

高雄榮民總醫院

非小細胞肺癌診療原則

肺癌醫療團隊擬定

這個指引是團隊成員根據實證醫學資料所做的共識聲明，來幫助醫師在特殊臨床狀況下做最適當的醫療決策。指引無法涵蓋所有的臨床狀況，醫師必須根據每個病人特殊的病況，下臨床判斷，做最適當的處置。

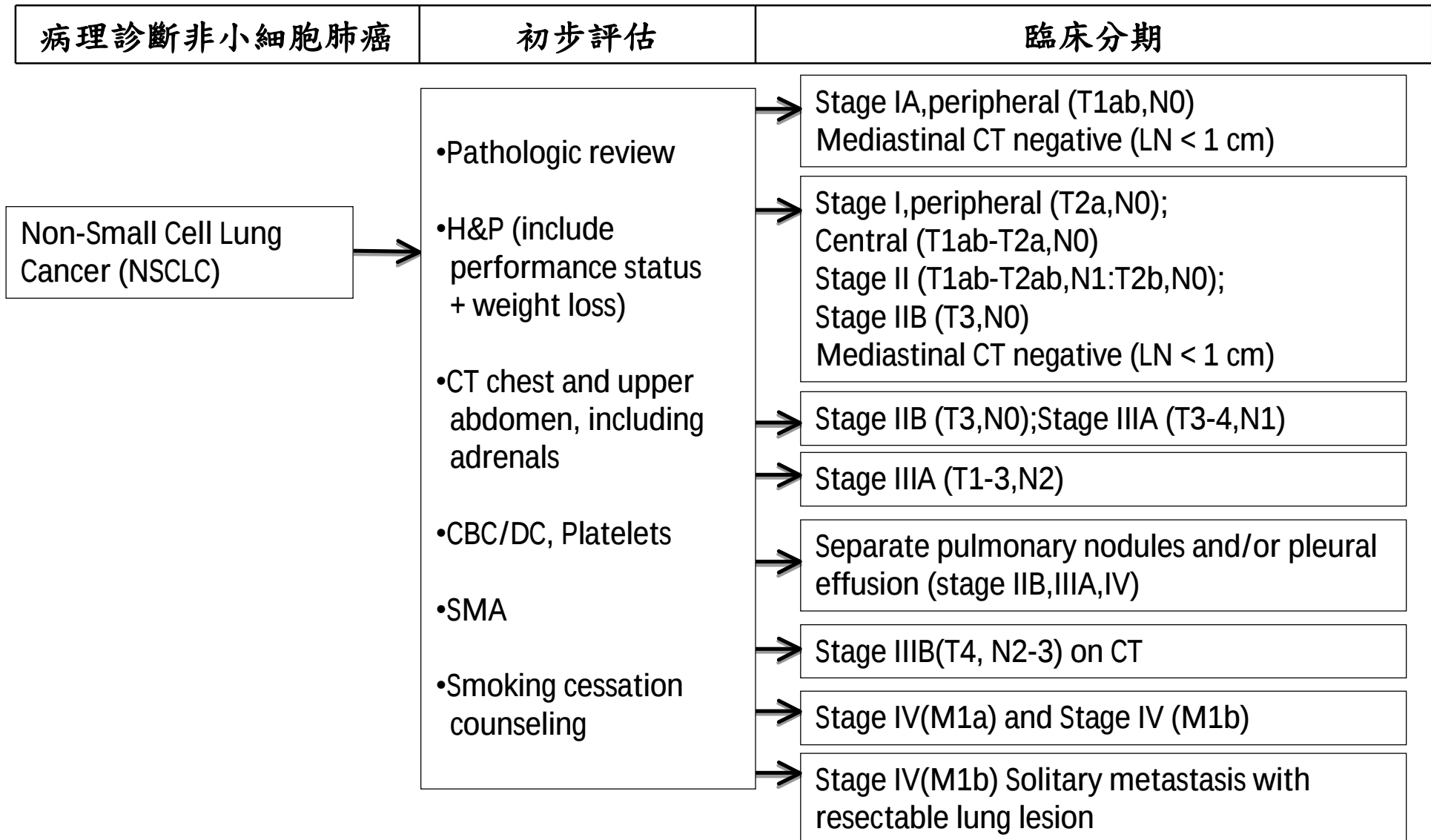
Reference: NCCN Clinical Practice Guideline in Oncology™, NSCLC, V.1.2010
台灣癌症臨床研究合作組織（TCOG）2003 肺癌臨床指引

