Small-cell lung cancer: ESMO Clinical Recommendations for diagnosis, treatment and follow-up

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incidence
The crude incidence of lung cancer in the European Union in 2002 was 55.5/100 000/year, mortality rate being 50.6/100 000/year. Rates among men were 87.7 and 80.1/100 000/year, and among women 24.8 and 22.4/100 000/year, respectively (GLOBOCAN 2002, http://www-dep.iarc.fr). Small-cell lung cancer (SCLC) accounts for 15–18% of all cases. In recent years the incidence of SCLC has decreased. SCLC is strongly associated with tobacco smoking.

diagnosis
Pathological diagnosis should be made according to the WHO classification. Biopsies can be obtained by flexible bronchoscopy, mediastinoscopy, endoscopic ultrasound, transthoracic needle aspiration, and thoracoscopy depending on the localization of the tumor. A biopsy from a metastatic lesion can substitute for a biopsy from the primary tumor. The least invasive approach should be used.

staging and risk assessment
Staging procedures should include medical history, physical examination, chest X-ray, complete blood count including differential count, liver, lung and renal function tests, LDH and sodium levels, and a CT scan of the chest and upper abdomen including the liver and adrenal glands.

In patients with symptoms or abnormal physical examination suggesting metastasis additional tests may include bone scintigraphy, contrast-enhanced CT scan or MRI of the brain, and bone marrow aspiration and biopsy. If extensive disease is detected by one test, further staging can be omitted [V, D].

Contrast-enhanced CT or MRI of the brain is recommended if chemoradiation with curative intent is under consideration. The role of combined FDG-PET/CT scanning is not defined.

Staging is performed according to either a two-stage system developed by the Veteran’s Administration Lung Cancer Study Group in the US dividing patients into limited and extensive disease groups, or to the TNM system.

limited disease
Limited disease is defined as a tumor, which can be encompassed in a single radiation port. Limited disease is confined to one hemithorax with regional lymph node metastasis including ipsilateral hilar, ipsilateral supraclavicular, mediastinal and/or contralateral hilar nodes.

extensive disease
Extensive disease is defined as any tumor that extends beyond the boundaries of a single radiation port, including patients with ipsilateral lung metastases, malignant pleural or pericardial effusion, and distant metastases.

treatment of limited disease
Limited disease patients should be treated with four to six cycles of etoposide/platinum, preferably etoposide/cisplatin, in combination with thoracic radiotherapy [I, A].

Thoracic radiotherapy increases local control and survival in limited disease patients [I, A]. A meta-analysis suggests that survival rates favor administering early thoracic radiotherapy concurrently with chemotherapy. The optimal dose and fractionation scheme are still unresolved, as is the role of elective mediastinal nodal irradiation. Therefore, etoposide/cisplatin with early concurrent radiotherapy is the standard of care for patients with limited disease suitable for this approach [II, B].

Patients with limited disease achieving a major response should be offered prophylactic cranial irradiation as it reduces risk of cerebral metastases and improves survival [I, A].
Multiple trials have shown that maintenance chemotherapy is not effective in improving survival [II, A].
In patients with very limited disease (i.e. T1-2, N0), surgical resection followed by postoperative chemotherapy and prophylactic cranial irradiation may be considered [III, D].

treatment of extensive disease
Extensive disease patient should be treated with cisplatin or carboplatin in combination with etoposide for four to six cycles [II, A].
Patients with response after chemotherapy should be offered prophylactic cranial irradiation as this treatment reduces the risk of brain relapse and prolongs survival [II, B].

second-line chemotherapy
Patients in good performance status relapsing after response to first-line chemotherapy should be considered for second-line chemotherapy as second-line chemotherapy increases survival [II, B]. No second-line chemotherapy has been proven superior to others.

response evaluation
Response evaluation is recommended during and at the completion of therapy. Initial positive imaging should be repeated [V, D].

follow-up
Although the optimal follow-up approach is controversial, it should be considered so that second line treatment may be offered. For patients who achieve long-term survival, monitoring for development of a second primary cancer may be considered. Smoking cessation is recommended.

note
Levels of evidence [I–V] and grades of recommendation [A–D] as used by the American Society of Clinical Oncology are given in square brackets. Statements without grading were considered justified standard clinical practice by the experts and the ESMO faculty.

literature