

# 高雄榮民總醫院

## 肺癌（非小細胞癌）診療原則

癌症中心 肺癌醫療團隊擬定

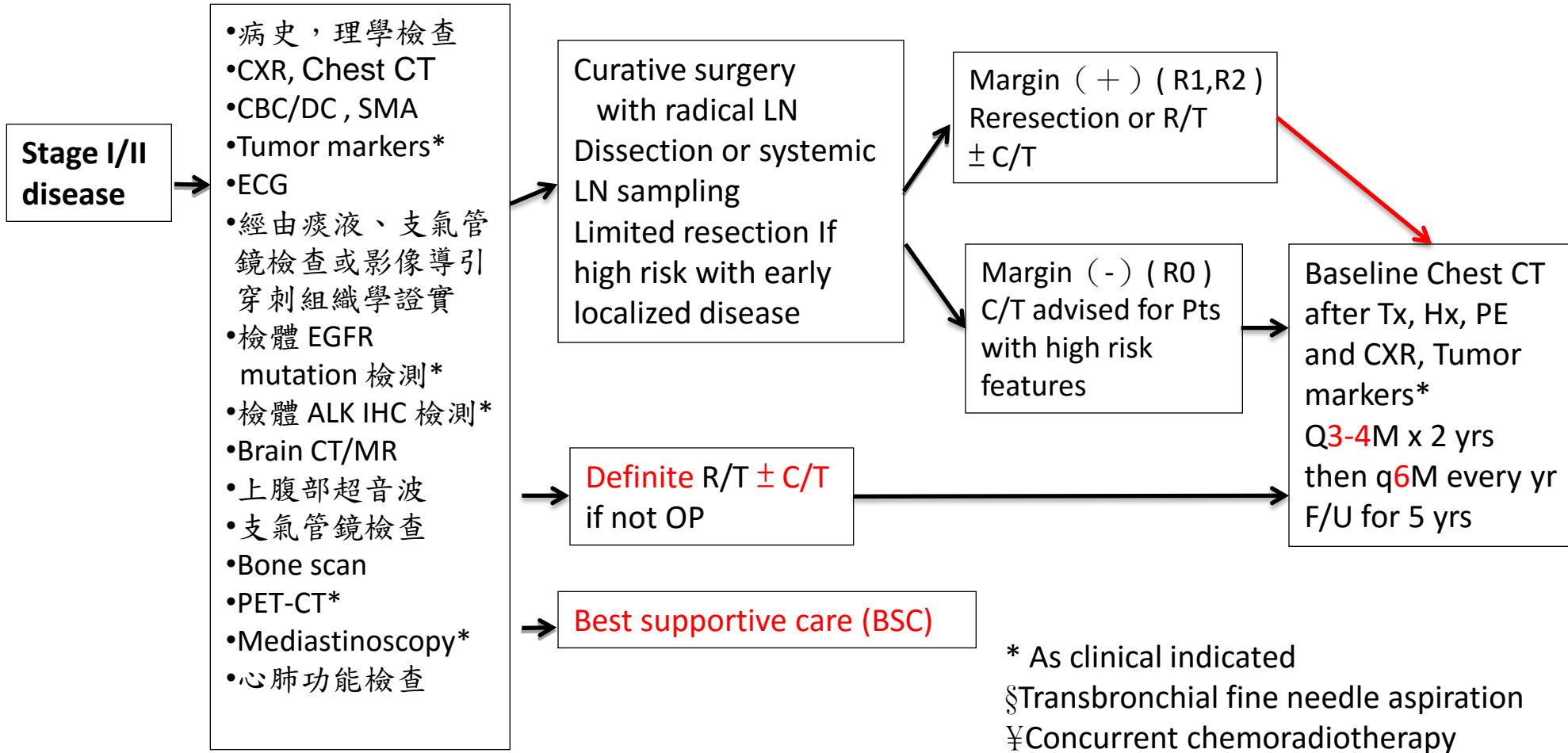
Reference: NCCN Clinical Practice Guideline in Oncology™ ,NSCLC, V.4.2016

