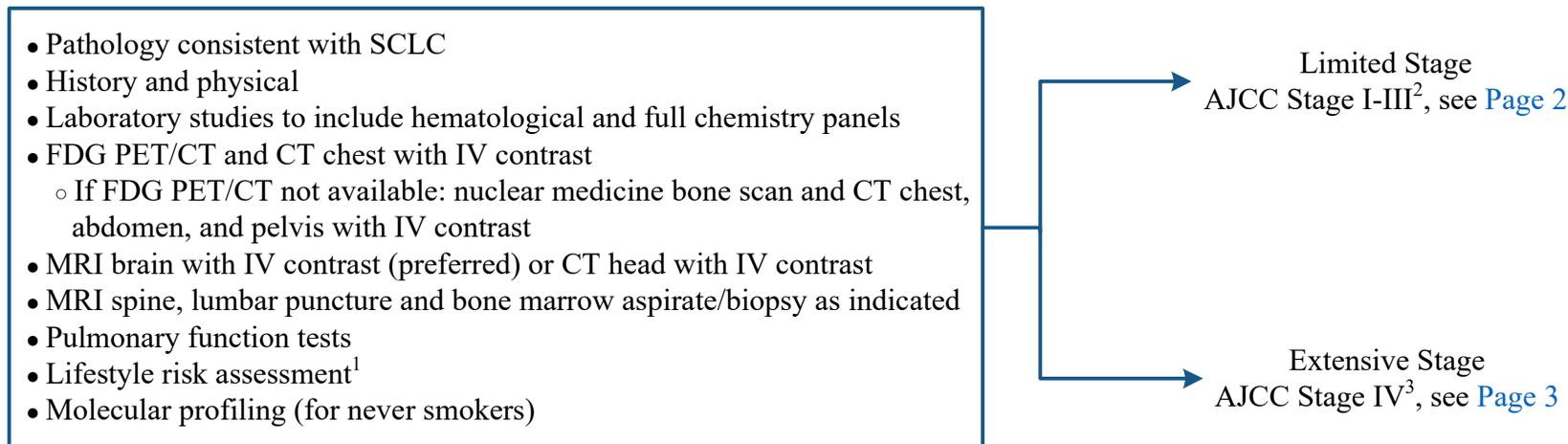


Disclaimer: This algorithm has been developed for MD Anderson using a multidisciplinary approach considering circumstances particular to MD Anderson's specific patient population, services and structure, and clinical information. This is not intended to replace the independent medical or professional judgment of physicians or other health care providers in the context of individual clinical circumstances to determine a patient's care. This algorithm should not be used to treat pregnant women.

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

INITIAL EVALUATION

STAGE



AJCC = American Joint Committee on Cancer

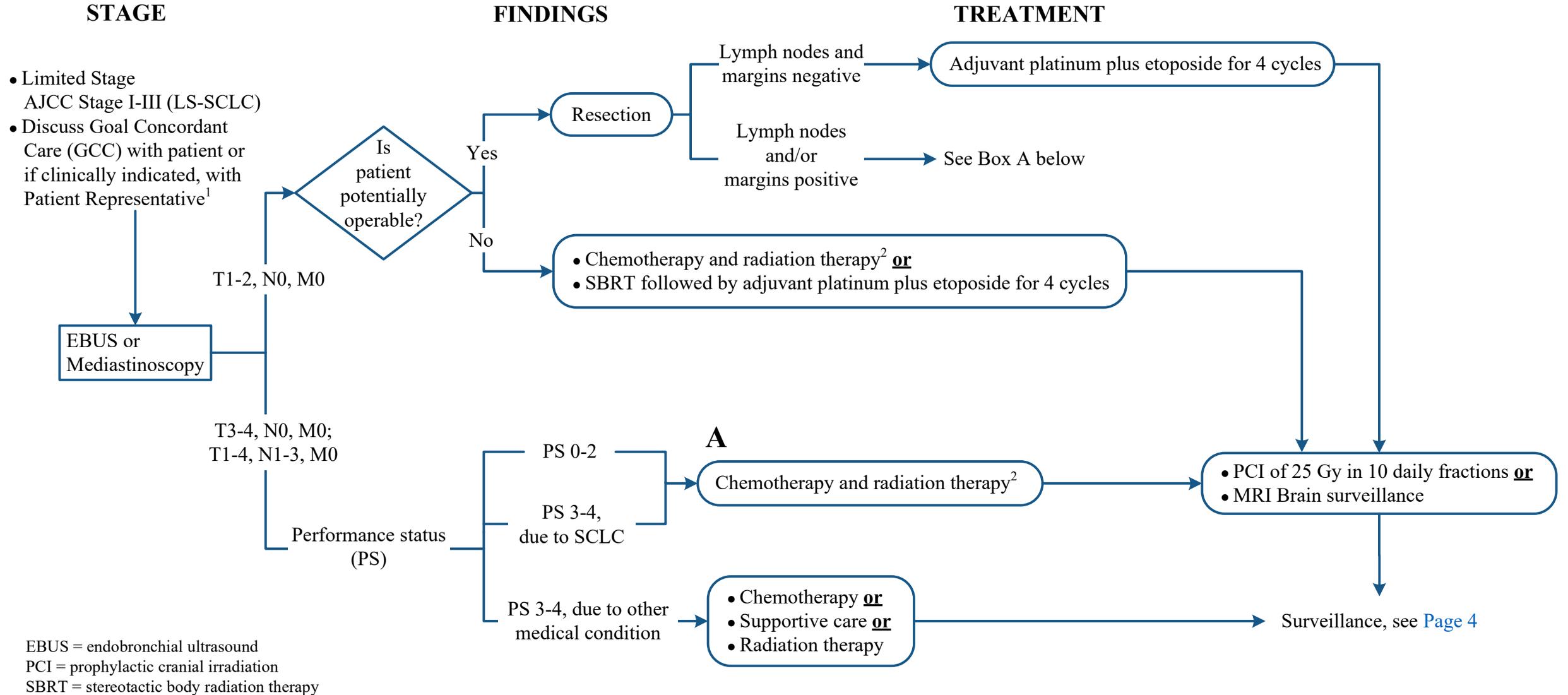
¹ See [Physical Activity](#), [Nutrition](#), and [Tobacco Cessation](#) algorithms; ongoing reassessment of lifestyle risks should be a part of routine clinical practice

