患者的治疗。
[yy]如果一线培美曲塞/铂类化疗方案联合使用了贝伐单抗。
[zz]如果未曾给予，对于PS 0-2患者的选择包括（尼鲁单抗、派姆单抗或阿特珠单抗）、多西他赛（2B类）、培美曲塞（2B类）、吉西他滨（2B类）或雷莫芦单抗+多西他赛（2B类）；PS 3-4患者的选择包括最佳支持治疗。进一步进展患者的选择是最佳支持治疗或临床试验。

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

SQUAMOUS CELL CARCINOMA 鳞癌

FIRST-LINE THERAPY
一线治疗

PS 0-2 → **Systemic therapy[vv]** 全身治疗 → **Tumor response evaluation[vv]** 肿瘤应答评估

- **Progression** 进展
  - PS 0-2 → 全身性免疫检查点抑制剂(首选)
    - 尼鲁单抗(1类)[ww]或派姆单抗(1类)[ss,xx]或阿特珠单抗(1类)[ww]

    或

    其他全身治疗[ss]：
    - 多西他赛或吉西他滨或雷莫芦单抗+多西他赛

    → **Progression[aaa]**
  - PS 3-4 → 最佳支持治疗 See NCCN Guidelines for Palliative Care
- **Response or stable disease** 有效或稳定 → **4–6 cycles (total)** 4–6周期(总) → **Tumor response evaluation[vv]** 肿瘤应答评估
  - **Progression** 进展 → **See Subsequent therapy, above** 见上述的后续治疗
  - **Response or stable disease** 有效或稳定 → 继续维持(2B类)[vv]
    - 吉西他滨

    或

    转换维持(2B类)[vv]
    - 多西他赛

    或

    密切观察

    → **Progression, see Subsequent therapy, above** 进展，见上述后续治疗

PS 3-4 → **Best supportive care** See NCCN Guidelines for Palliative Care

SUBSEQUENT THERAPY[vv]
后续治疗

[ss]如果未曾给予。
[vv]见晚期或转移性疾病全身治疗 (NSCL-F).
[ww]如果未曾给予派姆单抗。
[xx]FDA已批准派姆单抗用于经FDA批准的检验测定的肿瘤PD-L1表达水平≥1%的非小细胞肺癌患者的治疗。
[aaa]如果未曾给予，对于PS 0-2患者的选择包括（尼鲁单抗、派姆单抗或阿特珠单抗）、多西他赛（2B类）、吉西他滨（2B类）或雷莫芦单抗+多西他赛（2B类）；PS 3-4患者的选择包括最佳支持治疗。进一步进展患者的选择是最佳支持治疗或临床试验。

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病理学检查原则 (1 of 5)

病理学评估

- 病理学评估的目的是对肺癌组织学类型进行分类并确定AJCC推荐的所有分期参数[1]，包括肿瘤大小、侵犯范围（胸膜、支气管）、手术切缘是否足够以及有无淋巴结转移。[2,3] 此外，确定肿瘤特定的分子异常是预测肿瘤对越来越多的可用靶向药物敏感性或抵抗性的关键，这些药物主要是酪氨酸激酶抑制剂（TKIs）（见本节中的肺癌分子诊断研究）。[4,5]
- WHO肿瘤分类系统一直以来都为肺肿瘤提供分类基础，包括组织学类型、临床特征、分期需要考虑的事项以及肺癌的分子、基因和流行病学因素。[6,7]
- 在切除标本或小活检中病理诊断报告应包括WHO对肺恶性肿瘤描述的组织学分类。强烈反对使用细支气管肺泡癌（BAC）术语。
- 通用术语“非小细胞肺癌（NSCLC）”应避免作为一个单独的诊断术语。在进行免疫组化（IHC）染色的低分化癌小活检中，下列术语是可以接受的：“非小细胞肺癌倾向于腺癌”或“非小细胞肺癌倾向于鳞状细胞癌。”[8]在所有倾向于腺癌的NSCLC中强烈建议突变检测（如，表皮生长因子受体[EGFR] ）。
- 对于大多数的分子分析，福尔马林固定石蜡包埋的肿瘤是可以接受的。
- 在单独基于常规组织学不能可靠分类的标本中，强烈建议在小组织标本中限制使用免疫组化研究，从而保留关键的肿瘤组织用于分子研究，尤其是在晚期疾病患者中。对于大多数诊断问题，一个鳞状细胞癌标记（如p63、p40）和一个腺癌标记（如甲状腺转录因子-1、新天冬氨酸蛋白酶A）的有限组合应该足够。[8]

腺癌的分类[8]

- 原位腺癌（AIS；以前称为细支气管肺泡癌）：结节≤3cm、贴壁生长、黏液性、非黏液性或黏液/非黏液混合型。
- 微浸润腺癌（MIA）：结节≤3cm、浸润≤5mm、贴壁生长、黏液性、非黏液性或黏液/非黏液混合型。
- 浸润腺癌，主要生长方式：贴壁浸润>5mm、腺泡状、乳头状、微乳头状或伴有黏液的实性肿瘤。
- 浸润性腺癌变异型：黏液型腺癌、胶样型、胚胎型及肠型。

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

病理学检查原则(2 of 5)

免疫组化染色

- 强烈推荐明智、合理使用免疫组化以保留组织用于分子检测。只有在考虑所有资料包括常规H&E组织学、临床表现、影像学检查及病史之后才应该考虑使用免疫组化。
- 尽管与手术切除的标本相比，小活检标本的组织学亚型和免疫表型之间观察到的一致性总体而言是好的，但是，尝试对材料有限的小活检或免疫表型模棱两可的患者进行亚型诊断时建议应慎重。
- 应使用免疫组化鉴别原发性肺腺癌与下列肿瘤：鳞状细胞癌、大细胞癌、转移癌以及恶性间皮瘤；确定是否存在神经内分泌分化。[9-11]
- 原发性肺腺癌
  - 在肿瘤原发部位尚不明确的患者中，建议适当的免疫组化染色组合以排除肺转移性癌。[12]
  - 甲状腺转录因子1（TTF-1）是Nkx2基因家族的一种含同源结构域的核转录蛋白，在肺和甲状腺胚胎和成熟的上皮细胞中表达。在原发性肺腺癌中见到甲状腺转录因子1（TTF-1）免疫反应活性者大多数（70%–100%）为非黏液腺癌亚型。[13]肺的转移性腺癌中，除了转移性甲状腺癌外，甲状腺转录因子-1（TTF-1）几乎均阴性，但是在转移性甲状腺癌病例中，甲状腺球蛋白也是阳性的。
  - 新天冬氨酸蛋白酶A（Napsin A）——在正常肺泡II型上皮细胞和肾小管近端与远端表达的一种天门冬氨酸蛋白酶——似乎在80%以上的肺腺癌中表达，因此TTF-1辅助可能是有用的。[12]
  - 在既往分类为非小细胞肺癌非特指的小活检标本中，在细分腺癌或鳞状细胞癌诊断时，TTF-1（或Napsin A代替）和p63（或p40代替）组合可能是有用的。[8]
- 神经内分泌分化
  - CD56、嗜铬素以及突触素用于鉴别神经内分泌肿瘤。
- 恶性间皮瘤与肺腺癌
  - 鉴别肺腺癌与恶性间皮瘤（上皮型）可以根据组织学与临床印象、影像检查的相互关系以及如果需要有限的免疫标记组合做出诊断。[11]
    - ◊ 间皮瘤相对敏感且特异的免疫标记包括Wilm's肿瘤基因（WT-1）、钙结合蛋白、D2-40、HMBE-1和细胞角蛋白5/6（在腺癌中阴性）。[14,15]
    - ◊ 腺癌免疫活性抗体包括CEA、B72.3、Ber-EP4、MOC31、CD15、紧密连接蛋白-4和甲状腺转录因子-1（在间皮瘤中阴性）。[8,11]