# 非小細胞肺癌

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診斷	評估	初步治療	輔助治療	追蹤
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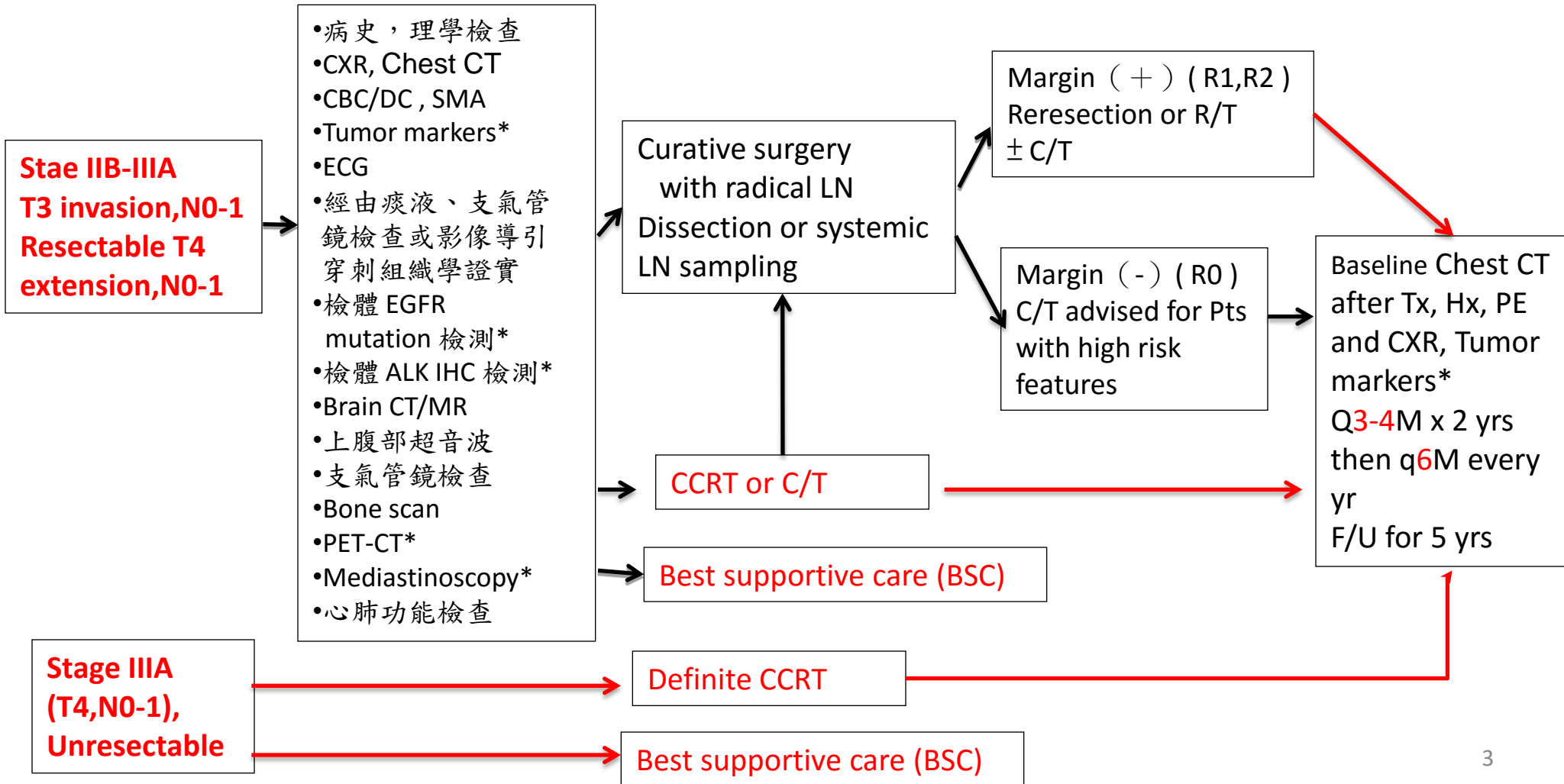