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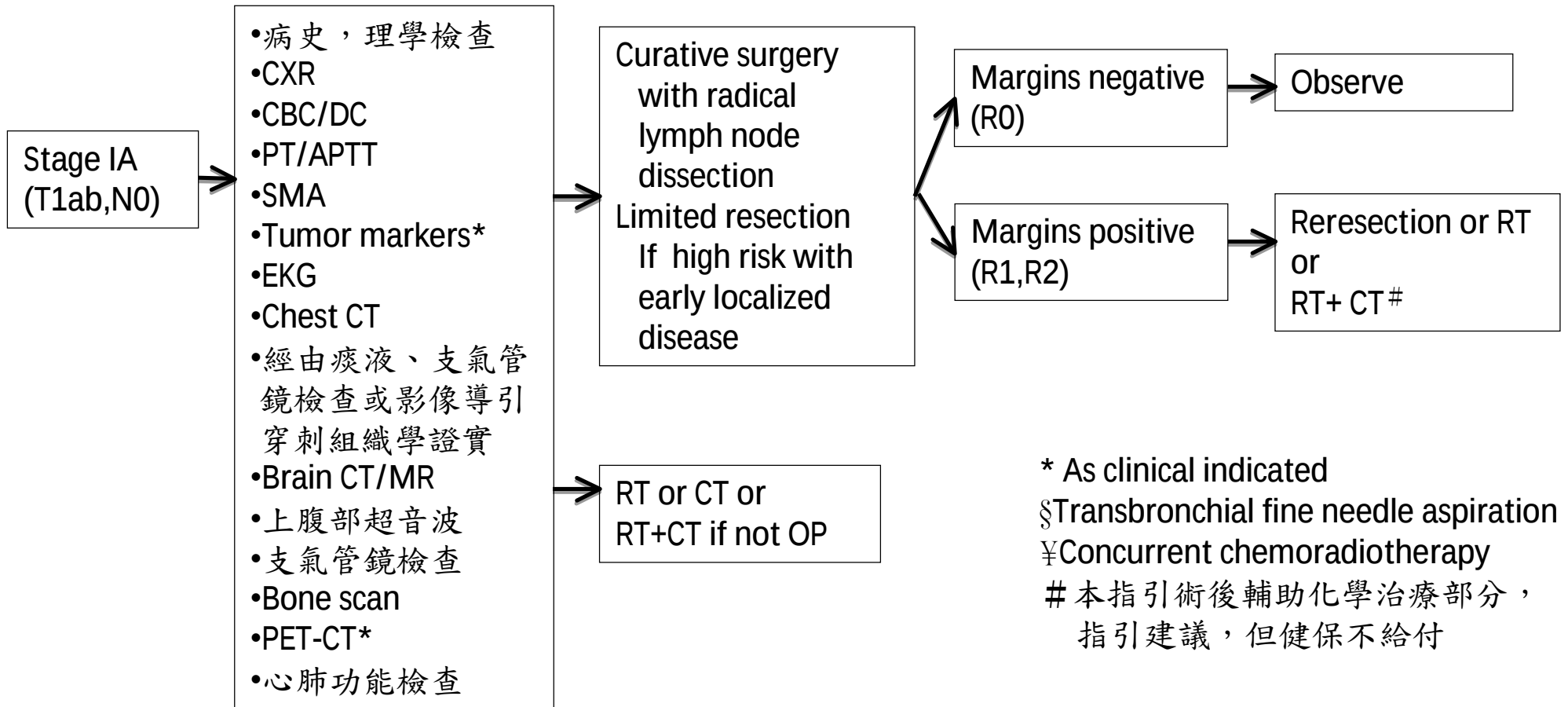
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診斷	評估	初步治療	手術發現	輔助治療
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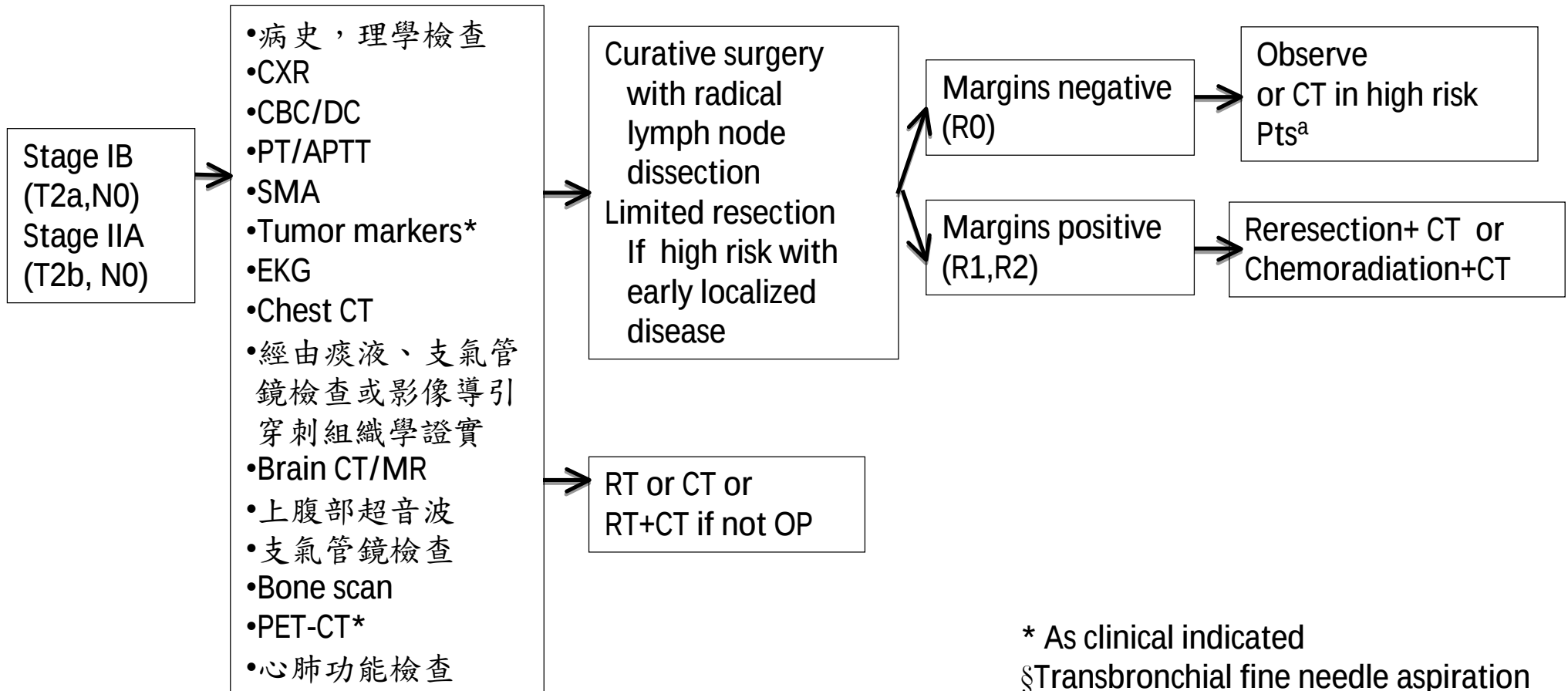
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診斷	評估	初步治療	手術發現	輔助治療
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* As clinical indicated

