Small Cell Lung Cancer

Overview and Recommendations

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Background

* [General information](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_f87e0ba7/#GUID-CAFF6889-F18F-4220-AC06-607686F10CDF):
  + Small cell lung cancer is a malignant epithelial tumor consisting of small cells with scant cytoplasm, ill-defined cellular borders, finely granular nuclear chromatin, and absent or inconspicuous nucleoli.
  + It is characterized by rapid doubling time, high growth fraction, and widespread metastases early in disease; patients often present with hematogenous metastases.
  + World Health Organization (WHO) [classifies](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_f87e0ba7/#TYPES__SNIPPET-POINTER_126094451) small cell lung cancer as a neuroendocrine tumor; it can be further classified as pure small cell lung cancer or combined small cell lung cancer.
  + Small cell lung cancer is suspected in patients with a history of cigarette smoking, coughing, hemoptysis, wheezing, fever, dyspnea, and/or chest pain.
* [Epidemiology](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_f87e0ba7/#GUID-653A9595-6697-4EA8-9B93-6D5DBC809DF7):
  + An estimated 228,150 new cases of lung and bronchus cancer are expected worldwide in 2019. Small cell lung cancer accounts for about 13%-15% of lung cancer cases.
  + The annual incidence has decreased over the past 30 years in industrialized countries, likely due to decreased rate of smoking in these regions.
  + [From 2009 to 2015 there were 33,824 total cases](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_f87e0ba7/#INCIDENCE) of small cell cancer of lung or bronchus in the United States; of these, about 75% of patients had metastatic disease at diagnosis.
  + The most common risk factor for small cell lung cancer is [cigarette smoking](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_f87e0ba7/#TOPIC_YTJ_MJT_TJB).

Evaluation

* The initial [evaluation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_f87e0ba7/#TESTING_OVERVIEW) to establish diagnosis includes:
  + blood tests ([Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_f87e0ba7/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF))
  + chest x-ray
  + IV contrast-enhanced computed tomography (CT) of chest, abdomen, and pelvis or of chest extending through liver and adrenal glands ([Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_f87e0ba7/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF))
* Confirm the diagnosis in patients with radiographic/clinical evidence of small cell lung cancer with the least invasive biopsy/pathology method as dictated by the patient’s presentation ([Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_f87e0ba7/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)). Options include sputum cytology, thoracentesis, bronchoscopy including transbronchial needle aspiration (TBNA), fine needle aspiration (FNA), and transthoracic needle aspiration (TTNA).
* Pretreatment testing aimed at staging typically includes:
  + brain magnetic resonance imaging (MRI) preferred or IV contrast-enhanced brain CT to detect brain metastases ([Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_f87e0ba7/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF));
  + bone scan ([Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_f87e0ba7/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF));
  + positron emission tomography (PET)/CT from skull base to mid-thigh if suspect limited stage or need clarification of stage ([Conditional recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_f87e0ba7/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)).
* Additional workup (if it is not done previously) for suspected limited stage disease includes:
  + pulmonary function tests in patients being evaluated for surgery or definitive radiation therapy ([Conditional recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_f87e0ba7/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF));
  + bone MRI or x-ray if PET/CT is inconclusive, followed by bone biopsy if MRI or bone scan is inconclusive ([Conditional recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_f87e0ba7/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF));
  + head MRI or CT in addition to PET, or abdominal CT plus bone scan in patients with clinical stage I disease considering definitive surgery ([Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_f87e0ba7/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF));
  + thoracentesis with cytologic analysis if pleural effusion is present ([Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_f87e0ba7/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)) and can be safely accessed;
  + bone marrow aspiration and biopsy in select patients with presentation suggestive of bone marrow invasion, including signs of blood-bone marrow barrier rupture (such as nucleated red blood cells on peripheral blood smear [peripheral blood erythroblasts]), or abnormal blood count (such as neutropenia and thrombocytopenia) ([Conditional recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_f87e0ba7/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)).
* Additional workup for never smokers with extensive stage disease includes molecular profiling to clarify diagnosis and evaluate possible targeted therapies ([Conditional recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_f87e0ba7/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)).