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診斷	評估	初步治療	輔助治療	追蹤
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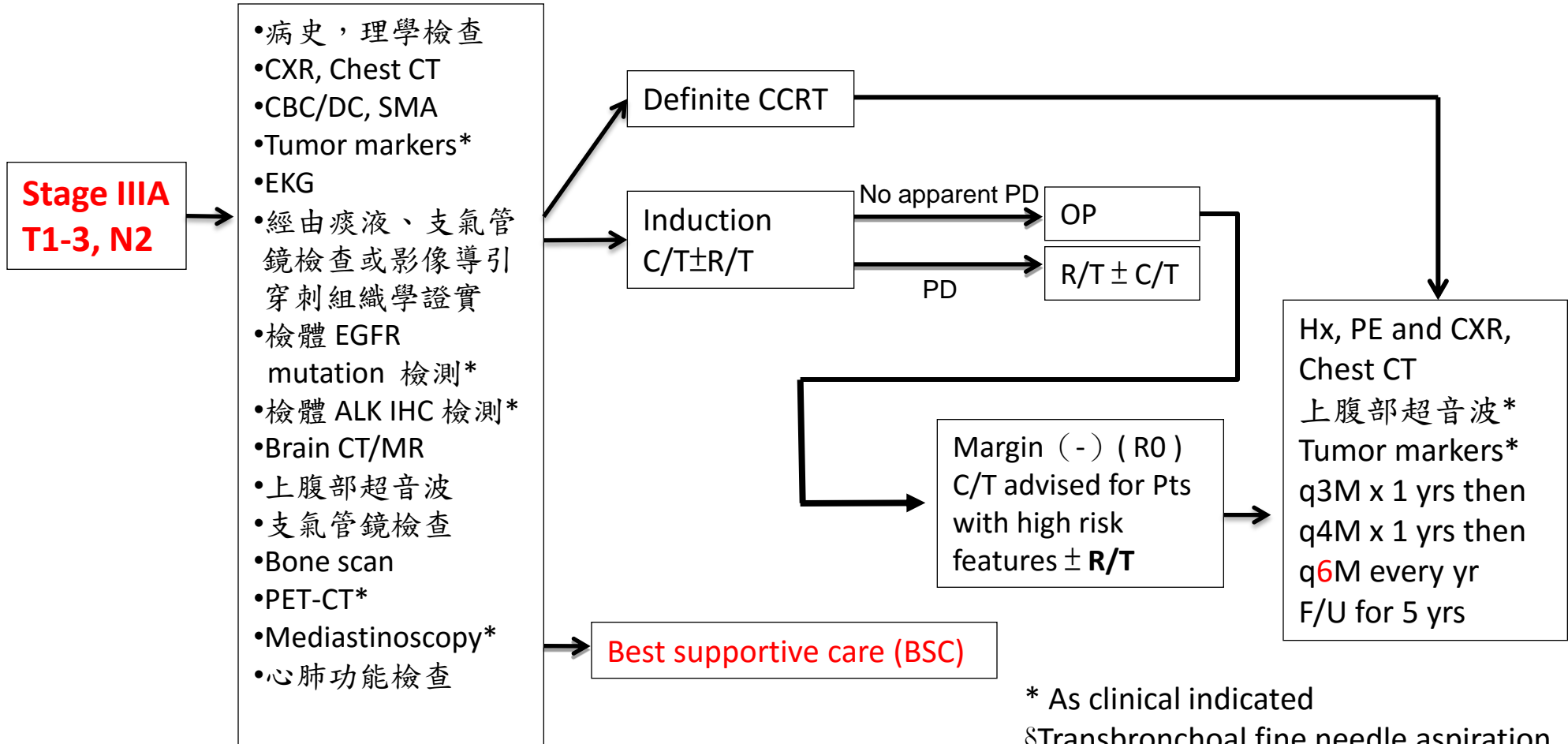


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診斷	評估	初步治療	輔助治療	追蹤
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\* As clinical indicated

§ Transbronchoal fine needle aspiration

¥ Concurrent chemoradiotherapy 4

# 非小細胞肺癌

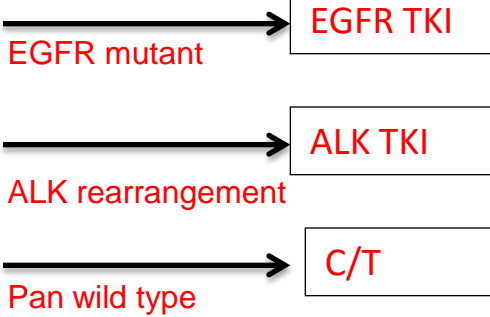
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診斷	評估	初步治療	重新評估	進一步治療	追蹤
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Stage IIIB  
(T4N2-3)

- 病史，理學檢查
- CXR, Chest CT
- CBC/DC, SMA
- Tumor markers\*
- ECG
- 經由痰液、支氣管鏡檢查或影像導引穿刺或表淺淋巴結抽吸組織學證實
- 檢體 EGFR mutation 檢測\*
- 檢體 ALK IHC 檢測\*
- Mediastinoscopy\* for N2/N3 disease
- Brain CT/MR\*
- 上腹部超音波
- 支氣管鏡檢查
- Bone scan\*, PET-CT\*
- 心肺功能檢查