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

病理学检查原则 (3 of 5)

肺癌的分子诊断研究

- ***EGFR*和*KRAS***
  - ***EGFR*通常出现于上皮细胞表面，在多种人类恶性肿瘤中经常过表达。表皮生长因子受体活化突变的存在是肺癌患者选择合理治疗的一个关键的生物学决定因素。**
  - EGFR突变——尤其是19外显子缺失和21外显子（L858R，L861）、18外显子（G719X，G719）和20外显子（S768I）突变——之间显著相关并且对EGFR-TKI敏感。[16-19]
  - 20外显子插入突变可预测对酪氨酸激酶抑制剂临床可达到的耐药水平。[20,21]
  - 不到1%的肺癌患者存在EGFR和KRAS基因叠加突变。[22]
  - ***KRAS*突变与EGFR TKI原发耐药相关，因此，KRAS基因测序对于选择EGFR TKI治疗的候选患者可能是有用的。[23]KRAS检测可识别出不会从进一步分子诊断检测获益的患者。**
  - 腺癌EGFR突变的发生率西方患者是10%，而亚洲患者高达50%，在非吸烟者、女性以及非黏液癌中EGFR突变率更高。在非亚洲裔、吸烟者和黏液腺癌中KRAS突变最常见。[24]最常见的EGFR突变导致21外显子（L858R）第858位氨基酸的亮氨酸取代了精氨酸和19外显子框架内缺失。突变在贴壁生长模式（原细支气管肺泡癌）的非黏液性肺腺癌和乳头状（和/或微乳头状）肺腺癌中更常见。
  - KRAS突变与对EGFR TKI治疗原发性耐药有关。获得性耐药与EGFR激酶结构域内的第二位点突变（如T790M）、另一种激酶扩增（如MET）、非小细胞肺癌组织学转化为小细胞肺癌以及上皮-间质转化（EMT）有关。
- ***ALK***
  - 间变性淋巴瘤激酶（ALK）基因重排是ALK和各伴侣基因之间的融合，包括棘皮动物微管结合蛋白4（EML4）。[25]ALK融合已在非小细胞肺癌患者的一个亚型中识别出来，代表非小细胞肺癌患者一个独特亚型，ALK抑制剂对其可能是一种非常有效的治疗策略。[26]克唑替尼、色瑞替尼和阿雷替尼是口服的ALK抑制剂，FDA已批准用于治疗有ALK基因重排（即ALK阳性）的转移性非小细胞肺癌患者。
  - ***ALK*非小细胞肺癌最常出现在一个独特的非小细胞肺癌患者亚组中，同时伴有许多共同临床特征的非小细胞肺癌患者可能存在EGFR突变。[27,28] 然而，大多数情况下，ALK重排和EGFR突变是互相排斥的。[27, 29-31]**
  - 目前检测ALK非小细胞肺癌的标准方法是荧光原位杂交（FISH）。检测ALK蛋白表达相应的抗体与方法可用于快速筛查ALK重排的肺腺癌，选择的病例可随后经FISH检测证实。[32]

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病理学检查原则 (4 of 5)

肺癌的分子诊断研究

- ***ROS-1***
  - 尽管ROS1是一个独特的受体酪氨酸激酶，但是ROS1与ALK具有高度的同源性（在激酶结构域中约50%，在ATP结合位点中约75%）。[33]
  - 大多数ROS1阳性的非小细胞肺癌患者对第一代ALK抑制剂克唑替尼应答；然而，某些其他ALK抑制剂如阿雷替尼对ROS1阳性的非小细胞肺癌似乎无效。[34]
  - 1%–2%的非小细胞肺癌患者存在ROS1基因重排。[34]与ALK重排检测相似，ROS1也用FISH检测。[35]
- ***PD-L1***
  - 免疫检查点抑制剂的靶点是程序性死亡受体1（PD-1）或其配体——程序性死亡配体1（PD-L1）。[36]
  - PD-1表达于T细胞，并调节外周组织中T细胞的活化。PD-1有两个配体，PD-L1（也称为B7-H1或CD274）和PD-L2（B7-DC或CD273）。这些配体广泛表达于各种免疫效应细胞、抗原呈递细胞和肿瘤细胞。肿瘤细胞上的PD-L1配体与PD-1结合并激活，产生一系列的细胞间作用，引起T细胞失活并降低增殖。
  - 在非小细胞肺癌中治疗的重点是用抗PD-L1或PD-1的单克隆抗体阻断PD-1与肿瘤细胞和免疫效应细胞的配体PD-L1之间的相互作用。[37]
  - 抗PD-L1免疫组化可能是一个用于选择更可能对免疫检查点抑制剂应答的非小细胞肺癌患者生物标志物，但是开发的各种疗法，每一种都使用不同的抗PD-L1 IHC检测，加剧了病理学家和肿瘤学家的困扰。[37,38]
  - PD-L1检测结果阳性的定义取决于使用的生物标记法。[37]对于一线派姆单抗治疗，PD-L1表达水平≥50%为阳性检测结果。

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病理学检查原则 (5 of 5) - 参考文献

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外科治疗原则 (1 of 4)

评估

- 判断可切除性、手术分期以及肺切除术应该由通过职业认证的、以肺癌外科手术为主要执业经验的胸外科医生进行。
- 用CT和PET分期评估应在术前60天内进行。
- 手术切除是首选的局部治疗方式（其他方式包括射频消融、冷冻疗法和立体定向消融放疗）。所有考虑根治性局部治疗的患者均应咨询胸部肿瘤外科医生。对于高危患者，如果考虑立体定向消融放疗，推荐多学科评估（包括放射肿瘤学家）。
- 在开始任何非急诊治疗前，应决定治疗的总计划和必要的影像学检查。
- 胸外科医生应积极参加肺癌患者的多学科讨论和会议（如多学科门诊和/或肿瘤委员会）。
- 应对主动吸烟者提供戒烟指导和教育 (NCCN 戒烟指南). 尽管主动吸烟者略微增加术后肺部并发症的发生率，但这不应视为手术的一个禁止性危险因素。外科医生不应该单纯由于吸烟状态拒绝为患者手术，因为对于延长早期肺癌患者的生存期，手术占主导地位。