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

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



¹ GCC should be initiated by the Primary Oncologist. If Primary Oncologist is unavailable, Primary Team/Attending Physician to initiate GCC discussion and notify Primary Oncologist. Patients, or if clinically indicated, the Patient Representative should be informed of therapeutic and/or palliative options. GCC discussion should be consistent, timely, and re-evaluated as clinically indicated. The Advance Care Planning (ACP) note should be used to document GCC discussion. Refer to [GCC home page](#) (for internal use only).

² Start radiation therapy within the first 2 cycles of chemotherapy

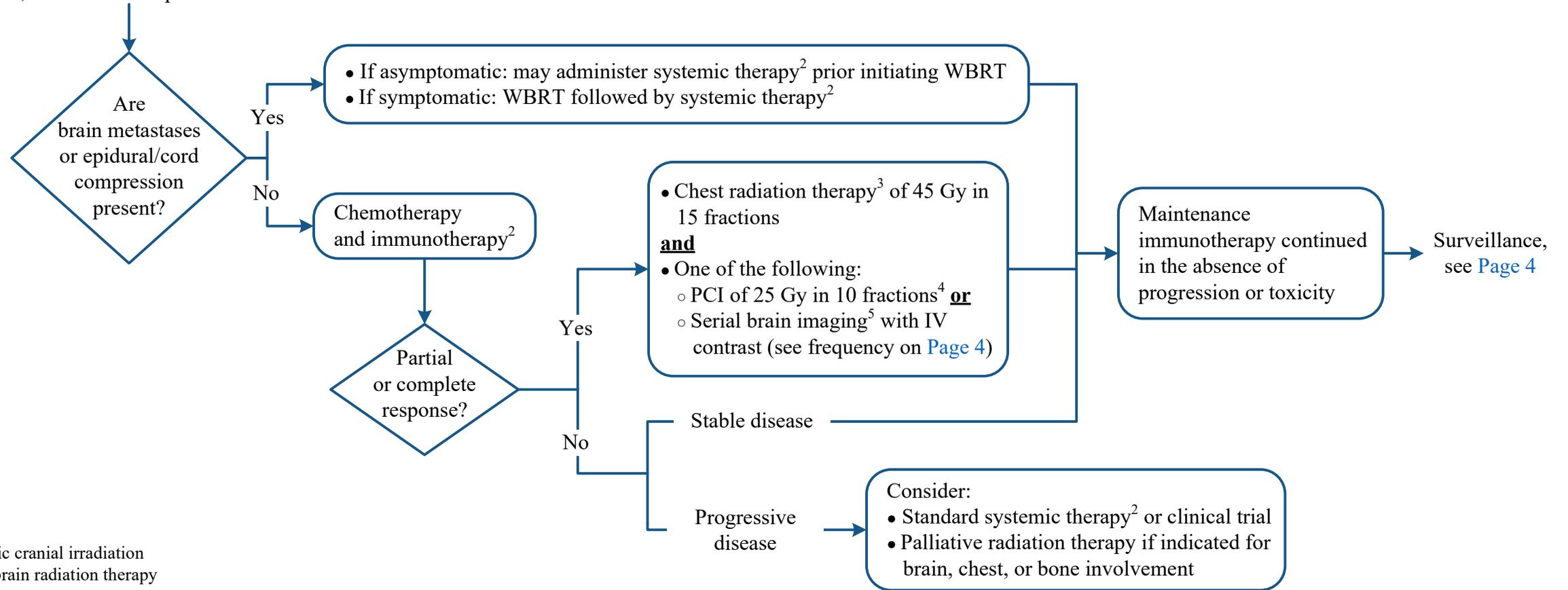
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Note: Consider Clinical Trials as treatment options for eligible patients.