§Transbronchial fine needle aspiration

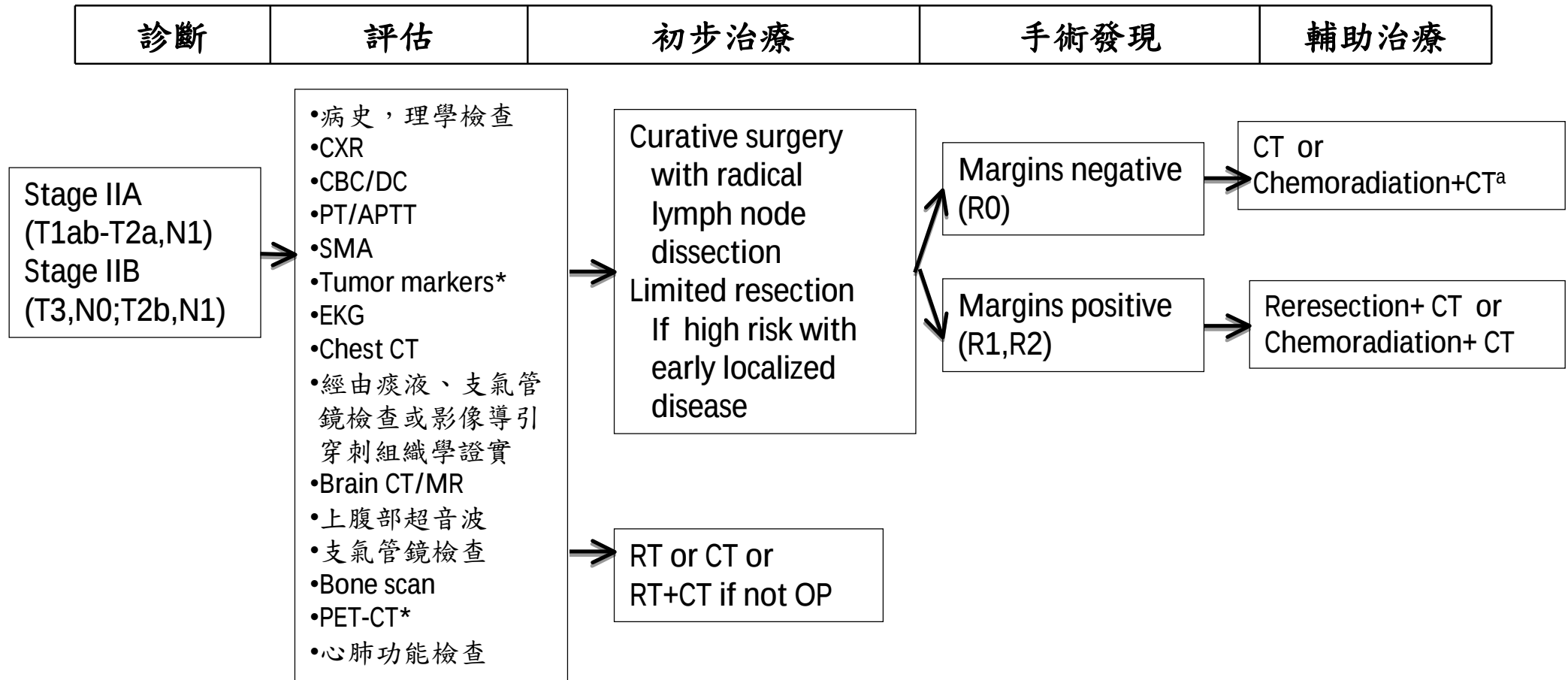
¥Concurrent chemoradiotherapy

^ahigh risk Pts are defined by poorly differentiated tumors, Vascular invasion, wedge resection, minimal margins, tumor > 4 cm, visceral pleural involvement, Nx

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^a Inadequate mediastinal LN dissection, extracapsular spread, multiple positive hilar nodes, close margins.