Definite CCRT

Best supportive care (BSC)

病史，理學檢查  
CXR,  
tumor markers\*  
q3M x 1 yr, then  
q4M x 1 yr, then  
Q6-12M x 3yrs

\* As clinical indicated

§ Transbronchoal fine needle aspiration

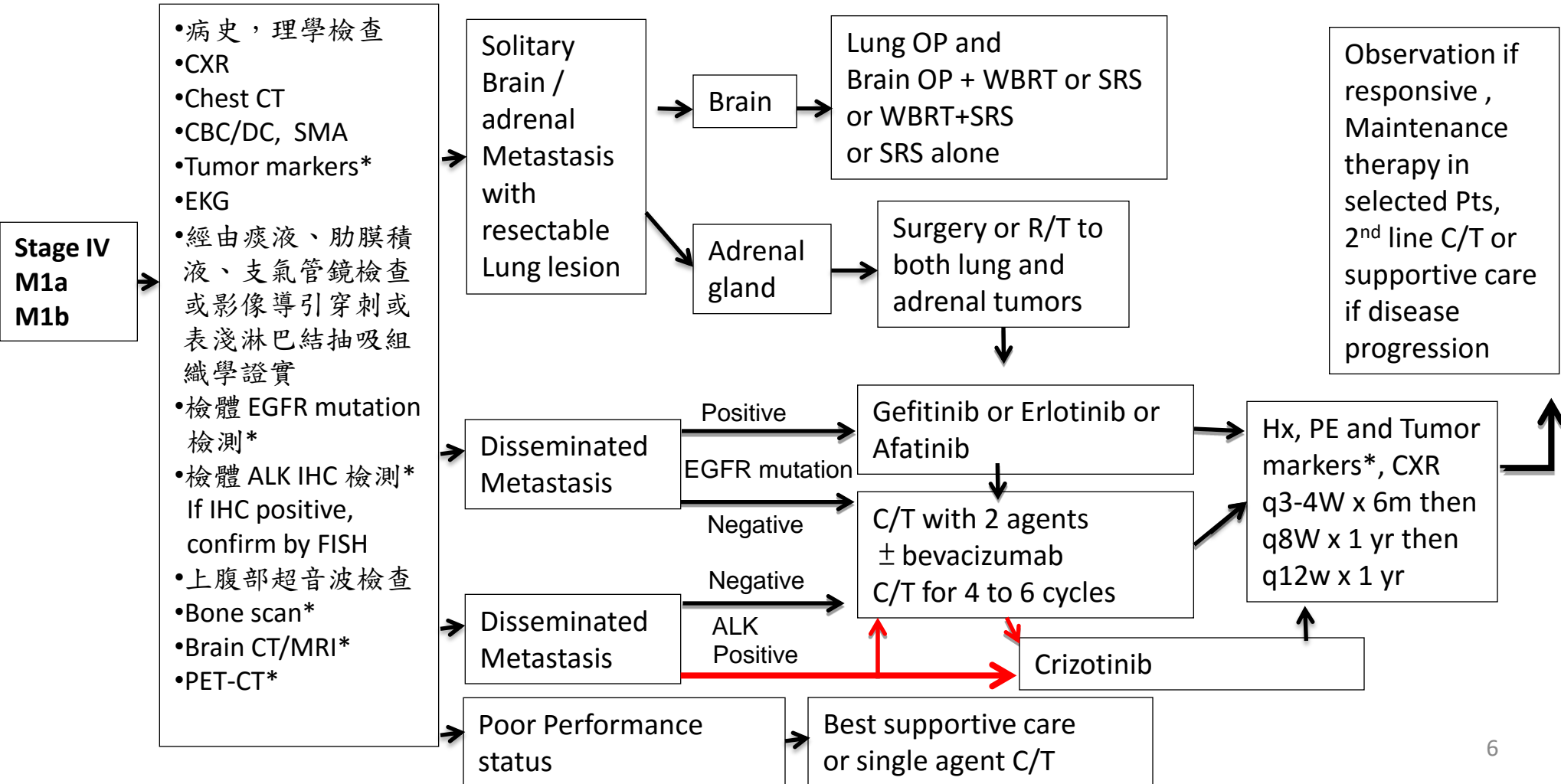