STAGE

- Extensive Stage AJCC Stage IV (ES-SCLC)
- Discuss GCC with patient or if clinically indicated, with Patient Representative¹

TREATMENT



PCI = prophylactic cranial irradiation
 WBRT = whole brain radiation therapy

¹ GCC should be initiated by the Primary Oncologist. If Primary Oncologist is unavailable, Primary Team/Attending Physician to initiate GCC discussion and notify Primary Oncologist. Patients, or if clinically indicated, the Patient Representative should be informed of therapeutic and/or palliative options. GCC discussion should be consistent, timely, and re-evaluated as clinically indicated. The Advance Care Planning (ACP) note should be used to document GCC discussion. Refer to [GCC home page](#) (for internal use only).

² Refer to Principles of Systemic Therapy on [Page 5](#)

³ For selected patients with residual thoracic disease and low-bulk extrathoracic metastatic disease that has responded to systemic therapy

⁴ The role of PCI is controversial in ES-SCLC (without brain metastasis) and is an option to selected patients. Consider holding immunotherapy during radiation.

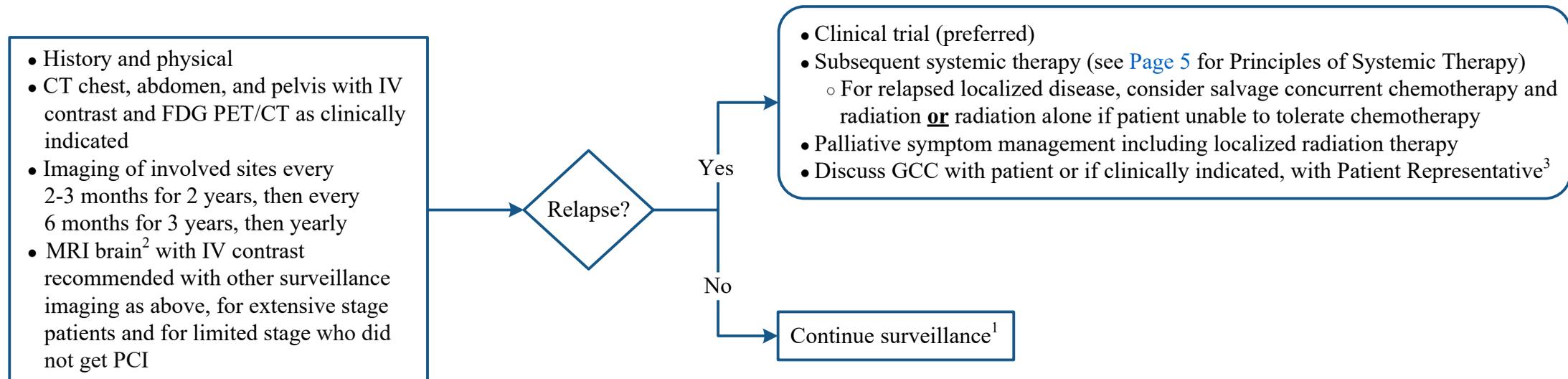
⁵ MRI brain preferred over CT as it is more sensitive in identifying brain metastases

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SURVEILLANCE¹

SALVAGE/PALLIATION



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

³ GCC should be initiated by the Primary Oncologist. If Primary Oncologist is unavailable, Primary Team/Attending Physician to initiate GCC discussion and notify Primary Oncologist. Patients, or if clinically indicated, the Patient Representative should be informed of therapeutic and/or palliative options. GCC discussion should be consistent, timely, and re-evaluated as clinically indicated. The Advance Care Planning (ACP) note should be used to document GCC discussion. Refer to [GCC home page](#) (for internal use only).