Management

Management of Limited Stage Disease

* If limited stage disease and negative pathologic mediastinal staging, perform lobectomy and mediastinal lymph node dissection or sampling ([Conditional recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_f87e0ba7/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)), then follow with adjuvant treatment, based on findings from lymph node dissection or sampling.
  + If lymph nodes are negative, offer 4 cycles of systemic therapy ([Conditional recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_f87e0ba7/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)).
  + If lymph nodes are positive, offer sequential or concurrent systemic therapy with or without mediastinal radiation therapy ([Conditional recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_f87e0ba7/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)).
* If limited stage disease and positive pathologic mediastinal imaging or limited stage disease in excess of T1-T2, N0:
  + for performance status (PS) 0-2, offer initial treatment with concurrent systemic therapy plus thoracic radiation therapy ([Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_f87e0ba7/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF));
  + for performance status 3-4 due to small cell lung cancer, offer systemic therapy with or without either concurrent or sequential radiation therapy ([Conditional recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_f87e0ba7/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF));
  + for performance status 3-4 not due to small cell lung cancer, offer an individualized treatment plan, including use of supportive care ([Conditional recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_f87e0ba7/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)).
* If limited stage disease and medically inoperable or decision not to pursue surgical resection, options include either stereotactic ablative radiation therapy (SABR) followed by adjuvant systemic therapy or concurrent chemoradiation ([Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_f87e0ba7/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)).
* Offer adjuvant prophylactic cranial irradiation to patients with limited stage disease and a complete or partial response to initial therapy ([Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_f87e0ba7/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)).

Management of Extensive Stage Disease

* For patients with extensive stage disease:
  + If no localized symptomatic sites or brain metastases, offer supportive care and base additional treatment on performance status.
    - For performance status 0-2 or 3-4 due to small cell lung cancer, offer combination systemic therapy ([Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_f87e0ba7/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)).
    - For performance status 3-4 not due to small cell lung cancer, may offer an individualized treatment plan and consider best supportive care ([Conditional recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_f87e0ba7/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)).
  + If localized symptomatic sites with superior vena cava syndrome, lobar obstruction, or bone metastases, treatment options include:
    - systemic therapy with or without radiation therapy to symptomatic sites ([Conditional recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_f87e0ba7/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF));
    - orthopedic stabilization and palliative external beam radiation therapy, for patients with high risk of fracture due to osseous impairment ([Conditional recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_f87e0ba7/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)).
  + If spinal cord compression, consider radiation therapy to symptomatic sites before systemic therapy (unless immediate systemic therapy is indicated) ([Conditional recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_f87e0ba7/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)).
  + If brain metastases:
    - consider systemic therapy before brain radiation therapy if patient is asymptomatic ([Conditional recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_f87e0ba7/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF));
    - consider brain radiation therapy before systemic therapy (unless immediate systemic therapy is indicated) if patient is symptomatic ([Conditional recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_f87e0ba7/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)).
  + For patients with a complete or partial response to initial therapy, options include adjuvant prophylactic cranial irradiation ([Conditional recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_f87e0ba7/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)) or magnetic resonance imaging (MRI) surveillance of brain ([Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_f87e0ba7/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)). May also offer sequential thoracic radiation therapy after systemic therapy, particularly in those with residual thoracic disease and low-bulk metastatic disease ([Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_f87e0ba7/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)).

Surveillance

* Surveillance for patients with small cell lung cancer includes ([Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_f87e0ba7/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)):
  + routine history and physical with assessment of symptoms
  + computed tomography (CT) of chest, abdomen, and pelvis
  + MRI or CT of brain
  + intervention for smoking cessation
  + survivorship care plan

Management of Relapsed or Progressive Disease

* Offer palliative management of symptoms to all patients with relapsing or progressive disease at any time during treatment regardless of PS, including localized radiation therapy to symptomatic sites ([Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_f87e0ba7/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)).
* For patients with relapsing or progressive disease and PS 0-2, offer subsequent systemic therapy with response assessment by chest/abdomen/pelvic CT with contrast after every 2-3 cycles ([Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_f87e0ba7/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)).
  + If response, continue therapy until disease progression or unacceptable toxicity ([Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_f87e0ba7/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)).
  + If no response or unacceptable toxicity and PS remains 0-2, options include subsequent systemic therapy and palliative management of symptoms including localized radiation therapy to symptomatic sites ([Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_f87e0ba7/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)).