¥ Concurrent chemoradiotherapy

# 非小細胞肺癌

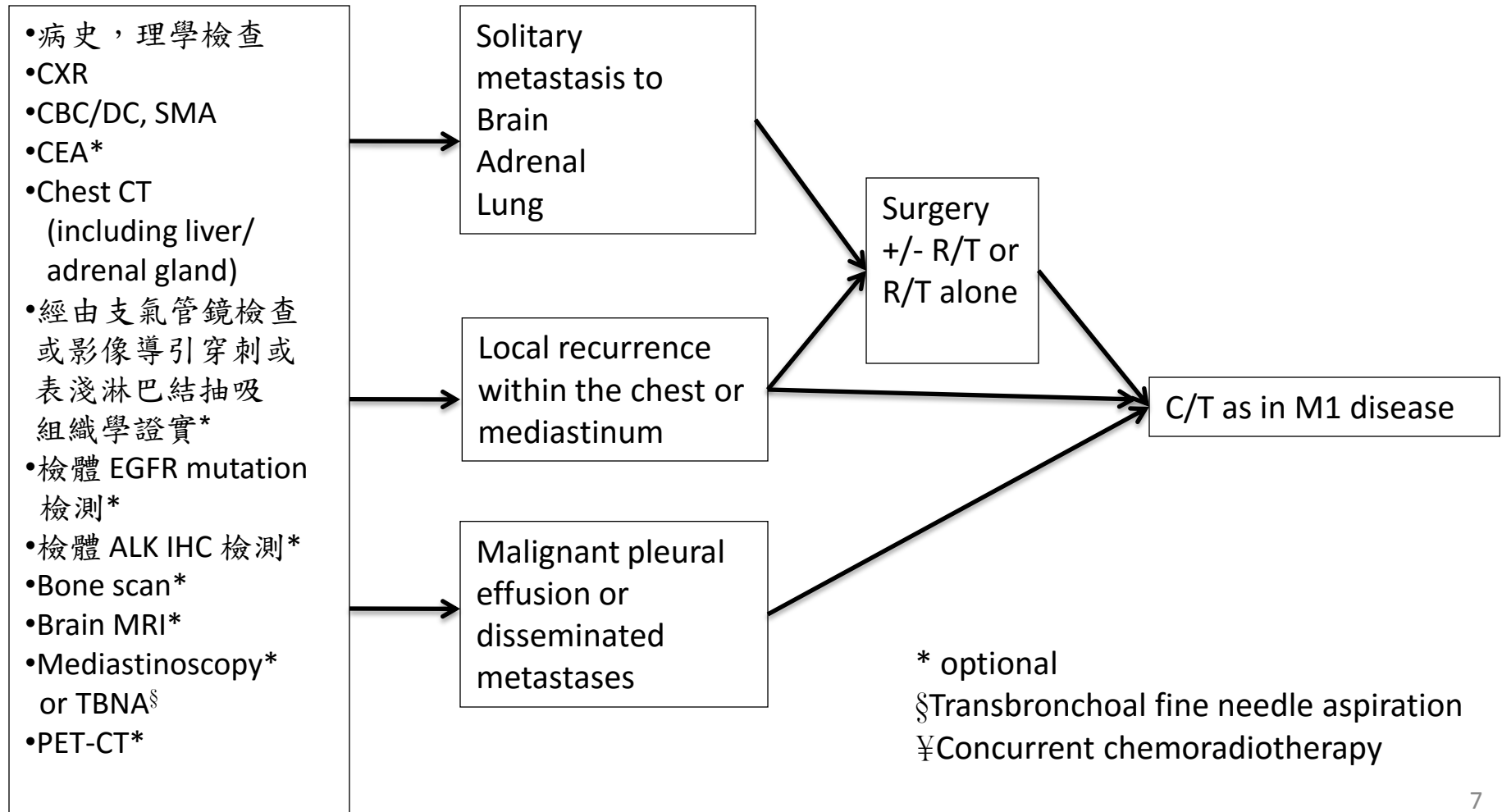
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診斷	評估	治療	重新評估	治療
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## 復發