* As clinical indicated

§ Transbronchial fine needle aspiration

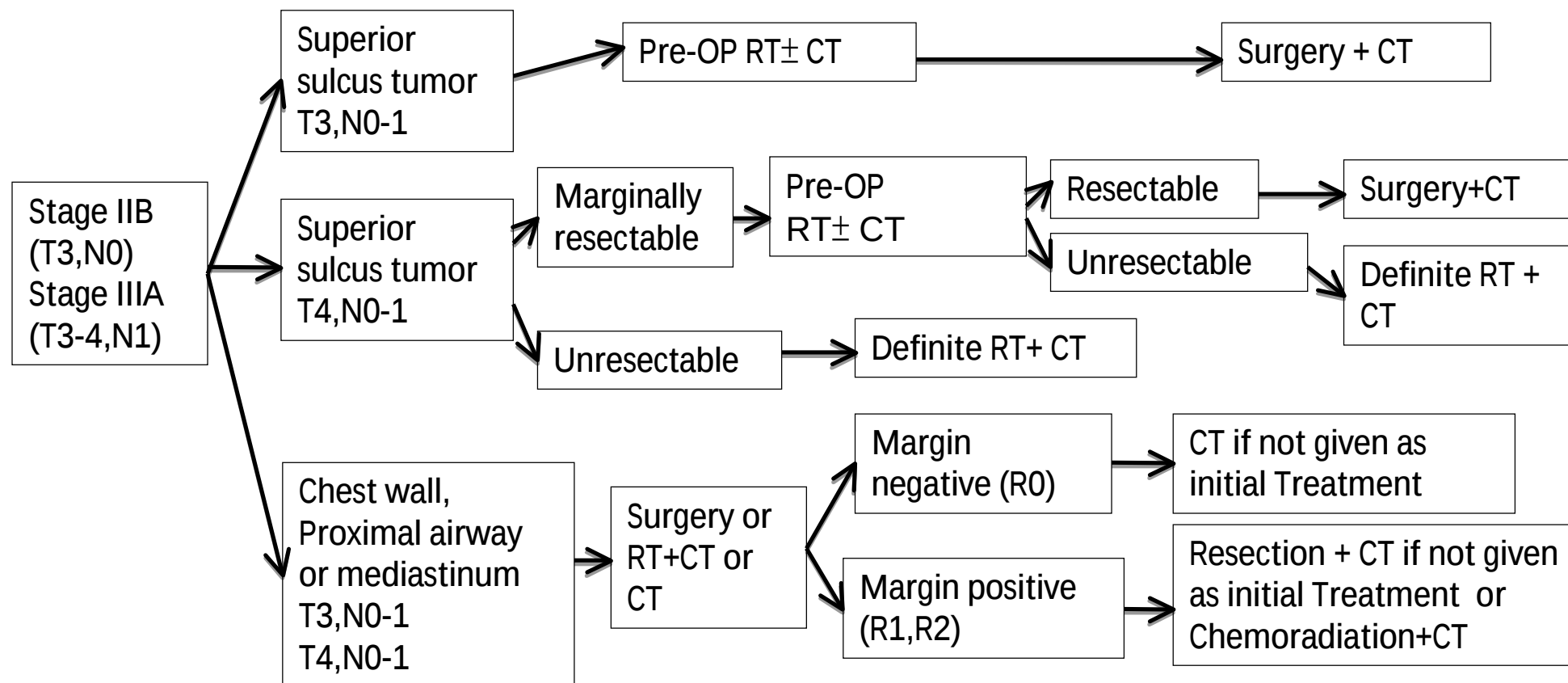
¥ Concurrent chemoradiotherapy

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診斷	臨床評估	初步治療	輔助治療
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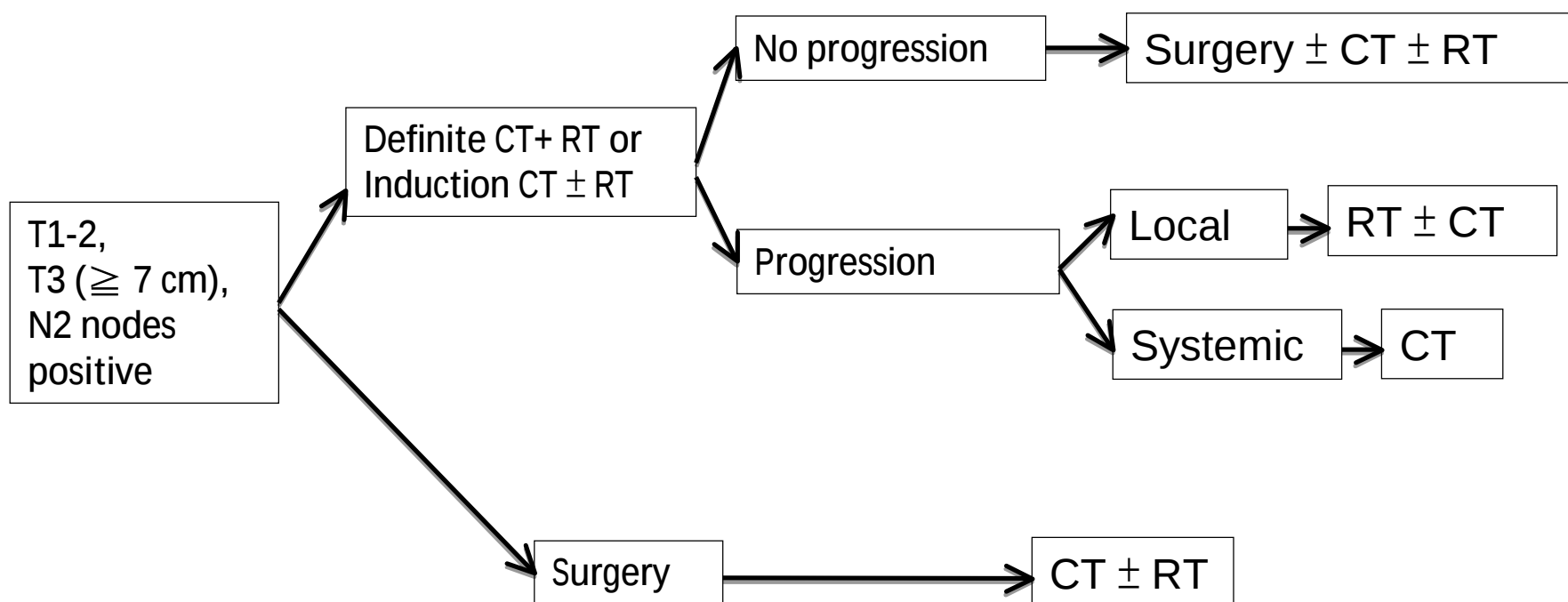
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診斷

初步治療

輔助治療

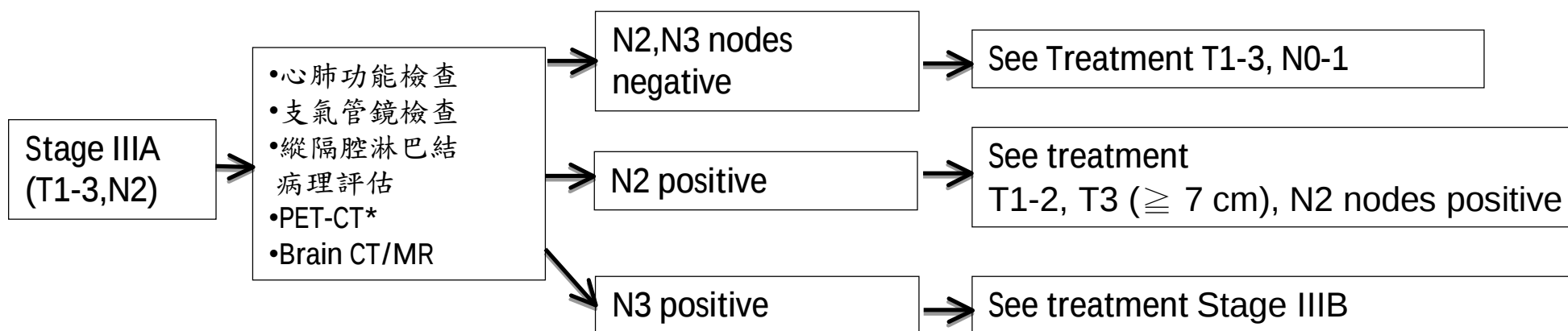


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診斷	評估	縱隔腔淋巴結發現 及可切除性	治療
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* As clinical indicated

