Small Cell Lung Cancer (SCLC)

Note: Consider Clinical Trials as treatment options for eligible patients.

INITIAL EVALUATION

- Pathology consistent with SCLC
- History and physical
- Laboratory studies to include hematological and full chemistry panels
- FDG PET/CT and CT chest with IV contrast
  - If FDG PET/CT not available: nuclear medicine bone scan and CT chest, abdomen, and pelvis with IV contrast
- MRI brain with IV contrast (preferred) or CT head with IV contrast
- MRI spine, lumbar puncture and bone marrow aspirate/biopsy as indicated
- Pulmonary function tests
- Lifestyle risk assessment[1]
- Molecular profiling (for never smokers)

STAGE

Limited Stage
AJCC Stage I-III[2], see Page 2

Extensive Stage
AJCC Stage IV[3], see Page 3

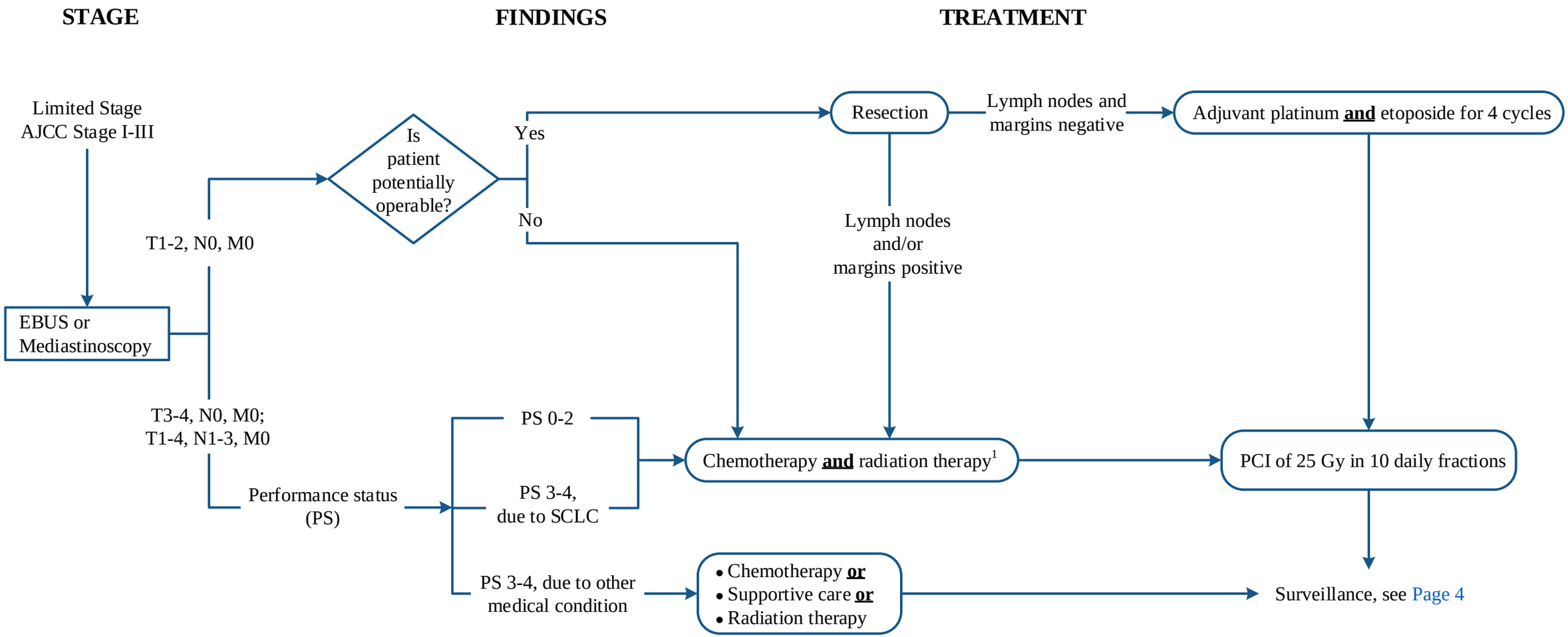
AJCC = American Joint Committee on Cancer

[1] See Physical Activity, Nutrition, and Tobacco Cessation algorithms; ongoing reassessment of lifestyle risks should be a part of routine clinical practice
[2] Limited stage: Stage I-III (T any, N any, M0) per AJCC 8th edition or disease confined to the ipsilateral hemithorax within a single radiation port
[3] Extensive stage: Stage IV (T any, N any, M 1a/b) per AJCC 8th edition or disease beyond ipsilateral hemithorax or malignant pleural effusion or obvious metastatic disease

Department of Clinical Effectiveness V11
Approved by The Executive Committee of the Medical Staff on 10/20/2020

Small Cell Lung Cancer (SCLC)

Note: Consider Clinical Trials as treatment options for eligible patients.