# 非小細胞肺癌

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## 一線化學治療處方

Published C/T Regimens	Schedule
Cisplatin 60-75 mg/m <sup>2</sup> , IV, D15 + Vinorelbine 25 mg/m <sup>2</sup> , IV, D1,8,15	Q28 d x 4-6 cycles
Cisplatin 60-75 mg/m <sup>2</sup> , IV, D8 + Vinorelbine 60-75 mg/m <sup>2</sup> , PO, D1,8	Q21 d x 4-6 cycles
Cisplatin 60-75 mg/m <sup>2</sup> , IV, D15 + Docetaxel 30 mg/m <sup>2</sup> , IV, D1,8,15	Q28 d x 4-6 cycles
Cisplatin 60-75 mg/m <sup>2</sup> , IV, D15 + Paclitaxel 60 mg/m <sup>2</sup> , IV, D1,8,15	Q28 d x 4-6 cycles
Cisplatin 60-75 mg/m <sup>2</sup> , IV, D15 + Gemcitabine 900-1000 mg/m <sup>2</sup> , IV, D1,8,15	Q28 d x 4-6 cycles
Cisplatin 60-75 mg/m <sup>2</sup> , IV, D1 + *Pemetrexed 500 mg/m <sup>2</sup> , IV, D1	Q21 d x 4-6 cycles
Gefitinib 250 mg po qd ( EGFR mutant )	Till PD or unacceptable toxicity
Erlotinib 150 mg po qd ( EGFR mutant )	Till PD or unacceptable toxicity
Afatinib 40 mg po qd ( EGFR mutant )	Till PD or unacceptable toxicity
Crizotinib 250 mg po bid (ALK rearrangement)	Till PD or unacceptable toxicity

若腎功能不佳，CCr < 60 ml/min，cisplatin 可以 carboplatin AUC 4-6 取代

若是 nonsquamous histology，沒有 bevacizumab 的 contraindication，platinum doublet 可以併用 bevacizumab

\* 使用於不是 squamous cell carcinoma 組織學型態的病人



## 一線的化學治療處方（年紀大，體能狀況不佳）

Published C/T Regimens	Schedule
Gefitinib 250 mg PO QD ( EGFR mutant )	Till PD or unacceptable toxicity
Erlotinib 150 mg PO QD ( EGFR mutant )	Till PD or unacceptable toxicity
Afatinib 40 mg po qd ( EGFR mutant )	Till PD or unacceptable toxicity
<b>Pemetrexed 500 mg/m<sup>2</sup>, IV, D1</b>	<b>Q21 d x 4-6 cycles</b>
Docetaxel 30 mg/m <sup>2</sup> , IV, D1,8,15	Q28 d x 4-6 cycles
Paclitaxel 60 mg/m <sup>2</sup> , IV, D1,8,15	Q28 d x 4-6 cycles
Gemcitabine 900-1000 mg/m <sup>2</sup> , IV, D1,8,15	Q28 d x 4-6 cycles
Vinorelbine 25 mg/ m <sup>2</sup> IV, D1,8,15	Q28 d x 4-6 cycles
Vinorelbine 60-75 mg/m <sup>2</sup> , PO, D1,8	Q21 d x 4-6 cycles
Crizotinib (ALK rearrangement)	Till PD or unacceptable toxicity

\* 一線，二線及二線之後的化學治療，術後輔助化學治療，依據病人年齡、性別、組織學型態、體能狀況、器官功能狀況、副作用的考量（血液學毒性、掉髮、皮疹、色素沈著、周邊神經病變等）、曾接受過的治療、病人的喜好、及分子生物標記來選擇病人的化學治療處方，給於客製化（personalized treatment）的治療。

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## 維持治療處方

Published C/T Regimens	Schedule
*Pemetrexed 500 mg/m <sup>2</sup> IV D1	Q21 d Till PD or unacceptable toxicity
*Erlotinib 150 mg PO QD	Till PD or unacceptable toxicity
*Docetaxel 30 mg/m <sup>2</sup> , IV, D1,8,15	Q28 d Till PD or unacceptable toxicity
#Gemcitabine 900-1000 mg/m <sup>2</sup> , IV, D1,8,15	Q28d Till PD or unacceptable toxicity
#Bevacizumab 7.5 mg/kg IV q3w	Q21d Till PD or unacceptable toxicity
#Pemetrexed 500 mg/m <sup>2</sup> IV + Bevacizumab 7.5 mg/kg IV	Q21d Till PD or unacceptable toxicity