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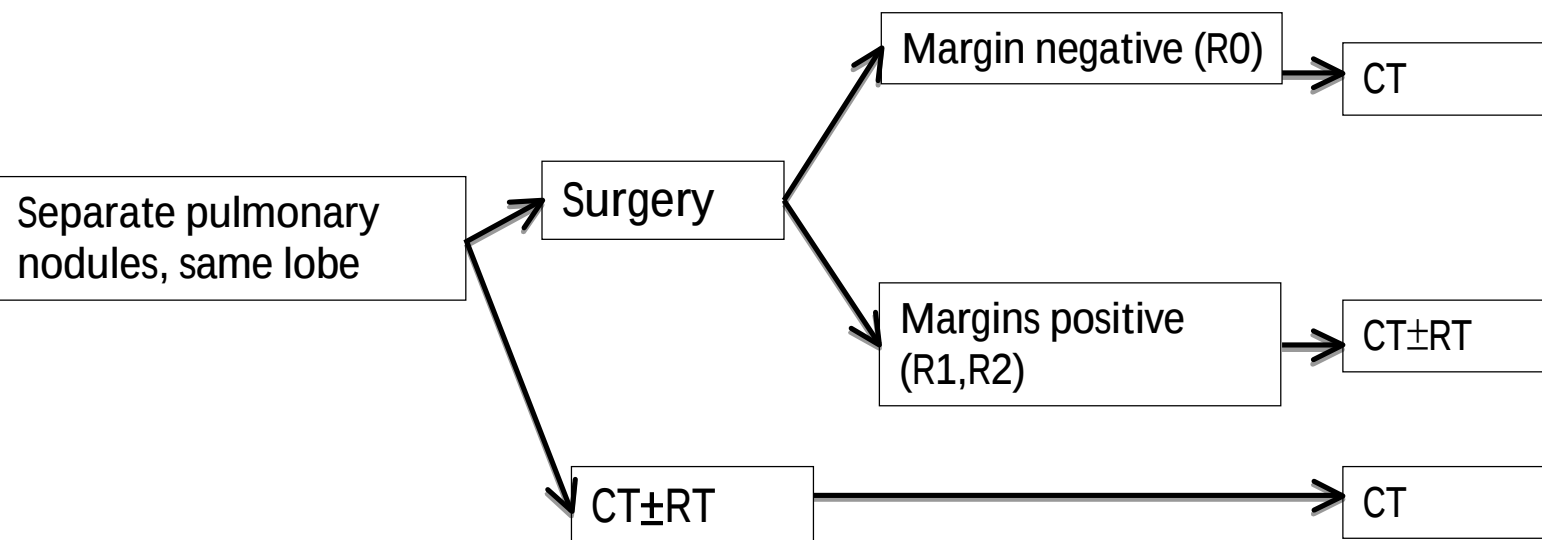
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診斷

初步治療

輔助治療



Stage IIIA (T4,N0-1)
Unresectable
(without effusion)