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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/m² IV on Day 1 and etoposide 120 mg/m² IV on Days 1, 2, 3
- Cisplatin 75 mg/m² IV on Day 1 and etoposide 100 mg/m² IV on Days 1, 2, 3
- Cisplatin 25 mg/m² IV on Days 1, 2, 3 and etoposide 100 mg/m² Days 1, 2, 3
- Carboplatin AUC 5-6 IV on Day 1 and etoposide 100 mg/m² 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/m² 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 or atezolizumab 1,680 mg Day 1 every 28 days
- Carboplatin AUC 5-6 IV on Day 1 and etoposide 100 mg/m² 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/m² IV on Day 1 and etoposide 100 mg/m² 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
 - Temozolomide PO
 - Vinorelbine
 - Etoposide PO
 - Gemcitabine
 - Irinotecan
 - If immunotherapy naïve
 - Nivolumab^a with or without ipilimumab
 - Pembrolizumab^a

Growth factor use with systemic therapy and other related considerations

- The use of myeloid growth factors is not recommended during concurrent systemic therapy plus radiation therapy
- Outside of radiation therapy, consider chemotherapy dose reduction or growth factor support for patients with performance status of 2 or age ≥ 70 years
- In patients with ES-SCLC, trilaciclib may be used as prophylactic option for chemotherapy-induced myelosuppression prior to receiving platinum/etoposide or topotecan on days of chemotherapy

^a Indication for SCLC has been withdrawn from the U.S. market, off-label use can be considered on a case-by-case basis

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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

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SUGGESTED READINGS

National Comprehensive Cancer Network. (2022). *Small Cell Lung Cancer* (NCCN Guideline Version 3.2023). 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. *The Lancet Oncology*, *10*(5), 467-474. [https://doi.org/10.1016/S1470-2045\(09\)70101-9](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](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](https://doi.org/10.1016/S1470-2045(17)30318-2)

Extensive Stage SCLC

Hart, L. L., Ferrarotto, R., Andric, Z. G., Beck, J. T., Subramanian, J., Radosavljevic, D. Z., . . . Hussein, M. A. (2021). Myelopreservation with trilaciclib in patients receiving topotecan for small cell lung cancer: Results from a randomized, double-blind, placebo-controlled phase II study. *Advances in Therapy*, *38*(1), 350-365. <https://doi.org/10.1007/s12325-020-01538-0>

Horn, L., Mansfield, A. S., Szcżęsna, A., Havel, L., Krzakowski, M., Hochmair, M. J., . . . Liu, S. V. (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. W. (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](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. Y., 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](https://doi.org/10.1016/S0140-6736(14)61085-0)

Trigo, J., Subbiah, V., Besse, B., Moreno, V., López, R., Sala, M. A., . . . Paz-Ares, L. (2020). Lurbinectedin as second-line treatment for patients with small-cell lung cancer: A single-arm, open-label, phase 2 basket trial. *The Lancet Oncology*, *21*(5), 645-654. [https://doi.org/10.1016/S1470-2045\(20\)30068-1](https://doi.org/10.1016/S1470-2045(20)30068-1)

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DEVELOPMENT CREDITS

This practice algorithm is based on majority expert opinion of the Thoracic Oncology Center providers at the University of Texas MD Anderson Cancer Center. It was developed using a multidisciplinary approach that included input from the following:

Core Development Team Leads

Joe Chang, MD, PhD (Radiation Oncology)

Carl Gay, MD, PhD (Thoracic/Head & Neck Medical Oncology)

Workgroup Members

George Blumenschein, MD (Thoracic/Head & Neck Medical Oncology)

Lauren Byers, MD (Thoracic/Head & Neck Medical Oncology)

Brett Carter, MD (Thoracic Imaging)

Wendy Garcia, BS[♦]

John Heymach, MD, PhD (Thoracic/Head & Neck Medical Oncology)

Wayne Hofstetter, MD (Thoracic & Cardiovascular Surgery)

Whitney Lewis, PharmD (Pharmacy Clinical Programs)

Zhongxing Liao, MD (Radiation Oncology)

Reza Mehran, MD (Thoracic & Cardiovascular Surgery)

Marcelo Vailati Negrao, MD (Thoracic/Head & Neck Medical Oncology)

David Rice, MD (Thoracic & Cardiovascular Surgery)

Jack Roth, MD (Thoracic & Cardiovascular Surgery-Research)

Stephen Swisher, MD (Surgery)

Ara Vaporciyan, MD (Thoracic & Cardiovascular Surgery)

Garrett Walsh, MD (Thoracic & Cardiovascular Surgery)

James Welsh, MD (Radiation Oncology)

Milena Zhang, PharmD[♦]

[♦] Clinical Effectiveness Development Team