Lung cancer is the leading cause of cancer-related deaths in men and women worldwide.\textsuperscript{1} It is also the leading cause of cancer mortality in Ireland, accounting for almost 20% of all cancer deaths.\textsuperscript{2}

Approximately 95% of all lung cancers are classified as either small cell lung cancer (SCLC) or non-small cell lung cancer (NSCLC). NSCLC is any type of epithelial lung cancer other than SCLC. NSCLC is the most common type of lung cancer accounting for approximately 80% of lung cancers. SCLC accounts for approximately 15% of bronchogenic carcinomas and is considered distinct from NSCLC because of its clinical and biologic characteristics. SCLC exhibits aggressive behaviour with rapid growth and early spread to distant sites.

Without treatment, SCLC has the most aggressive clinical course of any type of lung cancer, with median survival from diagnosis of only two to four months. Compared with other cell types of lung cancer, SCLC is more responsive to chemotherapy and radiation therapy. However, a cure is difficult to achieve because SCLC has a greater tendency to be widely disseminated by the time of diagnosis.

It is the cancer most commonly associated with paraneoplastic syndromes, including Lambert-Eaton myasthenic syndrome, syndrome of inappropriate antidiuretic hormone secretion (SIADH) and paraneoplastic cerebellar degeneration.\textsuperscript{3}

Efficient and correct diagnosis and staging of SCLC are key in improving survival with good quality of life, writes Dr Elaine Wallace

**Clinical Focus: Lung Cancer**

**Small cell lung cancer: staging, treatment and prognosis**

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**Evaluation**

The main issues to establish in a patient with suspected lung cancer are:

- The cell type (NSCLC vs SCLC)
- The stage of the disease
- The functional status of the patient.

It is necessary to distinguish whether the disease is SCLC or NSCLC in order to plan treatment and, because of this, a tissue diagnosis is vital.

**Staging**

In general a two-stage system is used for SCLC: limited-stage disease and extensive-stage disease. Limited-stage disease is confined to the hemithorax of origin, the mediastinum or the supraclavicular lymph nodes. Extensive-stage disease is present beyond one hemithorax. This distinction is important as patients with limited-stage disease may benefit from thoracic radiotherapy in addition to systemic chemotherapy.

**Performance status**

A patient’s performance status also dictates the type of treatment regime employed. Performance status can be assessed using a variety of assessment tools including the Eastern Co-operative Oncology Group (ECOG) scale and Karnofsky Performance Status (KPS) scale.\textsuperscript{4,5}

The KPS uses a 100-point scale and 11 measures to describe a patient’s abilities to engage in activities and perform work. The ECOG uses a five-point scale and has been shown in a comparative study to be a better predictor of prognosis.\textsuperscript{6}

**Treatment**

All patients should be discussed at a multidisciplinary forum with access to a full lung cancer team so that appropriate treatment can be efficiently arranged. Appropriate treatment for SCLC is determined predominantly by the stage of disease, but also by assessment of a patient’s performance status, co-morbidities and any associated weight loss. Where performance status is poor or co-morbidities severe, treatment may largely be palliative.

**Limited-stage disease**

At the time of diagnosis, approximately 30% of patients with SCLC will have limited-stage disease. Standard treatment options with limited-stage SCLC include:

- Chemotherapy and radiation therapy
- Combination chemotherapy alone
- Surgery followed by chemotherapy or radiotherapy
- Prophylactic cranial radiotherapy.

SCLC is believed to be a systemic disease at diagnosis, thus surgery plays no significant role in its management. Patients diagnosed with limited-stage disease who smoke should be encouraged to stop smoking before undergoing treatment as continued smoking may compromise cure rates.\textsuperscript{7}

Chemotherapy improves the survival of patients with limited-stage disease or extensive-stage disease, but it is curative in only a minority of patients.\textsuperscript{8,9} Although long-term survivors have been reported among patients who received either surgery or chemotherapy alone, chemotherapy combined with thoracic radiotherapy is considered the standard of care.

Adding thoracic radiotherapy increases absolute survival by approximately 5% over chemotherapy alone.\textsuperscript{10,11} The optimal timing of thoracic radiotherapy relative to chemotherapy has been evaluated in multiple trials and meta-analyses with the weight of evidence suggesting a small benefit to early thoracic radiotherapy.\textsuperscript{12-14}

Prophylactic cranial radiation helps prevent central nervous system (CNS) recurrence and can improve survival in patients who have had a complete response to chemo-radiation.\textsuperscript{15,16}

**Extensive-stage disease**

Patients with tumours that have spread beyond the supraclavicular areas are said to have extensive-stage disease and have
Table 1

Prognostic factors of survival in SCLC

- Limited disease
- Good performance status
- Female gender
- No significant weight loss
- White cell count
- Platelet count
- Lactate dehydrogenase (LDH)

A worse prognosis than patients with limited-stage disease. Chemotherapy for extensive-stage SCLC is commonly given as a two-drug combination with platinum-based compounds in doses associated with at least moderate toxic effects. Commonly used chemotherapeutic regimens include carboplatin/etoposide, cisplatin/etoposide, cisplatin/irinotecan and cyclophosphamide/doxorubicin/vincristine. Cisplatin is associated with significant toxic effects and requires fluid hydration, which can be problematic in patients with cardiovascular disease. Carboplatin is active in SCLC, is dosed according to renal function and is associated with less non-haematological toxic effects. Doses and schedules used in current regimes yield response rates of 50-80% and complete response rates of 0-30% in patients with extensive-stage disease. Palliative whole-brain radiotherapy should be used for radio-logically-proven cranial metastases. Radiotherapy should also be considered for the palliation of other metastatic lesions requiring symptom control.

Prognosis

The most important prognostic factor is the stage of disease at presentation. Patients with involvement of the CNS or liver at the time of diagnosis have a significantly worse outcome. A number of biochemical factors including white cell count, platelet count and lactate dehydrogenase (LDH) have also been found to independently correlate with outcome (see Table 1).

Factors of survival

Regardless of stage, the current prognosis for patients with SCLC is poor despite improvements in diagnosis and therapy during the past 25 years. The overall survival at five years is approximately 5-10%. For patients with limited-stage disease, median survival of six to 12 months is reported with currently available therapy, but long-term disease-free survival is rare. Most of the two-year disease-free survivors come from the limited-stage disease group. Earlier diagnosis, efficient and correct diagnosis and staging, and modern multidisciplinary management of SCLC have led to improved short-term and long-term survival with good quality of life. A recent trial of early versus standard referral to specialist palliative care has shown that early palliative care intervention results in improved quality of life and survival. Thus the early integration of palliative care into the disease-specific therapies for patients with advanced lung cancer should be considered.

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References