切除术

- 对于大多数非小细胞肺癌患者解剖性肺切除术是首选。
- 亚肺叶切除术——肺段切除术和楔形切除术切缘肺组织应达到≥2cm或≥结节的大小。
- 亚肺叶切除还应该对N1和N2淋巴结适当取样活检，除非在技术上做不到不显著增加手术风险。
- 在选择性患者中，肺段切除术（首选）或楔形切除术是合理的，原因如下：
  - 肺储备差或并存其他重大疾病，禁忌行叶切除术
  - 周围性结节≤2cm，至少具有下列一个特征：
    - ◊ 纯原位腺癌组织学
    - ◊ 在CT上结节磨玻璃样表现≥50%
    - ◊ 放射学监测证实倍增时间长（≥400天）
- 对于无解剖或外科手术禁忌症的患者，只要不违反肿瘤学标准和胸部手术切除原则，就应认真考虑电视辅助胸腔镜手术或微创手术（包括机器人辅助手术）。
- 具有电视辅助胸腔镜手术丰富经验的大型中心，在选择的患者中，电视辅助胸腔镜肺叶切除术可改善近期疗效（即，减轻疼痛、缩短住院时间、功能恢复更快、并发症少）而不影响癌症结局。
- 如果可获得合适的解剖性切除且切缘阴性，保留肺组织的解剖性切除术（袖状肺叶切除术）是优于全肺切除术的首选。
- T3（侵犯）和T4局部侵犯肿瘤要求将累及组织整块切除达到切缘阴性。如果外科医生或中心不能确定是否可能完全切除，则考虑另外征求大型专科中心的手术意见。

切缘和淋巴结评估(见 NSCL-B2 of 4)

[1]周围性定义为肺组织的外三分之一。

手术在ⅢA（N2）期非小细胞肺癌患者中的地位 (见 NSCL-B 2 of 4 through NSCL-B 4 of 4)

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

外科治疗原则 (2 of 4)

切缘和淋巴结评估

- 手术病理的相互关系对于评估明显靠近切缘或切缘阳性是至关重要的，因为这可能并不代表真正的切缘或可能并不真正表示局部复发危险区域（如，单独进行隆突下淋巴结清扫时，主或中间段支气管的内侧面；当胸膜缘靠近主动脉并未与主动脉黏连时）。
- 肺癌切除应常规进行N1与N2淋巴结清扫和定位——最少对3个N2淋巴结取样或行完全淋巴结清扫术。
- 对于ⅢA（N2）期患者的切除，需要正规的同侧纵隔淋巴结清扫。
- 完全切除术要求切缘阴性、系统淋巴结清扫或取样并且最上纵隔淋巴结肿瘤阴性。无论何时，只要有切缘受累、阳性淋巴结未切除或胸腔积液或心包积液阳性，则该切除术定义为不完全切除。完全切除称为R0，镜下阳性的切除术为R1，而肉眼可见残余肿瘤为R2。
- 病理分期为II期或以上的患者应转诊到肿瘤内科进行评估。
- 对于手术切除的ⅢA期考虑转诊到放射肿瘤学家。

手术在ⅢA（N2）期非小细胞肺癌患者中的地位

在病理学证实的N2患者中手术的地位仍存在争议。[1] 两项随机试验评估了手术在这类人群中的地位，但均未显示手术在总生存方面获益。[2,3] 然而，该人群具有异质性，因此，该小组认为，这些试验未充分评估N2异质性而存在的细微差别以及在特定的临床情况下手术可能的肿瘤学获益。

- 因为纵隔淋巴结病变的存在对预后和治疗决策有深远的影响，因此，在治疗开始前应尽最大努力通过影像学和创伤性分期确定有无N2病变。（NSCL-1，NSCL-2和NSCL-6）
- 在肺部分切除术时发现有隐匿性N2淋巴结阳性的患者，应该按照既定方案切除和正规的纵隔淋巴结清扫术。在接受电视胸腔镜检查过程中如果发现N2病变，外科医生可考虑中止计划的程序，给予术前诱导治疗；但也可以选择继续完成计划的程序。

- N2淋巴结阳性的患者，在开始治疗前，应由多学科团队，包括在实践中以胸部肿瘤为主、通过职业认证的胸外科医生决定是否手术。[4]

- 存在N2淋巴结阳性大大增加了N3淋巴结阳性的可能性。纵隔病理评估必须包括隆突下和对侧淋巴结。支气管内超声±内镜超声为微创纵隔病理分期提供了其他的技术手段，与纵隔镜互补。即便采用这些方式，重要的是，在确定最终的治疗决策前还需要充分评估累及站的数量并活检证实无对侧淋巴结受累。

手术在ⅢA（N2）期非小细胞肺癌患者中的地位继续讨论 NSCL-B 3 of 4 through NSCL-B 4 of 4

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

外科治疗原则 (3 of 4)

手术在ⅢA（N2）期非小细胞肺癌患者中的地位

- 与首次纵隔镜检查相比，重复纵隔镜检查，虽然有可能，但技术上困难且准确性较低。一个合适的策略是在初始治疗前的评估中进行支气管内超声（±内镜超声），将纵隔镜淋巴结再分期保留在新辅助治疗后。[5]
- 单个淋巴结小于3cm的患者可以考虑综合治疗，包括手术切除。[1,6,7]
- 诱导治疗后再分期很难解释，但应该进行CT±PET检查以排除疾病进展或转移灶在间歇期增大。
- 纵隔阴性的患者，新辅助治疗后预后更好。[7,8]
- 在NCCN成员单位中，50%使用新辅助放化疗，另外50%使用新辅助化疗。如果术前未给予放疗而术后给予，总生存期似乎相似。[5,9] 新辅助放化疗具有更高的病理完全缓解率及纵隔淋巴结阴性率。[10] 然而，达到这种疗效的代价是更高的急性毒性发生率和费用增加。
- 当新辅助放化疗使用低于标准的根治性治疗量时，应尽力减少手术评估可能造成的任何放疗中断。治疗中断超过1周是不可接受的。
- 当无法适时手术评估时，不应使用新辅助放化疗策略。在个别情况下，另外一种选择是，在得到胸外科医生同意的前提下，在重新评估并考虑手术前完成根治性放化疗。[11,12] 在根治量放疗后，如果外科医生或中心不能断定切除的可行性或安全性，则考虑另外征求大型专科中心的手术意见。这些操作在切除时需要考虑放射野内软组织瓣覆盖的其他事项可能也是有益的。

