SMALL CELL LUNG CANCER

Introduction

- Small cell lung cancer makes up about 15 percent of all lung cancers. It occurs almost exclusively in smokers, particularly heavy smokers, and former smokers.
- It is usually aggressive cancer that tends to grow and spread quickly.
- Small cell lung cancer (SCLC) is distinguished from non-small cell lung cancer (NSCLC) by its rapid doubling time, high growth fraction, and the early development of metastases.
- Although SCLC is highly responsive to both chemotherapy and radiotherapy (RT), it commonly relapses within months despite treatment.
- Since SCLC usually presents with disseminated disease, treatment strategies are mainly systemic.
- Although chemoradiation resulted in significant improvements in patient`s disease control for both the limited case and some of the extensive-stage disease, the long-term prognosis remains poor.

Initial Evaluation and Workup

- History and clinical examination
- Pathology review
- Laboratory tests:
  - CBC,
  - Biochemistry including serum LDH. LDH elevation reflects the bulk of the tumor and considered an aversive prognostic feature.
- Imaging:
  - Chest radiography
  - Computed tomography (CT) scan chest and abdomen
  - Magnetic resonance imaging (MRI) or CT scan brain
- Bone scan/NAF Scan is the current modality to test for bone metastases

Additional workup tools:

- Bone marrow aspiration cytology and biopsy: if abnormalities as would be suggested clinically and/or by peripheral smear.
- Thoracentesis:
  - Diagnostic through a cell block
  - Therapeutic to relief patient`s symptoms.
- Pulmonary function tests, echocardiography as indicated for selected cases.