#Continuous maintenance therapy：在沒有疾病惡化的情況下，一線化學治療 4-6 個療程後，持續使用一線化學治療配方中的一個藥物。使用於不是 squamous cell carcinoma 組織學型態的病人。

\* Switch maintenance therapy：在沒有疾病惡化的情況下，一線化學治療 4-6 個療程後，使用與一線化學治療配方不同的藥物。

## 二線及二線之後的化學治療處方

Published C/T Regimens	Schedule
Gefitinib 250 mg PO QD	Till PD or unacceptable toxicity
Erlotinib 150 mg PO QD	Till PD or unacceptable toxicity
<b>Crizotinib 250 mg po bid (ALK rearrangement)</b>	<b>Till PD or unacceptable toxicity</b>
*Ceritinib 750 mg po qd (ALK rearrangement)	Till PD or unacceptable toxicity
Docetaxel 30 mg/m <sup>2</sup> , IV, D1,8,15	Q28 d x 4-6 cycles
#Pemetrexed 500 mg/m <sup>2</sup> , IV, D1	Q21 d x 4-6 cycles
Paclitaxel 60 mg/m <sup>2</sup> , IV, D1,8,15	Q28 d x 4-6 cycles
Gemcitabine 900-1000 mg/m <sup>2</sup> , IV, D1,8,15	Q28 d x 4-6 cycles
Vinorelbine 25 mg/ m <sup>2</sup> IV, D1,8,15	Q28 d x 4-6 cycles
Vinorelbine 60-75 mg/m <sup>2</sup> , PO, D1,8	Q21 d x 4-6 cycles

\* 一線 crizotinib 治療惡化或不耐受

\* 一線，二線及二線之後的化學治療，術後輔助化學治療，依據分子生物標記、病人年齡、性別、組織學型態、體能狀況、器官功能狀況、副作用的考量（血液學毒性、掉髮、皮疹、色素沈著、周邊神經病變等）、曾接受過的治療、及病人的喜好來選擇病人的化學治療處方，給於客製化（personalized treatment）的治療。

# 使用於不是 squamous cell carcinoma 組織學型態的病人

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## 術前新輔助化學治療處方

Published C/T Regimens	Schedule
Cisplatin 60-75 mg/m <sup>2</sup> , IV, D15 Vinorelbine 25 mg/m <sup>2</sup> , IV, D1,8,15	Q28 d x 3-4 cycles
Cisplatin 60-75 mg/m <sup>2</sup> , IV, D8 Vinorelbine 60-75 mg/m <sup>2</sup> , PO, D1,8	Q21 d x 3-4 cycles
Cisplatin 60-75 mg/m <sup>2</sup> , IV, D15 Docetaxel 30 mg/m <sup>2</sup> , IV, D1,8,15	Q28 d x 3-4 cycles
Cisplatin 60-75 mg/m <sup>2</sup> , IV, D15 Paclitaxel 60 mg/m <sup>2</sup> , IV, D1,8,15	Q28 d x 3-4 cycles
Cisplatin 60-75 mg/m <sup>2</sup> , IV, D15. Gemcitabine 900-1000 mg/m <sup>2</sup> , IV, D1,8,15.	Q28 d x 3-4 cycles
Cisplatin 60-75 mg/m <sup>2</sup> , IV, D1 #Pemetrexed 500 mg/m <sup>2</sup> , IV, D1	Q21 d x 3-4 cycles

若腎功能不佳，CCr < 60 ml/min，cisplatin 可以 carboplatin AUC 4-6 取代

# 使用於不是 squamous cell carcinoma 組織學型態的病人

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## 術後輔助化學治療處方

Published C/T Regimens	Schedule
Cisplatin 60-75 mg/m <sup>2</sup> , IV, D15 Vinorelbine 25 mg/m <sup>2</sup> , IV, D1,8,15	Q28 d x 4 cycles
Cisplatin 60-75 mg/m <sup>2</sup> , IV, D15 Vinorelbine 60-75 mg/m <sup>2</sup> , PO, D1,8	Q21 d x 4 cycles
Cisplatin 60-75 mg/m <sup>2</sup> , IV, D15 Docetaxel 30 mg/m <sup>2</sup> , IV, D1,8,15	Q28 d x 4 cycles
Cisplatin 60-75 mg/m <sup>2</sup> , IV, D15 Paclitaxel 60 mg/m <sup>2</sup> , IV, D1,8,15	Q28 d x 4 cycles
Cisplatin 60-75 mg/m <sup>2</sup> , IV, D15. Gemcitabine 900-1000 mg/m <sup>2</sup> , IV, D1,8,15.	Q28 d x 4 cycles
Cisplatin 60-75 mg/m <sup>2</sup> , IV, D1 #Pemetrexed 500 mg/m <sup>2</sup> , IV, D1	Q21 d x 4 cycles
Tagafur/Uracil 300-500 mg PO QD *	Maintenance for 2 years