- 一项大型多中心试验的数据显示，新辅助放化疗后肺切除的并发症发生率和死亡率令人无法接受。[2] 但是，目前还不清楚，单纯新辅助化疗是否也是如此。[13-16] 另外，很多研究小组都质疑该协作组的发现，单机构的经验证明诱导治疗后肺切除术是安全的。此外，对于可手术的ⅢA（N2）患者，与诱导化疗相比，并没有证据表明诱导方案中加入放疗可改善预后。[17]

NCCN在2010年向成员机构发放了一份关于他们如何治疗N2疾病患者的调查问卷。他们的反馈结果显示了其在遇到这一棘手的临床问题时的实际工作模式。

a) 一个N2淋巴结站受累，淋巴结小于3cm，将考虑手术：(90.5%)

b) 一个以上的N2淋巴结站受累，只要淋巴结不大于3cm，会考虑手术：(47.6%)

c) 在纵隔初步评估时使用支气管内超声± 超声内镜：(80%)

d) 在新辅助治疗后，对纵隔进行病理评估，以便在术前做出最后决定：(40.5%)

e) 根据初步评估，患者很可能需要肺切除术时，将考虑新辅助治疗然后手术：(54.8%)

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

外科治疗原则 (4 of 4)

The Role of Surgery in Patients With Stage IIIA (N2) NSCLC - References

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放射治疗原则 (1 of 10)

一般原则 (见 表 1. 放射治疗常用缩写)

- 应该由通过职业认证、临床实践中主要从事肺癌放疗的放射肿瘤学家确定合理的放疗（RT）。
- 作为根治性或姑息性治疗，在所有分期的非小细胞肺癌中放疗均有潜在的作用。放射肿瘤学作为多学科评估或讨论的一部分，对所有非小细胞肺癌患者均
- 现代放疗的关键目的是肿瘤控制最大化，同时使治疗毒性最小化。最低技术标准是根据CT设计的三维适形放疗。[1]
- 当需要安全的根治性放疗时，可合理使用更先进的技术。这些技术包括（但不限于）4D-CT和/或PET/CT模拟、IMRT（调强放疗）/VMAT（旋转容积调强放疗）、IGRT（影像引导放射治疗技术）、运动管理及质子治疗 (https://www.astro.org/Daily-Practice/ Reimbursement/Model-Policies/Model-Policies/). 采用先进技术与老旧技术的非随机对照证明，降低毒性并改善生存。[2-4] I在一项根治性化/放疗治疗III期非小细胞肺癌的前瞻性试验（RTOG 0617）中，与三维适形放疗相比，尽管调强放疗组IIIB期比例较高且治疗体积较大，但是，调强放疗降低高级别放射性肺炎近60%而生存和肿瘤控制结果相似；[5] 因此，在这种情况下，适形调强放疗优于三维适形放疗。
- 使用先进技术的中心应实施并记录具体的质量保证措施。治疗计划与交付两者均外部认证是理想的，就像RTOG临床试验采用先进技术所要求的那样。有用的参考文献包括美国放射学会实践参数与技术标准 (http://www.acr.org/~/media/ACR/Documents/ PGTS/toc.pdf).

早期非小细胞肺癌（I期，某些淋巴结阴性的IIA期）

- 对于那些因内科因素不能手术或在开胸评价术后拒绝手术的患者，推荐立体定向消融放疗（SABR）（也称为SBRT）。在非随机和以人群为基础的对比中，因内科因素不能手术或老年患者，立体定向消融放疗（SABR）获得的原发肿瘤控制率和总生存率可媲美肺叶切除术且优于三维适形放疗。[6-11]
- 立体定向消融放疗（SABR）也是手术风险较高患者（能够耐受亚肺叶切除而非肺叶切除术[如年龄≥75岁]、肺功能差）一个合适的选择。立体定向消融放疗（SABR）达到的癌症特异性生存和原发肿瘤控制可媲美亚肺叶切除。[12-13]
- 比较立体定向消融放疗（SABR）与肺叶切除术治疗可手术患者的两项随机试验（单独未完成入组）的联合分析发现，与手术相比，SABR具有类似的癌症特异性结局，并且，SABR改善毒性和生存。[14] 该分析并未提供充分的数据改变良好手术候选者的治疗标准，但加强了立体定向消融放疗（SABR）治疗具有手术相对禁忌症或拒绝手术的患者的指征。
- 由于协会没有制定SABR方案，因此，更适度的超分割或剂量加强的常规分割三维适形放疗方案是次优替代选择。[15-17]
- 在接受手术的患者中，不推荐术后放疗（PORT），除非是切缘阳性或升期为N2（见本节中的局部晚期非小细胞肺癌）。

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

放射治疗原则 (2 of 10)

局部晚期非小细胞肺癌（ⅡA-ⅢA期）

- 不能手术的ⅡA期（淋巴结阳性）和ⅢA期患者的标准治疗是同步化/放疗。[18-20]
  通过采用支持治疗处理急性毒性，应避免放疗中断和减量。
- 序贯化/放疗或单纯放疗适于无法耐受同步治疗的体弱患者。[21,22]
  加速放疗方案可能是有益的，特别是如果同步化疗不能耐受（即，以序贯或单纯放疗的方式）。[23,24]
- 术前或术后放疗都有地位。
  - P对于可切除的ⅢA期（最低限度的N2且可肺叶切除治疗）[25]患者，术前同步化/放疗是一个选择，并推荐用于可切除的肺上沟瘤。[26,27]
  - P对于可切除的ⅢA期[28,29]患者，术前化疗和术后放疗是一个备选方案。在三联疗法（术前或术后化疗）中，无公认的放疗最佳时机，是有争议的。[30,31]
  - 在三联疗法中，应该在所有治疗开始之前确定可切除性。当考虑ⅢA期非小细胞肺癌外科治疗时，前期多学科会诊是特别重要的。
  - 临床I/ⅡA期、手术升期至N2+的患者，多项非随机分析认为，术后放疗（PORT）作为术后化疗的辅助手段似乎显著改善生存。[32,33] 虽然无公认的最佳顺序，但是，术后放疗（PORT）通常在术后化疗后给予。在医学上适合的患者[34-36]，术后放疗（PORT）同时化疗可安全实施，并建议积极切除边缘。[37]
  - 对于病理分期N0-1的患者，不建议术后放疗（PORT），因为已发现与死亡率增加有关，起码在使用老的放疗技术时是这样。[38]

晚期/转移性非小细胞肺癌（IV期）

- 推荐放疗用于缓解或预防局部症状（如疼痛、出血或梗阻）。
- 对孤立或局限的转移部位（寡转移）（包括但不限于脑、肺、肾上腺）根治性局部治疗，在一小部分精心挑选的、一般状况良好、胸内病变也已经接受根治性治疗的患者中，可延长生存期。对寡转移根治性放疗，特别是立体定向放疗消融（SABR），如果对受累部位可以安全地实施，在这种情况下是一个合适的选择。[39,40]
- 见 中枢神经系统肿瘤NCCN指南 关于脑转移瘤的放疗。