CT±RT

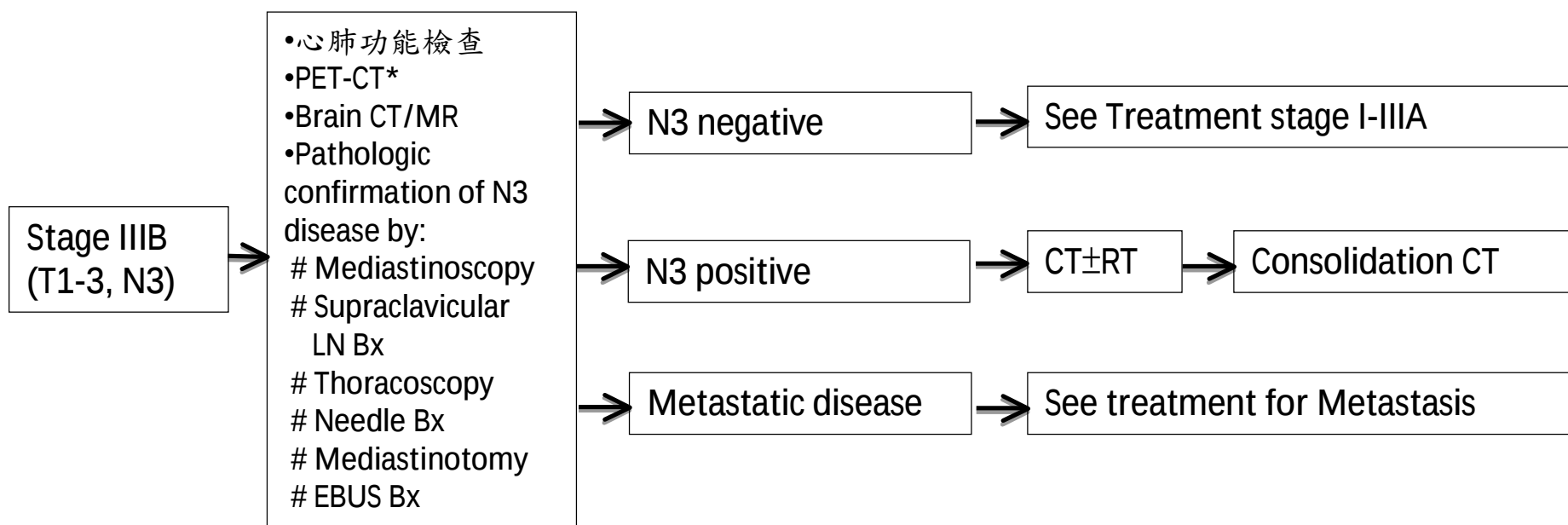
CT

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診斷	評估	縱隔腔淋巴結發現 及可切除性	治療
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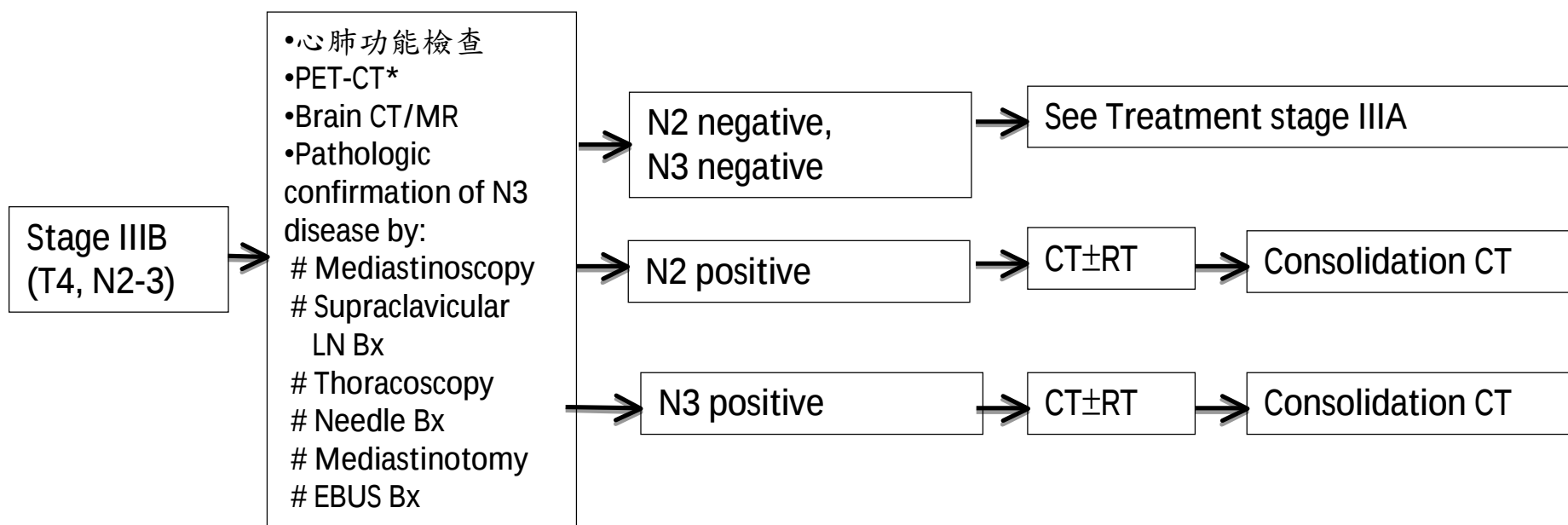
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診斷	評估	縱隔腔淋巴結發現 及可切除性	治療
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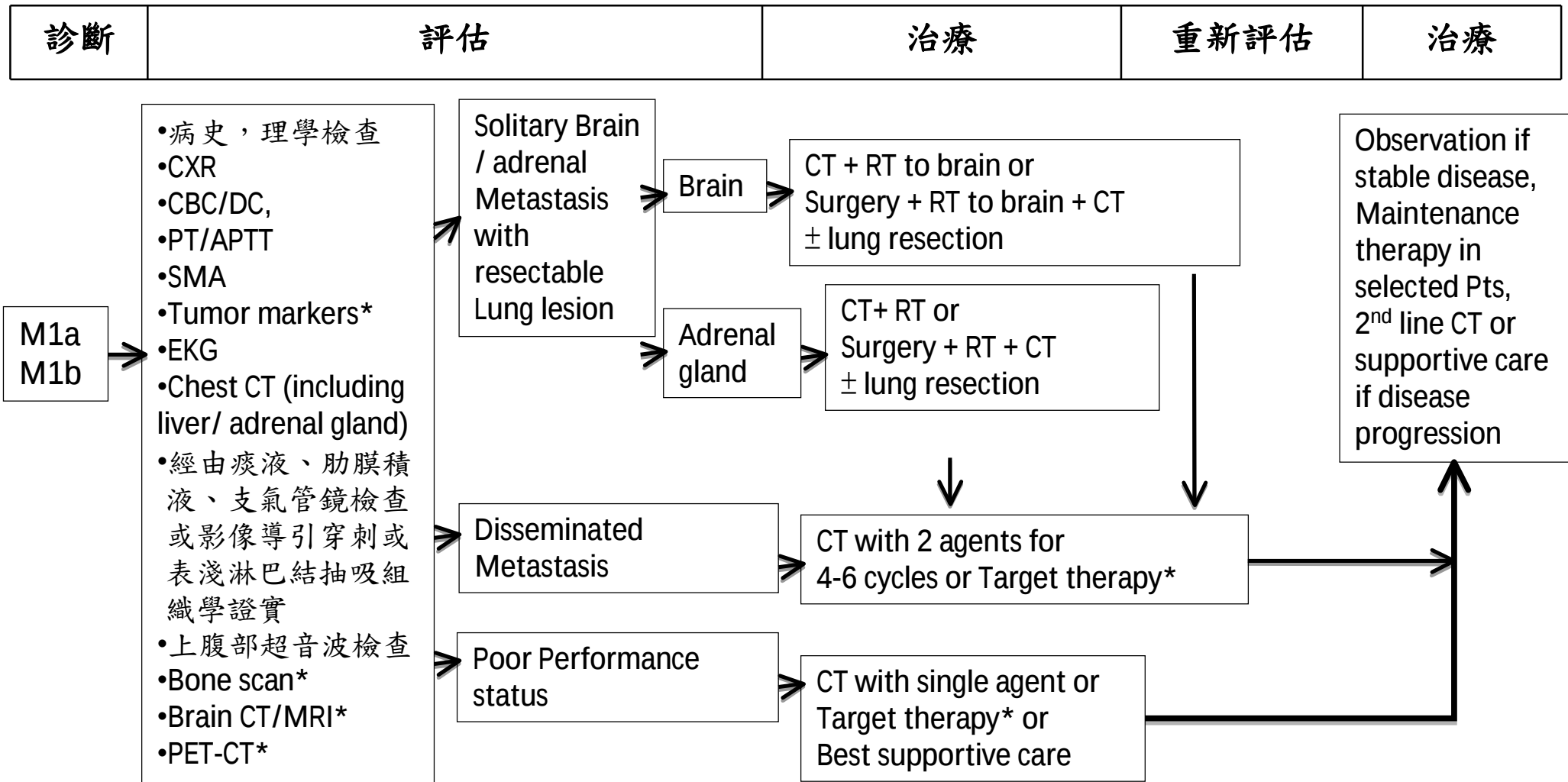