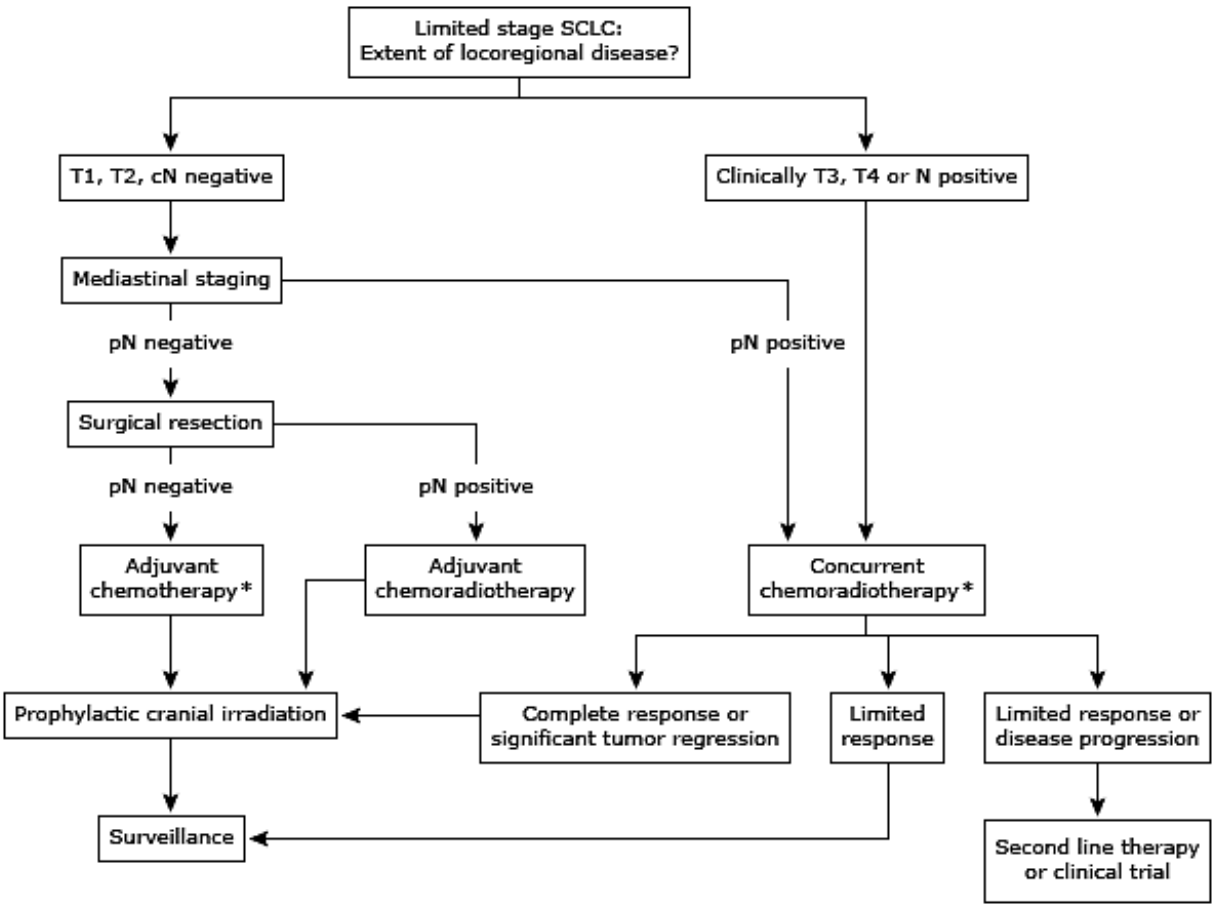
Staging of SCLC

- Patients with small-cell lung cancer are traditionally classified as having either:
  - Limited-stage or
  - Extensive-stage disease.
- Many experts recommended that small cell lung cancer should also to be classified using the TNM staging system.

Limited-stage disease (LD):

- Limited-stage small cell lung cancer is defined as cancer that is encompassed within one radiation port.
- Limited-stage disease correlates with stage I, II, or III cancer and representing one-third of patients at the time of initial presentation.
- Most people with limited-stage small-cell lung cancer are treated with chemotherapy with introducing thoracic radiation therapy as early as possible, currently given along with the second cycle of chemotherapy.
- Those who achieved a good response will be offered the chance of prophylactic cranial irradiation (PCI).
- Recently, there has been a role of surgery in selected patients with limited-stage small-cell lung cancer after careful discussion at the thoracic MDT.

The Management Approach for Patients with Limited Stage LD Small Cell Lung Cancer



Surgery in Multimodality Treatment for LD-SCLC

Surgery as initial therapy:

- Surgery is recommended for patients who:
  - Present with a solitary pulmonary nodule;
  - Have no evidence of hilar or mediastinal nodal involvement;
  - Have no distant metastases; and
  - Have no contraindications to surgery.
- Patients who will be considered candidates for primary resection should undergo extensive evaluation for mediastinal involvement and distant metastases.
- This evaluation should include
  - PET-CT and
  - Brain imaging.
- Invasive staging of the mediastinum by:
  - Endobronchial ultrasound (EBUS) or
  - Mediastinoscopy even if there is no evidence of mediastinal involvement by imaging.

Chemotherapy

- The current standard of care for patients with LD-SCLC consists of:
  - Four to six cycles of combination chemotherapy of the current standard cisplatin plus etoposide [EP]
  - Concurrent thoracic radiotherapy, along with chemotherapy, usually administered with the second cycle.
- Carboplatin can be an alternative if cisplatin is contraindicated for reasons such as:
  - Preexisting neuropathy,
  - Hearing loss,
  - Renal insufficiency.
- The number of chemotherapy cycles would depend on:
  - Patient`s tolerance;
  - Disease responsiveness; and
  - Side effects of the treatment.
- Prophylactic cranial irradiation (PCI) is generally recommended for patients with a complete response or significant tumor regression at the completion of chemotherapy.

Extensive-Stage Disease (ED)

- It is defined as patients with small cell lung cancer spreading to the other lung, liver, adrenal glands, bones, or brain.