Note: All recommendations are category 2A unless otherwise indicated.
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放射治疗原则 (3 of 10)

靶体积、处方剂量和正常组织剂量限制 (见 Tables 2–5 on NSCL-C 7 of 10 and NSCL-C 8 of 10)

- 国际辐射单位与测量委员会（ICRU）62和83报告详述了目前三维放疗和适形调强放疗靶体积的定义。大体靶区（GTV）包括在影像学和病理学评估时已知的病变范围（原发灶和淋巴结），临床靶区（CTV）包括推测的微观范围或播散区域，而计划靶区（PTV）包括靶区运动范围（ITV）（包括目标运动的边界）加定位与机械设备变化（误差）调整的边界。
  http://www.rtog.org/CoreLab/ContouringAtlases/LungAtlas.aspx
- 通过制动（固定）、运动管理和影像学引导放疗（IGRT）技术可以缩小计划靶区（PTV）边界。
- 正常结构轮廓勾画的一致性是评估计划安全性的关键。（美国）肿瘤放射治疗协作组织（RTOG）共识的肺轮廓勾画图集是一个有用的资源。
  http://www.rtog.org/CoreLab/ContouringAtlases/LungAtlas.aspx
- 常用的处方剂量和正常组织剂量的限制，总结于表2至表5。这均基于已发表的经验、正在进行的试验、历史数据、模型以及经验判断。[41,42]有用的参考资料包括QUANTEC项目最近对正常器官剂量反应的复习评论。[43-47]

~~早期淋巴结阴性的立体定向消融放疗~~

- 立体定向消融放疗（SABR）的高剂量强度和适形性要求计划靶区（PTV）降至最小。
  - 对于立体定向消融放疗（SABR），与非强化方案相比，生物学等效剂量（BED）≥100Gy的强化方案具有更好的局部控制和生存。[48] 在美国，只有分割≤5的方案才能符合立体定向放疗任意计费代码的定义，但是，时间更长的方案也略微更合适。[48,49] 对于中心型肿瘤（定义变为近端支气管树和/或邻接纵隔胸膜2cm内）甚至超中心型肿瘤（定义为紧邻支气管树），4-10分割风险调整的立体定向消融方案似乎是安全有效的，[50-53] 而54-60Gy/3f是不安全的，应该避免。RTOG 0813前瞻性研究了5分割方案的最大耐受剂量，初步结果显示50 Gy/5f没有高级别的毒性。[55]
- 立体定向消融放疗（SABR）最常用于达5cm的肿瘤，而选择性的更大的孤立性肿瘤如果保证正常组织的限制剂量可以安全地治疗。[54,56]
  - 处方剂量不能完全说明实际给予的剂量，这同样在很大程度上取决于如何处方剂量（等中心与等剂量体积覆盖PTV的比例）、剂量不均匀的程度、是否使用组织密度不均匀校正以及剂量计算法则的类型。[57,58] 当理解或仿效既往研究方案时，必须考虑所有这些因素。

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放射治疗原则 (4 of 10)

局部晚期/常规分割放疗

- 累及野照射（IFI）而非选择性淋巴结照射（ENI）允许增加肿瘤剂量并可降低单独淋巴结复发风险，特别是在PET/CT分期的病人中。[59-63] 两项随机试验发现，与选择性淋巴结照射（ENI）相比，累及野照射（IFI）改善了生存，可能是因为其能够剂量递增。[64] 为了使肿瘤根治量最优化，累及野照射（IFI）是合理的。[65]

- 根治性放疗最常用的处方剂量是60-70Gy，2Gy/f。应给予至少60Gy的剂量。[66] 在非随机对照中，单纯增加放疗剂量[67]、序贯化/放疗[68]或同步化/放疗[69]具有更好的生存。尽管最佳的放疗剂量强度仍然是一个悬而未决的问题，但是，目前不推荐常规使用74Gy的更高剂量。[70-74] 一项meta分析显示，加速分割放疗方案和个体化强化加速放疗剂量改善生存，[75] 目前正在一项随机试验（RTOG 1106）中评估。

- 45-54Gy，1.8-2Gy/f是标准的术前剂量。[76] 术前化放疗可安全地给予根治性放疗剂量，并可获得极佳的淋巴结清除率和生存率，[77-80] 但是在高剂量放疗后，需要有胸部手术技巧经验以使手术并发症风险将至最低。

- 在术后放疗（PORT）中，临床靶体积（CTV）包括支气管残端及高危引流淋巴结区。[81] 完全切除术后的标准剂量是50-54Gy，1.8-2Gy/f，但对于高危区域包括淋巴结囊外扩散区域或镜下切缘阳性区域可给予推量照射。[32,33,82] 肺剂量限制应该更加谨慎，因为术后耐受性似乎降低。正在进行的欧洲肺ART试验为术后放疗（PORT）技术提供了有用的指南。[83]

晚期/姑息性放疗

- 姑息性放疗的剂量与分割应根据治疗的目标、症状、一般情况和后勤方面的考量进行个体化治疗。较短程放疗与较长程放疗疼痛缓解相似，但更可能需要再治疗，[84-87]因此，对于一般情况差和/或预期寿命较短的患者是首选。为了缓解胸部症状，较高剂量/较长疗程的胸部放疗（如≥30Gy/10f）可适当改善生存和症状，尤其是在一般情况良好的患者中。[88,89] 当准许使用更高剂量（> 30 Gy）时，应该使用技术减少正常组织的照射（至少三维适形放疗以及包括调强放疗或酌情使用质子治疗）。

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放射治疗原则 (5 of 10)

放射治疗模拟、计划和交付

- 应使用适当固定设备在放疗位置获得的CT扫描进行模拟，在中心型肿瘤或淋巴结病变的患者中，为更好地勾画靶/器官，建议静脉造影±口服对比剂。由于静脉造影可以影响组织的非均匀性校正计算，因此，当进行强烈增强时，可能需要密度蒙罩或使用增强前扫描。

- PET/CT明显提高靶标精度[90]，尤其是对于显著肺不张和有静脉造影CT禁忌症的患者。一项对比PET/CT与单纯CT制定放疗计划的随机试验证明，PET/CT放疗计划可增加排除徒劳无效的根治性放疗、减少复发并且有改善总生存的趋势[91]。考虑到非小细胞肺癌的快速发展潜力[92,93]，应最好在治疗前4周内获得PET/CT。理想情况下，获得治疗位置的PET/CT。