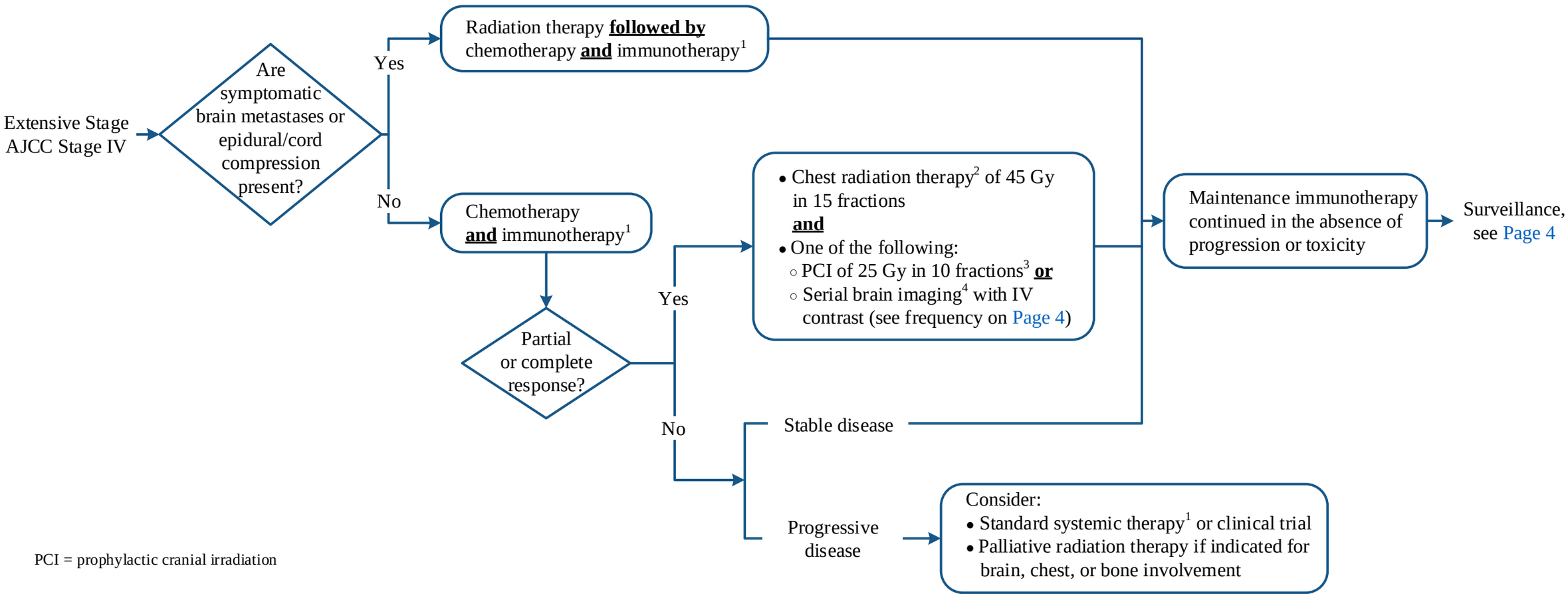
EBUS = endobronchial ultrasound
PCI = prophylactic cranial irradiation

[1] Start radiation therapy within the first 2 cycles of chemotherapy

Small Cell Lung Cancer (SCLC)

Note: Consider Clinical Trials as treatment options for eligible patients.

STAGE **TREATMENT**



PCI = prophylactic cranial irradiation

[1] Refer to Principles of Systemic Therapy on Page 5
[2] For selected patients with residual thoracic disease and low-bulk extrathoracic metastatic disease that has responded to systemic therapy
[3] Consider holding immunotherapy during radiation
[4] MRI brain preferred over CT as it is more sensitive in identifying brain metastases

Small Cell Lung Cancer (SCLC)

Note: Consider Clinical Trials as treatment options for eligible patients.

