Introduction to ACRODeck

- The goal of ACRODeck is to introduce standard treatments of oncologic malignancies for early radiation oncology residents.

- Please note that there is often considerable variation in standard treatment recommendations.

- Moreover, the landscape of oncology is ever-changing; for practice changing landmark studies and feedback, please email: resident@acro.org.
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SCLC classically appears as a large hilar mass with bulky mediastinal adenopathy

Clinical Presentation and Differential Diagnosis

- SCLC typically presents with cough, weight loss, and dyspnea
  - Symptoms of hemoptysis, hoarseness, brachial plexopathy, SVC syndrome may also be present
  - 3-5% of cases will present with paraneoplastic symptoms

- Most cases present with extensive disease

- Differential Diagnosis:
  - Neoplasm (NSCLC, SCLC, metastases)
  - Infections (fungal, bacterial, parasitic)

<table>
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<tr>
<th>TABLE 27.2: Paraneoplastic Syndromes Commonly Diagnosed in SCLC</th>
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<tr>
<td><strong>SIADH</strong></td>
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<tr>
<td><strong>Cushing syndrome</strong></td>
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<td><strong>Lambert–Eaton</strong></td>
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Essentials of Clinical Radiation Oncology
In the case of emergent SVC syndrome, placement of an intravascular stent is critical.

**Initial Workup**

- **H/P & Labs**
  - Focus on smoking history and cessation
  - CBC, CMP, PFTs

- **Imaging**
  - CT CAP with contrast
  - PET CT
  - MRI Brain

- **Biopsy**
  - Typically done via bronchoscopy or CT guidance

- **Pathologic mediastinal staging**
  - Typically done via EBUS, EUS, or mediastinoscopy

- **Thoracentesis if pleural effusion is present**
Pathologic Mediastinal Lymph Node Evaluation

- **Endobronchial Ultrasound (EBUS)**
  - Can access nodes near the airways

- **Cervical Mediastinoscopy**
  - Can access nodes near the airways
  - Inserts scope through an incision above the sternum

- **Endoscopic Ultrasound (EUS)**
  - Can access nodes near the esophagus
  - Only modality that can reach levels 8-9

- **Anterior Mediastinoscopy (Chamberlain Procedure)**
  - Only modality that can reach levels 5-6
  - Inserts scope through an incision in the parasternal 2nd left intercostal space
Pathologic Mediastinal Lymph Node Evaluation

Consider performance status and comorbidities before pathologic mediastinal staging.
VA Staging

- **Limited Stage**
  - Confined to ipsilateral mediastinum and/or supraclavicular region

- **Extensive stage**
  - Not limited stage
    - Contralateral disease
    - Metastatic disease (including malignant effusions)

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LS-SCLC is also defined as “disease confined to a single radiation port”
AJCC Staging

- Nodal Staging:
  - N1: double digit LN levels
    - 10 – 14
  - N2: single digit LN levels
    - Excluding N3 disease
  - N3: contralateral LN levels and/or the level 1 station

While the VA staging is more common, AJCC is used to determine surgical / SBRT candidates.
Treatment Summary

**Limited Stage**

- **Radiotherapy**
  - BID Treatment: 45 Gy in 30 fx
  - Daily Treatment: 66 Gy in 33 fx
- **Chemotherapy**
  - Cisplatin & Etoposide

**Consider PCI vs. MRI Brain Surveillance**

**Extensive Stage**

- **Chemotherapy**
  - Carboplatin & Etoposide
- **Immunotherapy**
  - Atezolizumab

*Other radiotherapy fractionations are often used as well*
Prior to definitive treatment, pathologic mediastinal staging should be performed.

**T1-T2N0 (AJCC)**

- Lobectomy with mediastinal lymph node dissection
  - For positive margins and/or nodes, chemotherapy ± radiotherapy is considered

- If surgical resection is not performed (i.e.: medically operable patients), SBRT can be considered
Limited Stage (VA)

1. Concurrent chemoradiation
   - Chemotherapy = “Platinum-Doublet”
     - Cisplatin/Etoposide
     - Carboplatin/Etoposide (not an NCCN preferred regimen)
   - Radiation (start before cycle 2 of chemotherapy)
     - 45 Gy in 30 fx BID
     - or
     - 66 – 70 Gy (in 2 Gy fractions)

2. Prophylactic cranial irradiation (PCI) or Surveillance with MRI brain
Extensive Stage (VA)

1. Concurrent chemoimmunotherapy regimens (4 cycles)
   - Cisplatin/Etoposide + Durvalumab
   - Carboplatin/Etoposide + Durvalumab
   - Carboplatin/Etoposide + Atezolizumab

2. Maintenance Immunotherapy (PD-L1 inhibitors)
   - Atezolizumab or Durvalumab continued until disease progression or unacceptable toxicities
     - Consolidative radiation is considered during (or before) maintenance immunotherapy (and is being explored on the NRG RAPTOR trial)
     - Many doses are used: 30 Gy in 10 fx is an option

3. Prophylactic cranial irradiation (PCI) or Surveillance with MRI brain
Thoracic Radiation Dosing in LS-SCLC

- In 1999, Turrisi published a landmark trial establishing 45 Gy in 30 fx BID as standard of care

- In 2017, the CONVERT trial did not demonstrate superiority of 66 Gy in 33 fx
  - However, many institutions have adopted this regimen (as no detriment was seen between the 2 treatment arms)