- 肿瘤和器官的移动，尤其是由于呼吸，在模拟时对其应进行评估或计算在内。选择方案包括透视、吸气/呼气或慢扫描CT，或者，最理想的是4D-CT。

- 光子束能量应根据肿瘤的解剖学部位和光子束路径个体化。通常情况下，对于光子束在进入肿瘤之前通过低密度肺组织的情况，建议光子能量在4-10MV之间。当光子束进入肿瘤之前没有空气间隙（如，对于某些大纵隔肿瘤或肿瘤贴于胸壁）时，更高的能量可改善剂量分布，尤其是当使用一个较小的固定束角时。

- 由于横向电子散射作用的积累，因此建议在密度不均匀组织中采用组织不均质的校正和精确的剂量计算方法。不推荐用简单的笔形束算法进行异质性校正。[60]

- 当运动过度时，应控制呼吸运动。这包括（但不限于）腹部压迫强迫浅呼吸、周期性呼吸门控加速器束、肿瘤动态跟踪，主动呼吸控制（ABC）或指导/生物反馈技术。如果运动极小或靶区运动范围（ITV）小，包含移动靶区是合适的。美国医学物理学家协会（AAPM）工作组的76报告对呼吸运动管理的实施是有用的资源。[94]

- 当使用立体定向消融放疗（SABR）和3D-CRT/IMRT（三维适形放疗/调强放疗）靶区周围具有陡峭的剂量梯度时，当危及器官（OARs）非常接近高剂量区域时，以及当使用复杂的运动管理技术时，推荐使用影像引导放射治疗技术（IGRT）——包括（但不限于）正交双平面成像和容积成像（如锥形束CT[CBCT]或在轨CT）。

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

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Table 1. Commonly Used Abbreviations in Radiation Therapy

RT	Radiation Therapy or Radiotherapy
2D-RT	2-Dimensional RT
3D-CRT	3-Dimensional Conformal RT
4D-CT	4-Dimensional Computed Tomography
AAPM	American Association of Physicists in Medicine
ABC	Active Breathing Control
ACR	American College of Radiology
ASTRO	American Society for Radiation Oncology
BED	Biologically Effective Dose
CBCT	Cone-Beam CT
CTV*	Clinical Target Volume
ENI	Elective Nodal Irradiation
GTV*	Gross Tumor Volume

ICRU	International Commission on Radiation Units and Measurements
IFI	Involved Field Irradiation
IGRT	Image-Guided RT
IMRT	Intensity-Modulated RT
ITV*	Internal Target Volume
OAR	Organ at Risk
OBI	On-Board Imaging
PORT	Postoperative RT
PTV*	Planning Target Volume
QUANTEC	Quantitative Analysis of Normal Tissue Effects in the Clinic
RTOG	Radiation Therapy Oncology Group now part of NRG Oncology
SABR	Stereotactic Ablative RT, also known as Stereotactic Body RT (SBRT)
VMAT	Volumetric Modulated Arc Therapy

*Refer to ICRU Report 83 for detailed definitions.

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Table 2. Commonly Used Doses for SABR

Total Dose	# Fractions	Example Indications
25–34 Gy	1	Peripheral, small (<2 cm) tumors, esp. >1 cm from chest wall
45–60 Gy	3	Peripheral tumors and >1 cm from chest wall
48–50 Gy	4	Central or peripheral tumors <4–5 cm, especially <1 cm from chest wall
50–55 Gy	5	Central or peripheral tumors, especially <1 cm from chest wall
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

Please note - Tables 2–5 provide doses and constraints used commonly or in past clinical trials as useful references rather than specific recommendations.

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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

Please note: Tables 2–5 provide doses and constraints used commonly or in past clinical trials as useful references rather than specific recommendations.

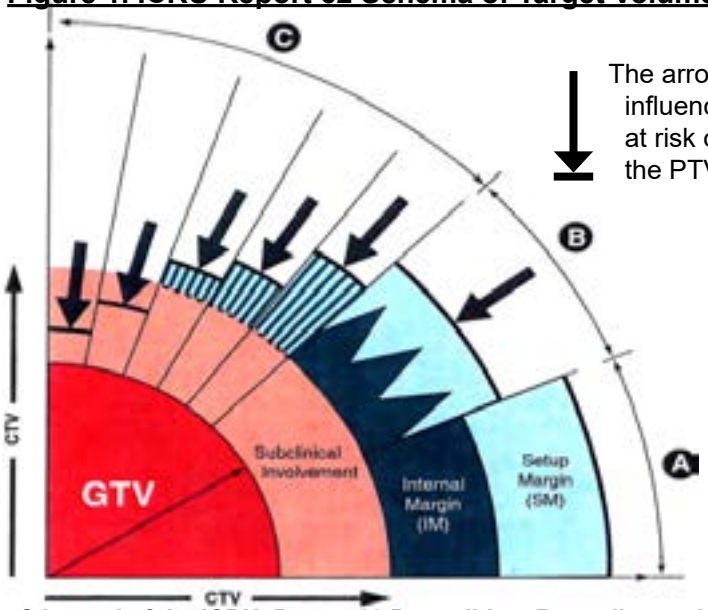
Table 5. Normal Tissue Dose-Volume Constraints for Conventionally Fractionated RT

OAR	Constraints in 30–35 Fractions
Spinal cord	Max ≤50 Gy
Lung	V20 ≤35%; V5 ≤65%; MLD ≤20 Gy
Heart**	V40 ≤80%; V45 ≤60%; V60 ≤30%; Mean ≤35 Gy
Esophagus	Mean ≤34 Gy; Max ≤105% of prescription dose
Brachial plexus	Max ≤66 Gy

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

**RTOG 0617 data suggest that even lower radiation doses to the heart than previously appreciated may be detrimental to survival after thoracic RT, and more stringent constraints may be appropriate.

Figure 1. ICRU Report 62 Schema of Target Volume Definitions



©Journal of the ICRU. Report 62 Prescribing, Recording and Reporting Photon Beam Therapy (Supplement to ICRU Report 50) 1999, Figure 2.16 from p 16.

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Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

新辅助与辅助治疗化疗方案

- **顺铂50mg/㎡ d1、8；长春瑞滨25mg/㎡ d1、8、15、22，每28天为1周期，共4周期[a]**
- **顺铂100mg/㎡ d1；长春瑞滨30mg/㎡ d1、8、15、22，每28天为1周期，共4周期[b,c]**
- **顺铂75-80mg/㎡ d1；长春瑞滨25–30mg/㎡ d1、8，每21天为1周期，共4周期**
- **顺铂100mg/㎡ d1；依托泊苷100mg/㎡ d1–3，每28天为1周期，共4周期[b]**
- **顺铂75mg/㎡ d1；吉西他滨1250mg/㎡ d1、8，每21天为1周期，共4周期[d]**
- **顺铂75mg/㎡ d1；多西他赛75mg/㎡ d1，每21天为1周期，共4周期[e]**
- **对于非鳞癌：顺铂75mg/㎡ d1，培美曲塞500mg/㎡ d1，每21天为1周期，共4周期[f]**

有合并症或不能耐受顺铂患者的化疗方案

紫杉醇200mg/㎡ d1，卡铂AUC 6 d1，每21天为1周期[g]

[a]Winton T, Livingston R, Johnson D, et al. Vinorelbine plus cisplatin vs. observation in resected non-small-lung cancer. N Engl J Med 2005;352:2589-2597.
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[g]Strauss GM, Herndon III JE, Maddaus MA, et al. Adjuvant paclitaxel plus carboplatin compared with observation in stage IB non-small cell lung cancer: CALGB 9633 with the Cancer and Leukemia Group B, Radiation Therapy Oncology Group, and North Central Cancer Treatment Group Study Groups. J Clin Oncol 2008;26:5043-5051.