Treatment Options:

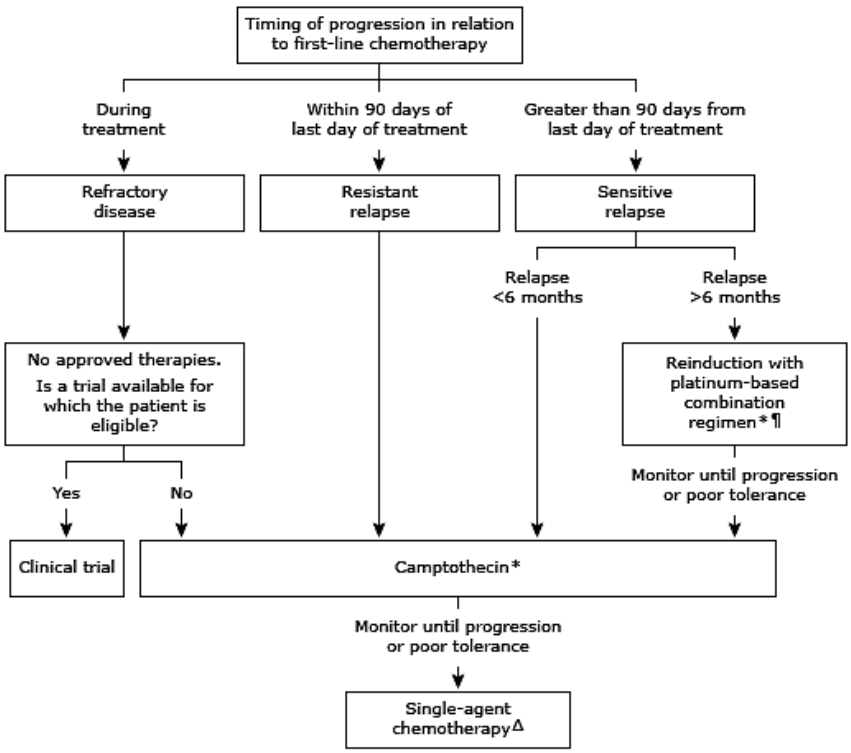
1) **Palliative Chemotherapy:**
   - Patients with extensive-stage small-cell lung cancer are generally treated with palliative chemotherapy utilizing cisplatin (or carboplatin) plus etoposide.
2) **Palliative Radiotherapy:**
   - Palliative radiation therapy would be offered for symptomatic metastatic sites.
3) **Local Therapies:**
   - Those who responded may be offered local therapies after discussion at thoracic MDT.

- Recently Atezolizumab has been combined to carboplatin and etoposide in the first-line setting as was shown on phase III trial with two months benefit on overall survival benefit as was outlined by IMpower 133 study.

Thoracic Radiation Therapy

- The plan of radiotherapy will be decided by our thoracic radiotherapy colleagues of the thoracic MDT.
- **Prophylactic cranial irradiation:**
  - Indicated for patients with a complete or very good partial response to their initial chemotherapy treatment.

Treatment of refractory and relapsed SCLC



Agents used on relapse:

Topotecan (Irinotecan)	**Gemcitabine**	**Vinoralbine**	**Temozolamide [not commonly** used due to high toxicity profile]

- **Nivolumab** as a second-line regimen based on the phase II trial [Checkmate 331 trial] that gained an accelerated the Food and Drug Administration (FDA) approval yielding a response rate relative risk (RR) of 12%.
- **Treatment duration and further lines of therapy**
  - The optimal duration of second-line treatment has not been clearly established. A commonly employed and acceptable approach is to continue treatment until disease progression or unacceptable toxicity occurs.
  - Third-line chemotherapy may be offered to patients who still have:
  - Adequate performance status after progression on two lines of chemotherapy (ECOG 0 to 2),
  - The discretion of the treating clinician through thoracic MDT and patient preferences.
- **Late relapses (after six months)**
  - These patients may be challenged with the initial protocol provided that the patient maintains a good performance status (Eastern Cooperative Oncology Group [ECOG] 0 to 2 after having 6-12 relapse-free intervals and so considered potentially eligible to derive a greater benefit from this approach.

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