SURVEILLANCE[1]

- History and physical
- CT chest, abdomen, and pelvis with IV contrast and FDG PET/CT as clinically indicated
- Imaging of involved sites every 2-3 months for 2 years, then every 6 months for 3 years, then yearly
- MRI brain[2] with IV contrast recommended with other surveillance imaging as above, for extensive stage patients and for limited stage who did not get PCI

Relapse?

SALVAGE/PALLIATION

Yes

- Clinical trial (preferred)
- Salvage chemotherapy **or** immunotherapy (see Page 5 for Principles of Systemic Therapy)
- Palliative symptom management including localized radiation therapy

No

Continue surveillance[1]

[1] For patients already on maintenance immunotherapy, continue in the absence of progression or toxicity
[2] MRI brain preferred over CT as it is more sensitive in identifying brain metastases

Note: Consider Clinical Trials as treatment options for eligible patients.

PRINCIPLES OF SYSTEMIC THERAPY

First-line therapy

Acceptable regimens for limited stage disease (maximum of 4-6 cycles) include:

- Cisplatin 60 mg/m^2 IV on Day 1 and etoposide 120 mg/m^2 IV on Days 1, 2, 3
- Cisplatin 75 mg/m^2 IV on Day 1 and etoposide 100 mg/m^2 IV on Days 1, 2, 3
- Carboplatin AUC 5-6 IV on Day 1 and etoposide 100 mg/m^2 IV on Days 1, 2, 3
- During systemic therapy plus radiation therapy, cisplatin/etoposide is recommended (category 1)

Acceptable regimens for extensive stage disease include:

- Carboplatin AUC 5 IV on Day 1 and etoposide 100 mg/m^2 IV on Days 1, 2, 3 and atezolizumab 1,200 mg Day 1 every 21 days for 4 cycles
  - Followed by maintenance atezolizumab 1,200 mg Day 1 every 21 days
- Carboplatin AUC 5-6 IV on Day 1 and etoposide 100 mg/m^2 IV on Days 1, 2, 3 and durvalumab 1,500 mg Day 1 every 21 days for 4 cycles
  - Followed by maintenance durvalumab 1,500 mg Day 1 every 28 days
- Cisplatin 75 mg/m^2 IV on Day 1 and etoposide 100 mg/m^2 IV on Days 1, 2, 3 and durvalumab 1,500 mg Day 1 every 21 days for 4 cycles
  - Followed by maintenance durvalumab 1,500 mg Day 1 every 28 days

Second-line or greater therapy

- Clinical trial (preferred)
- If relapse occurs > 6 months after completion of first-line therapy: original regimen
  - For patients who relapsed after 6 months, while on atezolizumab or durvalumab maintenance therapy, consider re-treatment with platinum plus etoposide alone (without atezolizumab or durvalumab)
- If relapse occurs ≤ 6 months and performance status 0-2:
  - Lurbinectedin
  - Topotecan PO or IV
  - Paclitaxel
  - Docetaxel
  - Irinotecan
  - Temozolomide PO
  - Vinorelbine
  - Etoposide PO
  - Gemcitabine
  - If immunotherapy naïve
    - Nivolumab plus ipilimumab
    - Pembrolizumab

Growth factor use with systemic therapy and other considerations

- The use of myeloid growth factors is not recommended during concurrent systemic therapy plus radiation therapy (category 1 or not using GM-CSF)
- Outside of radiation therapy, consider chemotherapy dose reduction or growth factor support for patients with performance status of 2 or age ≥ 70 years

Note: Consider Clinical Trials as treatment options for eligible patients.