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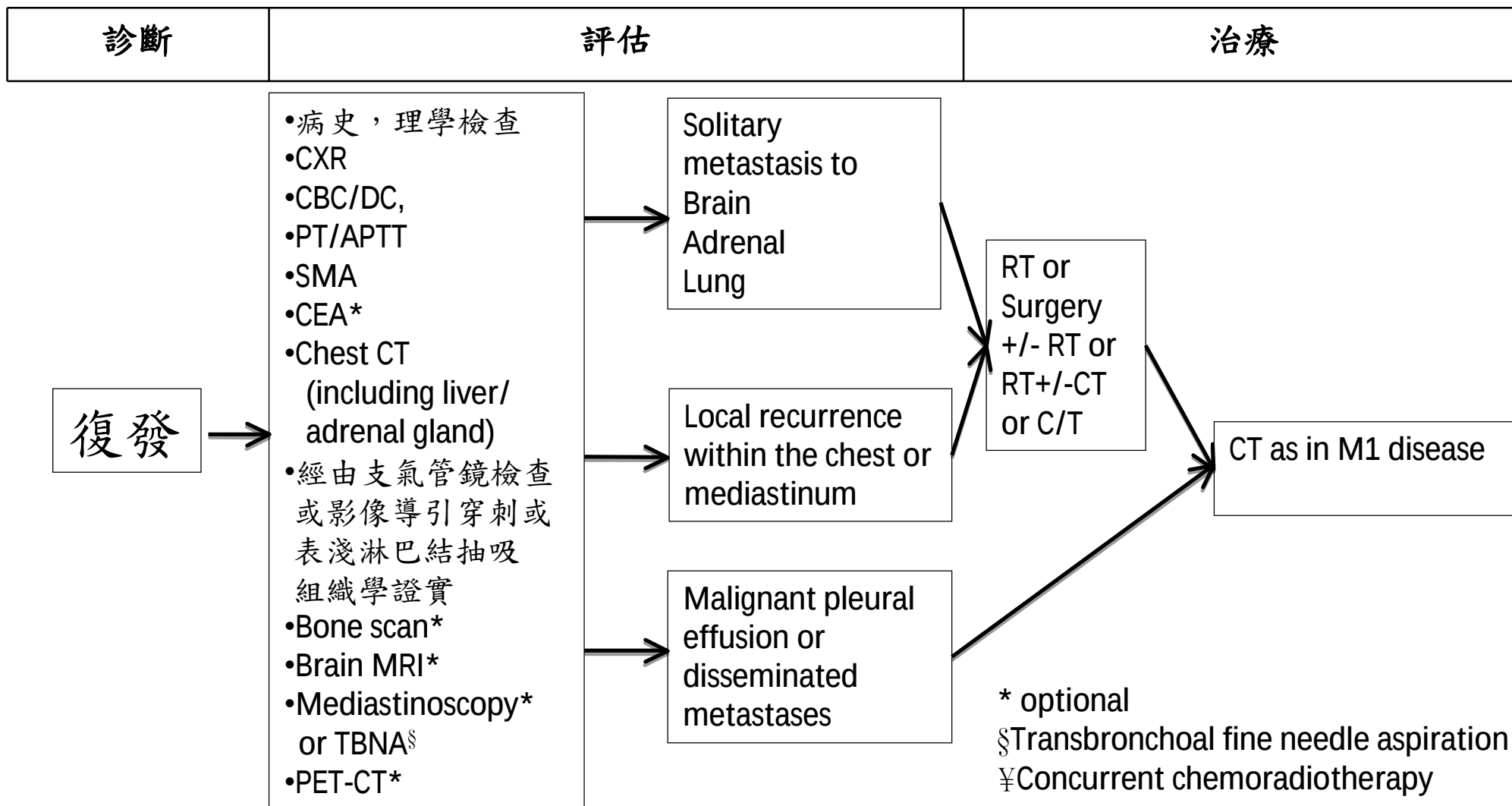


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一線化學治療處方

Published C/T Regimens	Schedule
Cisplatin 60-80 mg/m ² , IV, D15 Vinorelbine 25 mg/m ² , IV, D1,8,15	Q28 d x 4-6 cycles
Cisplatin 60-80 mg/m ² , IV, D15 Vinorelbine 60 mg/m ² , PO, D1,8,15	Q28 d x 4-6 cycles
Cisplatin 60-80 mg/m ² , IV, D15 Docetaxel 30 mg/m ² , IV, D1,8,15	Q28 d x 4-6 cycles
Cisplatin 60-80 mg/m ² , IV, D15 Paclitaxel 60 mg/m ² , IV, D1,8,15	Q28 d x 4-6 cycles
Cisplatin 60-80 mg/m ² , IV, D15 Gemcitabine 900-1000 mg/m ² , IV, D1,8,15	Q28 d x 4-6 cycles
Cisplatin 60-80 mg/m ² , IV, D1 Pemetrexed 500 mg/m ² , IV, D1	Q28 d x 4-6 cycles