若腎功能不佳，CCr < 60 ml/min，cisplatin 可以 carboplatin AUC 4-6 取代

# 使用於不是 squamous cell carcinoma 組織學型態的病人

# 非小細胞肺癌

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## 同步化學治療放射線治療處方

Published C/T Regimens	Schedule
Cisplatin 50-60 mg/m <sup>2</sup> , IV, D15 Vinorelbine 20-25 mg/m <sup>2</sup> , IV, D1,8,15	Q28 d x 4 cycles
Cisplatin 50-60 mg/m <sup>2</sup> , IV, D15 Docetaxel 20-25 mg/m <sup>2</sup> , IV, D1,8,15	Q28 d x 4 cycles
Cisplatin 50-60 mg/m <sup>2</sup> , IV, D15 Paclitaxel 45-50 mg/m <sup>2</sup> , IV, D1,8,15	Q28 d x 4 cycles
Cisplatin 50-60 mg/m <sup>2</sup> , IV, D1 #Pemetrexed 500 mg/m <sup>2</sup> , IV, D1	Q21 d x 4 cycles
Carboplatin AUC 4, IV, D1 #Pemetrexed 500 mg/m <sup>2</sup> , IV, D1	Q21 d x 4 cycles

若腎功能不佳，CCr < 60 ml/min，cisplatin 可以 carboplatin AUC 4取代

# 使用於不是 squamous cell carcinoma 組織學型態的病人

## References

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

## References

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



## References

31. Herbst RS, Prager D, Hermann R, et al: TRIBUTE: A phase III trial of erlotinib hydrochloride (OSI-774) combined with carboplatin and paclitaxel chemotherapy in advanced non–small-cell lung cancer. *J Clin Oncol* 23:5892-5899, 2005
32. Gatzemeier U, Pluzanska A, Szczesna A, et al: Phase III study of erlotinib in combination with cisplatin and gemcitabine in advanced non–smallcell lung cancer: The Tarceva Lung Cancer Investigation Trial. *J Clin Oncol* 25:1545-1552, 2007
33. Mok TS, Wu YL, Thongprasert S, et al: Gefitinib or carboplatin-paclitaxel in pulmonary adenocarcinoma. *N Engl J Med* 361:947-957, 2009
34. Pirker R, Pereira JR, Szczesna A, et al: Cetuximab plus chemotherapy in patients with advanced non-small-cell lung cancer (FLEX): An open-label randomised phase III trial. *Lancet* 373:1525-1531, 2009
35. Scagliotti G, Hanna N, Fossella F, et al: The differential efficacy of pemetrexed according to NSCLC histology: A review of two phase III studies. *Oncologist* 14:253-263, 2009
36. Yang CH, Shih JY, Chen KC, et al: Survival outcome and predictors of gefitinib antitumor activity in East Asian chemonaive patients with advanced nonsmall cell lung cancer. *Cancer* 107:1873-1882, 2006
37. Eberhard DA, Johnson BE, Amler LC, et al: Mutations in the epidermal growth factor receptor and in KRAS are predictive and prognostic indicators in patients with non–small-cell lung cancer treated with chemotherapy alone and in combination with erlotinib. *J Clin Oncol* 23:5900-5909, 2005
38. Harrington SE, Smith TJ: The role of chemotherapy at the end of life: “When is enough, enough?” *JAMA* 299:2667-2678, 2008
39. Curran WJ et al. Sequential vs concurrent chemoradiation for stage III non-small cell lung cancer: a randomized phase III trial RTOG 9410. *J Natl Cancer Inst.* 2011;103:1452-1460
40. Sequist LV, Yang JC et al. Phase III study of afatinib or cisplatin plus pemetrexed in patients with metastatic lung adenocarcinoma with EGFR mutations. *J Clin Oncol* 2013;31:3327-3334.
41. Shaw AT et al. Ceritinib in ALK-rearranged non-small-cell lung cancer. *N Engl J Med* 2014;370:1189-1197