

NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Health Technology Appraisal

Topotecan for the treatment of relapsed small cell lung cancer

Draft scope (Pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of topotecan for the treatment of relapsed small cell lung cancer.

Background

Small cell lung cancer (SCLC) is a type of lung cancer which grows rapidly, spreads quickly to distant sites. Common symptoms of SCLC include weight loss, malaise, bone pain, breathlessness and haemoptysis. SCLC is frequently associated with distinct paraneoplastic syndromes which are not due to direct invasion of adjacent tissues by the cancer or its metastases, for example, neurological or endocrine syndromes.

In 2003, lung cancer was the second most common cancer in men and third most common cancer in women, accounting for 31,900 new cases of lung cancer in England and Wales. SCLC constitutes about 20-25% of all lung cancers, an estimated 6,380 to 7,975 of the new cases. Of these, around 30 to 40% are classed as limited stage at diagnosis (tumour confined to one side of the chest or to the neck lymph nodes), while the remainder have extensive stage disease (defined as the presence of obvious metastatic disease). Because of the rapid growth pattern of SCLC, TNM staging classification is not well correlated with prognosis or survival, but simple staging into those with limited or extensive disease has some prognostic impact.

The prognosis of SCLC is poor; the life expectancy of those with untreated SCLC is about 3.5 months for limited disease and 6 weeks for extensive disease. Prognosis has been linked to serum sodium, albumin, and alkaline phosphatase, which are routine biochemical measures, as well as to performance status and extent of disease.

Current management usually consists of combination chemotherapy, which may include etoposide, cisplatin, cyclophosphamide, doxorubicin, and vincristine. Median survival with such cytotoxic treatment is approximately 14 to 18 months for limited disease and 9 to 12 months for extensive disease. Radiotherapy has an important role to play in the palliation of symptoms that may develop after relapse following chemotherapy. Cranial irradiation is often required as brain metastases are common. Surgery is only suitable for a small minority of patients with no evidence of local spread or metastasis.

The NICE lung cancer clinical guideline (2005) advises that:

- All patients with newly diagnosed SCLC should be offered a platinum-based chemotherapy, and multi-drug regimes.
- Patients with limited-stage SCLC should be offered thoracic irradiation concurrently with the first or second cycle of chemotherapy, or following completion of chemotherapy if there has been at least a good partial response within the thorax.
- For patients with extensive disease, thoracic irradiation should be considered following chemotherapy if there has been a complete response at distant sites and at least a good partial response within the thorax.
- Second-line chemotherapy should be offered to patients at relapse only if their disease responded to first-line chemotherapy.

The technology

Topotecan (Hycamtin, GlaxoSmithKline) acts by inhibiting topoisomerase I, an enzyme that is required for DNA replication, leading to cell death. It can be administered either orally or intravenously.

Intravenous topotecan holds a marketing authorisation as monotherapy for patients with relapsed small cell lung cancer [SCLC] for whom re-treatment with the first-line regimen is not considered appropriate.

There is currently no UK marketing authorisation for oral topotecan in SCLC. It is being investigated in ongoing randomised controlled trials (RCTs) for the treatment of extensive or limited SCLC, in patients who have relapsed after having had a complete or partial response to first-line therapy.

Intervention	<ul style="list-style-type: none"> • Oral/intravenous topotecan
Population(s)	Patients with small cell lung cancer that has relapsed following previous therapy.
Standard comparators	<ul style="list-style-type: none"> • cisplatin • etoposide • thoracic irradiation • other chemotherapy regimens including combinations of the above. • intravenous topotecan

Outcomes	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> • progression free survival • response rate • response duration • survival • adverse effects of treatment • health-related quality of life.
Economic analysis	<p>The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year.</p> <p>The time horizon for the economic evaluation should reflect the period over which relevant costs and benefits can reasonably be expected.</p> <p>Costs will be considered from an NHS and Personal Social Services perspective.</p>
Other considerations	<p>Guidance will only be issued in accordance with the marketing authorisation.</p> <p>If evidence allows subgroups of patient populations in whom the technology is clinically effective and cost effective should be considered. These may include subgroups by biochemical measures, performance status, prior therapy and extent of disease.</p>
Related NICE recommendations	<p>Related NICE clinical guideline:</p> <ul style="list-style-type: none"> • Clinical Guideline. Lung cancer: the diagnosis and treatment of lung cancer. CG24, February 2005 [review expected, February 2009].

Questions for consultation

- It is anticipated that this technology will be appraised through the Single Technology Appraisal (STA) process. Are there any reasons why this may not be appropriate?
- What chemotherapy regimens are the most commonly used in current clinical practice for the subsequent treatment of people who have relapsed after a complete or partial response to first-line therapy?

- Should the appraisal consider just oral or both oral and intravenous topotecan?
- Are there any groups in which topotecan is expected to be particularly clinically or cost effective or other groups that should be examined separately?