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联合放疗的化疗方案

同步化/放疗方案

- **顺铂50mg/㎡ d1、8、29、36；依托泊苷50mg/㎡ d1–5、29–33；同期胸部放疗[a,b,*,**]**
- **顺铂100mg/㎡ d1、29；长春花碱5mg/㎡ /周×5；同期胸部放疗[b,*,**]**
- **卡铂AUC 5 d1，培美曲塞500mg/㎡ d1，每21天为1周期，共4周期；同期胸部放疗[c]（非鳞癌）*,****
- **顺铂75mg/㎡ d1，培美曲塞500mg/㎡ d1，每21天重复共3周期；同期胸部放疗[d,e]（非鳞癌）*,** ± 追加4周期培美曲塞500mg/㎡****
- **紫杉醇45-50mg/㎡每周1次；卡铂AUC 2，同期胸部放疗[f,*,**] ± 追加2周期紫杉醇200mg/㎡加卡铂AUC 6****

序贯化/放疗方案（辅助）

- **顺铂100mg/㎡，d1、29；长春花碱5mg/㎡/周，d1、8、15、22、29；序贯放疗[b]**
- **紫杉醇200mg/㎡，3小时以上，d1；卡铂AUC 6，60分钟以上，d1，每3周为1周期共2周期，然后胸部放疗[g]**

*方案可作为新辅助/术前/诱导化放疗使用。
**方案可作为辅助或根治性同步化/放疗使用。

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[e]Senan S, Brade A, Wang LH, et al. PROCLAIM: randomized phase III trial of pemetrexed-cisplatin or etoposide-cisplatin plus thoracic radiation therapy followed by consolidation chemotherapy in locally advanced nonsquamous non-small-cell lung cancer. J Clin Oncol 2016;34:953-962.
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Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

晚期或转移性疾病的全身治疗 (1 OF 4)

晚期疾病：
- 应该给予最可能受益的、具有对医患双方都可接受的毒性的药物方案作为晚期肺癌的初始治疗。
- 分期、体重减轻、一般情况以及性别预测生存。
- 与最佳支持治疗相比，以铂类为基础的化疗延长生存期、提高症状控制率并可获得更好的生活质量。
- 在全身治疗的选择方面非小细胞肺癌的组织学是重要的。
- 患者接受新药/铂二联的疗效有个平台：总有效率（≈25%–35%）、至进展时间（4–6个月）、中位生存期（8–10个月）、1年生存率（30%–40%）、2年生存率（10%–15%）。
- PS 3–4、任何年龄段的患者均不能从细胞毒性治疗中获益，除了厄洛替尼、阿法替尼或吉非替尼用于治疗EGFR突变阳性和克唑替尼用于治疗ALK阳性的非鳞非小细胞肺癌或非小细胞肺癌非特指患者。

一线治疗
- 在组织学非鳞癌患者中，与顺铂/吉西他滨相比，顺铂/培美曲塞有优越的疗效和较低的毒性。
- 在组织学鳞癌患者中，与顺铂/培美曲塞相比，顺铂/吉西他滨有优越的疗效。
- 首选两药方案；第3个细胞毒药物增加有效率，但不改善生存。在选择性的患者中单药治疗可能是合理的。
- 1-2周期后疗效评估，然后每2-4周期1次或有临床指征时对已知部位强化或平扫CT检查。

维持治疗
- 继续维持治疗是指在4至6周期后疾病无进展者，使用至少一种一线给予的药物。转换维持治疗是指在4-6周期初始治疗后疾病无进展者，启动一线方案中不包含的另一个不同的药物。

后续治疗
- 每6-12周对已知部位强化或平扫CT检查评估疗效。

See First-line Systemic Therapy Options for Adenocarcinoma, Large cell, NSCLC NOS on NSCL-F (2 of 4)

See First-line Systemic Therapy Options for Squamous Cell Carcinoma on NSCL-F (3 of 4)

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

晚期或转移性疾病的全身治疗 (2 of 4)†

一线全身治疗方案

腺癌、大细胞肺癌、非小细胞肺癌非特指（PS 0-1）

- 贝伐单抗/卡铂/紫杉醇（1类）[1,*,**,***]
- 贝伐单抗/卡铂/培美曲塞[2,*,**,***]
- 贝伐单抗/顺铂/培美曲塞[3*,**,***]
- 卡铂/白蛋白结合型紫杉醇（1类）[4]
- 卡铂/多西他赛（1类）[5]
- 卡铂/依托泊苷（1类）[6,7]
- 卡铂/吉西他滨（1类）[8]
- 卡铂/紫杉醇（1类）[9]
- 卡铂/培美曲塞（1类）[10]
- 顺铂/多西他赛（1类）[5]
- 顺铂/依托泊苷（1类）[11]
- 顺铂/吉西他滨（1类）[9,12]
- 顺铂/紫杉醇（1类）[13]
- 顺铂/培美曲塞（1类）[12]
- 吉西他滨/多西他赛（1类）[14]
- 吉西他滨/长春瑞滨（1类）[15]

腺癌，大细胞肺癌，非小细胞肺癌非特指（PS 2）

- 白蛋白结合型紫杉醇[16]
- 卡铂/白蛋白结合型紫杉醇[17,18]
- 卡铂/多西他赛[5]
- 卡铂/依托泊苷[6,7]
- 卡铂/吉西他滨[8]
- 卡铂/紫杉醇[9]
- 卡铂/培美曲塞[10]
- 多西他赛[19,20]
- 吉西他滨[21-23]
- 吉西他滨/多西他赛[14]
- 吉西他滨/长春瑞滨[15]
- 紫杉醇[24-26]
- 培美曲塞[27]

†在接受紫杉醇或多西他赛的患者中，尽管预处理用药仍有过敏反应者，或标准预处理用药（即地塞米松、H2受体阻滞剂、H1受体阻滞剂）禁忌者，白蛋白结合型紫杉醇可以取代紫杉醇或多西他赛。