PRINCIPLES OF RADIATION THERAPY

Radiation therapy for Limited Stage disease

- Radiation therapy should be given 1.5 Gy twice a day (with at least 6 hours between fractions) to a total dose of 45 Gy. In circumstances where twice daily fractionation is not feasible, an acceptable alternate schedule is 1.8-2.0 Gy/day to a dose of 60-70 Gy.
- Radiation therapy should be administered concurrently with chemotherapy, ideally beginning during cycle 1 of chemotherapy
- Radiation therapy should be delivered to original tumor volume unless there is marked risk of radiation pneumonitis; decrease field as tumor shrinks
- In patients receiving radiation therapy or chemoradiation with curative intent, treatment interruptions or dose reductions for temporary and manageable toxicities, such as esophagitis and myelosuppression, should be avoided. Careful patient monitoring and aggressive supportive care are preferable to treatment breaks in potentially curable patients. Patients should be evaluated at least once per every 5 fractions to monitor weight changes and toxicity.
- 45 Gy in 30 fractions over 3 weeks would not be recommended with concurrent chemotherapy on Day 1, if the DVH shows V20 more than 35% of target lesion. If the GTV is too large to meet dose volume constraints, give one cycle of chemotherapy or go daily fraction of radiation and cone down of the GTV after re-simulation after 2-3 weeks treatment. This will apply for patients who have FEV1 or DLCO less than 30% of predicted value.
- Elective nodal radiation therapy is not recommended
- Appropriate schedule for PCI is 25 Gy in 10 fractions

DVH = dose volume histogram
GTV = gross tumor volume

SUGGESTED READINGS

National Comprehensive Cancer Network. (2020). *Small Cell Lung Cancer* (NCCN Guideline Version 3.2020). Retrieved from https://www.nccn.org/professionals/physician_gls/pdf/sclc.pdf

Prophylactic Cranial Irradiation (PCI)

PCI in Limited Stage SCLC

Le Péchoux, C., Dunant, A., Senan, S., Wolfson, A., Quoix, E., Faivre-Finn, C., . . . Laplanche, A. (2009). Standard-dose versus higher-dose prophylactic cranial irradiation (PCI) in patients with limited-stage small-cell lung cancer in complete remission after chemotherapy and thoracic radiotherapy (PCI 99-01, EORTC 22003-08004, RTOG 0212, and IFCT 99-01): A randomised clinical trial. *Lancet Oncology, 10*(5), 467-474. https://doi.org/10.1016/S1470-2045(09)70101-9

PCI in Extensive Stage SCLC

Slotman, B., Faivre-Finn, C., Kramer, G., Rankin, E., Snee, M., Hatton, M., . . . Senan, S. (2007). Prophylactic cranial irradiation in extensive small-cell lung cancer. *The New England Journal of Medicine, 357*(7), 664-672. https://doi.org/10.1056/NEJMoa071780

Takahashi, T., Yamanaka, T., Seto, T., Harada, H., Nokihara, H., Saka, H., . . .Yamamoto, N. (2017). Prophylactic cranial irradiation versus observation in patients with extensive-disease small-cell lung cancer: A multicentre, randomised, open-label, phase 3 trial. *The Lancet Oncology, 18*(5), 663-671. https://doi.org/10.1016/S1470-2045(17)30230-9

Limited Stage SCLC

Faivre-Finn, C., Snee, M., Ashcroft, L., Appel, W., Barlesi, F., Bhatnagar, A., . . . Blackhall, F. (2017). Concurrent once-daily versus twice-daily chemoradiotherapy in patients with limited-stage small-cell lung cancer (CONVERT): An open-label, phase 3, randomised, superiority trial. *The Lancet Oncology, 18*(8), 1116-1125. https://doi.org/10.1016/S1470-2045(17)30318-2

Extensive Stage SCLC

Horn, L., Mansfield, A. S., Szczęsna, A., Havel, L., Krzakowski, M., Hochmair, M., . . . Liu, S. (2018). First-line atezolizumab plus chemotherapy in extensive-stage small-cell lung cancer. *The New England Journal of Medicine, 379*(23), 2220-2229. https://doi.org/10.1056/NEJMoa1809064

Paz-Ares, L., Dvorkin, M., Chen, Y., Reinmuth, N., Hotta, K., Trukhin, D., . . . Goldman J. (2019). Durvalumab plus platinum-etoposide versus platinum-etoposide in first-line treatment of extensive-stage small-cell lung cancer (CASPIAN): A randomised, controlled, open-label, phase 3 trial. *The Lancet, 394*(10212), 1929-1939. https://doi.org/10.1016/S0140-6736(19)32222-6

Slotman, B. J., van Tinteren, H., Praag, J. O., Knegjens, J. L., El Sharouni, S., Hatton, M., . . . Senan, S. (2015). Use of thoracic radiotherapy for extensive stage small-cell lung cancer: A phase 3 randomised controlled trial. *The Lancet*, *385*(9962), 36-42. https://doi.org/10.1016/S0140-6736(14)61085-0

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