- Radiotherapy fractionation is an area of continued research:
  - 70 Gy in 35 fx daily (RTOG 0538)
  - 60 Gy in 40 BID (THORA Trial)
  - 42 Gy in 15 fx daily (Gronberg et al)
Thoracic RT Simulation

Simulation
- 4DCT (± IV contrast)
  - IV contrast strongly recommended for nodal disease
- Supine, arms above head in an arm-board

Other motion management techniques include compression and DIBH
If unable to meet dose constraints:
2 cycles of chemotherapy can be administered prior to resimulation for chemoRT

Thoracic Dose Constraints

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<th>Organ at Risk (OAR)</th>
<th>Qday Dose Constraint</th>
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<tr>
<td>Spinal Cord</td>
<td>Max ≤ 50 Gy*</td>
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| Lung                | \( V_{200Gy} \leq 35\% \)  
                      | Mean ≤ 20 Gy         |
| Heart               | \( V_{50Gy} \leq 25\% \)  
                      | Mean ≤ 20 Gy         |
| Esophagus           | Max ≤ 105% of prescription  
                      | \( V_{60Gy} \leq 17\% \)  
                      | Mean ≤ 34 Gy         |
| Brachial Plexus     | Max ≤ 66 Gy          |

*The spinal cord dose constraint for BID treatment is 41 Gy; most others are identical*
In the 1999 Turrisi trial, the rate of esophagitis was higher in the BID arm; this was not the case in CONVERT or RTOG 0538.

Radiation Toxicities

- Acute:
  - Fatigue
  - Skin Irritation
  - Cough
  - Esophagitis

- Subacute
  - Radiation Pneumonitis

- Chronic:
  - Chest Wall Pain
  - Rib Fracture
  - Cardiac Toxicity
  - Bronchopulmonary Hemorrhage/Fistula
  - Pulmonary Fibrosis
Radiation Pneumonitis

- Radiation pneumonitis typically presents 1 – 6 months after the completion of radiotherapy
  - Symptoms include cough, dyspnea, low-grade fevers, chest and pleuritic pain
  - Supplemental oxygen may be necessary

- The mainstay of treatment is steroids
  - There are a variety of dosing schedules, most including 40 – 60 mg steroids with a slow taper
    - Example 6-week schedule
      - Prednisone 60mg daily for 1 week
      - Prednisone 50mg daily for 1 week
      - Prednisone 40mg daily for 1 week
      - Prednisone 30mg daily for 1 week
      - Prednisone 20mg daily for 1 week
      - Prednisone 10mg daily for 1 week

Risk of grade 3+ pneumonitis was 2.9% on RTOG 0538
Prophylactic Cranial Irradiation

- The utility of PCI is an area of debate in radiation oncology
  - Side effects included profound fatigue, nausea, hair loss, impaired neurocognition
  - Worse neurotoxicity is seen in patients aged ≥ 60 years

- If offered (instead of MR brain surveillance):
  - Patients must have had a partial response or complete response to initial therapy (determined by MR Brain and CT CAP)
  - Patients must have a good performance status and not be neurocognitively impaired

- Dose
  - 25 Gy in 10 fx to the whole brain
  - May consider memantine and hippocampal avoidance using IMRT

- The MAVERICK trial is exploring replacing PCI with surveillance MRIs, although many institutions already have adopted this as standard
Prognosis

- Distant failure (intracranially) is the most common pattern of failure.
- Overall survival is dismal.
  - Median OS:
    - LS-SCLC: ~30 months
    - ES-SCLC: ~10 months
  - 5 Yr OS:
    - LS-SCLC: 25%
    - ES-SCLC: 5%

NRG-LU005 is exploring the role of maintenance immunotherapy in LS-SCLC.
Review
Review #1: CONVERT to Daily RT

What was the radiation regimen used in the CONVERT trial (PMID 28642008), which attempted to prove the superiority of daily RT?

(A) 30 Gy in 10 fx
(B) 45 Gy in 25 fx
(C) 66 Gy in 33 fx
(D) 70 Gy in 35 fx
Review #2: Dose Constraints

Per RTOG 0538, what is the spinal cord dose constraint for BID radiation in SCLC?

(A) 31 Gy
(B) 41 Gy
(C) 51 Gy
(D) 61 Gy
NRG CC003 is exploring the role of hippocampal avoidance for SCLC receiving WBRT

Review #3: PCI

Per Takashai’s phase 3 RCT of PCI vs. surveillance MRIs (PMID 28343976), how often were MRIs performed in the first year?

(A) Every month
(B) Every 3 months
(C) Every 6 months
(D) Every 12 months
Review #4: Consolidative RT in ES-SCLC

Per the CREST Trial (PMID 25230595), consolidative thoracic RT of 30 Gy improved which of the following:

(A) 1 yr OS
(B) 2 yr OS
(C) Neurocognition
(D) Grade 4 toxicity
Review #5: Stage IA

For peripheral stage IA disease, with negative mediastinal nodes demonstrated pathologically, what is the recommended treatment regimen per NCCN?

(A) Observation
(B) Immunotherapy alone
(C) Radiation alone
(D) Exploration/resection with mediastinal lymph node dissection
The pattern of failure for advanced lung cancer is typically distant

Answer Key

1. C
2. B
3. B
4. B
5. D