*应该给予贝伐单抗直至疾病进展。

**任何具有血小板减少高危和潜在出血风险的方案，联合贝伐单抗时均应谨慎。

***联合贝伐单抗是标准治疗：非鳞非小细胞肺癌并且近期无咯血史。贝伐单抗不应单药给予，除非最初联合化疗使用然后作为维持。

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

晚期或转移性疾病的全身治疗(3 of 4)†,††

一线全身治疗方案

鳞状细胞癌（PS 0-1）

- 卡铂/白蛋白结合型紫杉醇（1类）[4]
- 卡铂/多西他赛（1类）[5]
- 卡铂/吉西他滨（1类）[8]
- 卡铂/紫杉醇（1类）[9]
- 顺铂/多西他赛（1类）[5]
- 顺铂/依托泊苷（1类）[11]
- 顺铂/吉西他滨（1类）[9,12]
- 顺铂/紫杉醇（1类）[13]
- 吉西他滨/多西他赛（1类）[14]
- 吉西他滨/长春瑞滨（1类）[15]

鳞状细胞癌（PS 2）

- 白蛋白结合型紫杉醇[16]
- 卡铂/白蛋白结合型紫杉醇[17,18]
- 卡铂/多西他赛[5]
- 卡铂/依托泊苷[6,7]
- 卡铂/吉西他滨[8]
- 卡铂/紫杉醇[9]
- 多西他赛[19,20]
- 吉西他滨[21-23]
- 吉西他滨/多西他赛[14]
- 吉西他滨/长春瑞滨[15]
- 紫杉醇[24-26]

†在接受紫杉醇或多西他赛的患者中，尽管预处理用药仍有过敏反应者，或标准预处理用药（即地塞米松、H2受体阻滞剂、H1受体阻滞剂）禁忌者，白蛋白结合型紫杉醇可以取代紫杉醇或多西他赛。

††在NCCN机构中对于这些适应症，基于这些药物的疗效与安全性和其他可用药物的疗效与安全性相比较，顺铂/吉西他滨/奈昔妥珠单抗不用于一线、厄洛替尼或阿法替尼不用于二线。

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

晚期或转移性疾病的全身治疗 (4 of 4)

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癌症生存关怀

非小细胞肺癌长期随访指导

- 癌症监测
  - 病史与体格检查、胸部CT扫描±强化，每6 - 12个月1次共2年，之后，病史与体检和胸部平扫CT
  - 每次随访时评估吸烟状况；咨询并根据需要建议戒烟。
- 免疫接种
  - 流感疫苗接种每年1次
  - 带状疱疹疫苗
  - 酌情再次接种肺炎球菌疫苗

考虑健康促进与健康咨询[1]

- 保持健康的体重
- 采用一种积极运动的生活方式（定期体力活动：每周大部分日子30分钟中等强度的体力活动）
- 健康饮食，强调植物来源
- 如果饮酒，需要限制

其他健康监测

- 常规血压、胆固醇和血糖监测
- 骨健康：酌情骨密度检测
- 牙齿健康：常规牙科检查
- 日常防晒

资源

- 国家癌症研究所直面未来：癌症治疗后的生活
  http://www.cancer.gov/cancertopics/life-after-treatment/allpages

癌症筛查推荐[2,3]

这些推荐是针对平均风险的个体，而高危患者应该个体化。

- 结直肠癌：
  See NCCN Guidelines for Colorectal Cancer Screening
- 前列腺癌：
  See NCCN Guidelines for Prostate Cancer Early Detection
- 乳腺癌：
  See NCCN Guidelines for Breast Cancer Screening

[1]营养与体力活动防癌ACS指南：
http://www.cancer.org/healthy/eathealthygetactive/acsguidelinesonnutritionphysicalactivityforcancerprevention/index?sitearea=PED.
[2]纪念斯隆-凯特琳癌症中心筛查指南： https://www.mskcc.org/cancer-care/risk-assessment-screening/screening-guidelines.
[3]癌症早期发现美国癌症协会指南：
http://www.cancer.org/healthy/findcancerearly/cancerscreeningguidelines/american-cancer-society-guidelines-for-the-early-detection-of-cancer?sitearea=PED.

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具有遗传学改变患者的新兴靶向药物

遗传学改变（即驱动事件）	针对肺癌驱动事件可用、有效的靶向药物
BRAF* V600E突变 *非V600E突变的激酶活性以及对这些药物的应答各种各样。	维罗非尼[1,2] 达拉非尼[2,3] 达拉非尼+曲美替尼[4]
高水平MET扩增或MET外显子14跳跃突变	克唑替尼[5-9]
***RET*重排**	卡博替尼[10,11] 凡德他尼[12]
***HER2* 突变**	曲妥珠单抗[13] (2B类) 阿法替尼[14] (2B类)

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Table 1. 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 visualized by imaging or bronchoscopy
T0	No evidence of primary tumor
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)[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 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: 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 nodule(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 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	Distant Metastasis
MX	Distant metastasis cannot be assessed
M0	No distant metastasis
M1	Distant metastasis
M1a	Separate tumor nodule(s) in a contralateral lobe; tumor with pleural nodules or malignant 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 ≤5 cm or if size cannot be determined, and T2b if >5 cm but ≤7 cm.

[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 IASLC Lung Cancer Staging Project: Proposals for the revision of the TNM stage groupings in the forthcoming (seventh) edition of the TNM classification of malignant tumors. J Thorac Oncol 2007;2:706-714.

Table 2. Anatomic Stage and Prognostic Groups

Occult Carcinoma	**TX**	**N0**	**M0**
Stage 0	**Tis**	**N0**	**M0**
Stage IA	**T1a**	**N0**	**M0**
	T1b	**N0**	**M0**
Stage IB	**T2a**	**N0**	**M0**
Stage IIA	**T2b**	**N0**	**M0**
	T1a	**N1**	**M0**
	T1b	**N1**	**M0**
	T2a	**N1**	**M0**
Stage IIB	**T2b**	**N1**	**M0**
	T3	**N0**	**M0**

Stage 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 IIIB	**T1a**	**N3**	**M0**
	T1b	**N3**	**M0**
	T2a	**N3**	**M0**
	T2b	**N3**	**M0**
	T3	**N3**	**M0**
	T4	**N2**	**M0**
	T4	**N3**	**M0**
Stage IV	**Any T**	**Any N**	**M1a**
	Any T	**Any N**	**M1b**

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Table 3. Descriptors, T and M Categories, and Stage Grouping*

6th Edition T/M Descriptor	7th Edition T/M	N0	N1	N2	N3
T1 (≤2 cm)	T1a	IA	IIA	IIIA	IIIB
T1 (<2–3 cm)	T1b	IA	IIA	IIIA	IIIB
T2 (≤5 cm)	T2a	IB	**IIA**	IIIA	IIIB
T2 (<5–7 cm)	T2b	**IIA**	IIB	IIIA	IIIB
T2 (>7 cm)	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.

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