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

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一線化學治療處方（年紀大，體能狀況不佳，器官功能不佳）

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
Docetaxel 30 mg/m ² , IV, D1,8,15	Q28 d x 4-6 cycles
Paclitaxel 60 mg/m ² , IV, D1,8,15	Q28 d x 4-6 cycles
Gemcitabine 900-1000 mg/m ² , IV, D1,8,15	Q28 d x 4-6 cycles
Vinorelbine 25 mg/ m ² IV, D1,8,15	Q28 d x 4-6 cycles
Vinorelbine 60 mg/m ² , PO, D1,8,15	Q28 d x 4-6 cycles

* 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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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
Docetaxel 30 mg/m ² , IV, D1,8,15	Q28 d x 4-6 cycles
Pemetrexed 500 mg/m ² , IV, D1	Q28 d x 4-6 cycles
Paclitaxel* 60 mg/m ² , IV, D1,8,15	Q28 d x 4-6 cycles
Gemcitabine* 900-1000 mg/m ² , IV, D1,8,15	Q28 d x 4-6 cycles
Vinorelbine* 25 mg/ m ² IV, D1,8,15	Q28 d x 4-6 cycles
Vinorelbine* 60 mg/m ² , PO, D1,8,15	Q28 d x 4-6 cycles

* Alternative option

* 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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術後輔助化學治療處方

Published C/T Regimens	Schedule
Cisplatin 60-80 mg/m ² , IV, D15 Vinorelbine 25 mg/m ² , IV, D1,8,15	Q28 d x 4 cycles
Cisplatin 60-80 mg/m ² , IV, D15 Docetaxel 30 mg/m ² , IV, D1,8,15	Q28 d x 4 cycles
Cisplatin 60-80 mg/m ² , IV, D15 Paclitaxel 60 mg/m ² , IV, D1,8,15	Q28 d x 4 cycles
Cisplatin 60-80 mg/m ² , IV, D15. Gemcitabine 900-1000 mg/m ² , IV, D1,8,15.	Q28 d x 4 cycles
Cisplatin 60-80 mg/m ² , IV, D1 Pemetrexed 500 mg/m ² , IV, D1 *	Q28 d x 4 cycles
Cisplatin 60-80 mg/m ² , IV, D1 Etoposide 60-80 mg/m ² D1,2,3	Q28 d x 4 cycles
Tagafur/Uracil 300-500 mg PO QD *	Maintenance for 2 years

* For adenocarcinoma and large cell carcinoma

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

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術前新輔助化學治療處方

Published C/T Regimens	Schedule
Cisplatin 60-80 mg/m ² , IV, D15 Vinorelbine 25 mg/m ² , IV, D1,8,15	Q28 d x 4-6 cycles
Cisplatin 60-80 mg/m ² , IV, D8 Vinorelbine 60 mg/m ² , PO, D1,8,15	Q28 d x 4-6 cycles
Cisplatin 60-80 mg/m ² , IV, D15 Docetaxel 30 mg/m ² , IV, D1,8,15	Q28 d x 4-6 cycles
Cisplatin 60-80 mg/m ² , IV, D15 Paclitaxel 60 mg/m ² , IV, D1,8,15	Q28 d x 4-6 cycles
Cisplatin 60-80 mg/m ² , IV, D15 Gemcitabine 900-1000 mg/m ² , IV, D1,8,15	Q28 d x 4-6 cycles
Cisplatin 60-80 mg/m ² , IV, D1 Pemetrexed 500 mg/m ² , IV, D1	Q28 d x 4-6 cycles

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

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同步化學放射線治療化學治療處方

Published C/T Regimens	Schedule
Cisplatin 50-70 mg/m ² , IV, D15 Vinorelbine 15-20 mg/m ² , IV, D1,8,15	Q28 d
Cisplatin 50-70 mg/m ² , IV, D15 Docetaxel 20-25 mg/m ² , IV, D1,8,15	Q28 d
Cisplatin 50-70 mg/m ² , IV, D15 Paclitaxel 40-50 mg/m ² , IV, D1,8,15	Q28 d
Cisplatin 50-70 mg/m ² , IV, D1 Pemetrexed 400-500 mg/m ² , IV, D1	Q28 d

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

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放射線治療 Conventionally Fractionated Radiation Therapy 建議劑量

Treatment Type	Total Dose	Fraction Size	Treatment Duration
Preoperative	45-50 Gy	1.8-2 Gy	4-5 wks
Postoperative			
*Negative margins	50 Gy	1.8-2 Gy	4-5 wks
*Extracapsular nodal extension or microscopic positive margins	54-60 Gy	1.8-2 Gy	5-6 wks
*Gross residual tumors	60-70 Gy	1.8-2 Gy	6-7 wks
Definitive			
*Radiation alone or sequentital chemoradiation	64-70 Gy	2 Gy	6-7.5 wks
*Concurrent chemotherapy	60-70 Gy	2 Gy	6-7 wks
Palliative			
*Obstructive disease (SVC syndrome or obstructive pneumonia)	30-45 Gy	3 Gy	2-3 wks
*Bone metastasis with soft tissue mass	30 Gy	3 Gy	2 wks
*Bone metastasis without soft tissue mass	8 Gy	8 Gy	1 day

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, Tsiafaki 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 chemonative 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. Silvestri G, Pritchard R, Welch HG: Preferences for chemotherapy in patients with advanced ASCO Stage IV Non–Small-Cell Lung Cancer Guideline Update © 2009 by American Society of Clinical Oncology 25 non-small cell lung cancer: Descriptive study based on scripted interviews. *BMJ* 317:771-775, 1998