New and Emerging Technology Briefing

National Horizon Scanning Centre

BEC-2 for small cell lung cancer

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Horizon Scanning Review

Early assessments of new or emerging technologies contain time-limited information and should be used with due caution.

BEC-2 for small cell lung cancer

Summary

BEC-2 (Mitumomab) is a cancer vaccine administered with Baccillus Calmette-Guérin (BCG) for patients with limited small cell lung cancer. It is administered by 5 intradermal injections over 10 weeks after standard chemotherapy and radiation therapy have been completed. A published trial in 15 patients found increased survival and relapse-free survival compared to historical controls. A large phase III trial is ongoing and due to complete in mid 2003. BEC-2 is also in clinical trials for extensive small cell lung cancer.

Developer – Merck Pharmaceuticals (licensed from ImClone Systems)

Regulatory status – Phase III clinical trials.

Unit cost – Not determined at present.

- Impact on government policy and priorities – Cancer is a government priority area.
- Impact on patient care – Small cell lung cancer has a poor prognosis. We estimate that between 670 and 1,665 patients may be eligible for BEC-2 if it gets a licence for limited disease. If results from the phase III trial support those found in the pilot trial, BEC-2 may have the potential to improve survival and perhaps quality of life.
- Impact on service provision – BCG preparation needs special microbiological precautions and can be undertaken either centrally or locally. The administration and monitoring of the skin reaction to the 5 intradermal injections with BCG requires some training and will have some impact on health services.
- Impact on NHS resources – Without any estimate of likely cost we cannot make a prediction about the likely cost impact. We can say that any costs will be additional to current costs, but are unlikely to lead to any additional knock-on costs.

The technology

BEC-2 (Mitumomab) – Merck Pharmaceuticals, is a cancer vaccine that mimics the GD3 glycopeptide on the surface of small cell lung cancer cells. It is administered with Baccillus Calmette-Guérin (BCG) as an immune adjuvant, by 5 intradermal injections over 10 weeks after standard chemotherapy and radiation therapy have been completed

Patient group

Lung cancer is the most common cancer in men and the third most common in women. In 1997 there were 33,300 new cases of lung cancer in England and Wales (21,000 men and 12,300 women) with 29,400 deaths.[1] Small cell lung cancer constitutes about 20-25% of all lung cancer (6,660 to 8,325 cases) the remainder being non-small cell cancer.[2] Small cell lung

cancer is divided into limited disease (tumour confined to one side of the chest or to the neck lymph nodes) and extensive disease. Between 20-40% have limited disease on diagnosis (about 1,332 – 3,330 cases). A second primary cancer develops after treatment in 25-50% of cases.

People with small cell lung cancer and limited disease who undergo combined chemotherapy and radiotherapy have a median survival of 18-24 months. Those with extensive disease given palliative chemotherapy have a median survival of 10-12 months. About 5-10% of people with small cell cancer present with central nervous system involvement and half develop symptomatic brain metastases by 2 years. An estimated 50% of those with limited disease may still be in remission after initial chemotherapy and radiotherapy (670 – 1,665 people).[a]

Current treatment and alternatives

First line treatment is normally combination chemotherapy, commonly cyclophosphamide, doxorubicin and vincristine.[3] This combination can induce responses and temporary remission in 80-90% of people. Combination cisplatin and etoposide can produce similar benefits. Patients who respond to chemotherapy may also benefit from radiotherapy to the chest (to improve local tumour control) and the brain (to reduce the risk of metastases).

The National Institute for Clinical Excellence (NICE) are currently developing guidelines for the management of lung cancer. Guideline publication is anticipated for March 2004.

Cost

No cost has yet been determined for BEC-2.

Current research evidence

Effectiveness

A study administered BEC-2 to 15 patients with small cell lung cancer who had experienced a partial or complete response to standard chemotherapy.[4] Patients received a series of 5 intradermal immunisations consisting of 2.5mg of BEC-2 plus a reducing dose of BCG over a 10 week period (weeks 0, 2, 4, 6 and 10). Eight of the patients had extensive disease on diagnosis. Median overall survival measured from diagnosis was 20.5 months with the longest relapse-free intervals being observed in the patients with measurable anti-GD3 antibodies. The median time to relapse was 10.6 months for those with extensive disease, and had not been met by 47 months for those with limited disease. Comparison to an historical control group showed that the BEC-2/BCG group had an overall survival and relapse/progression-free survival far longer than expected.

The main adverse event is the local skin reaction to the BCG component of the vaccine. About 2-3% of patients appear to have general malaise.

Cost-effectiveness

No economic evaluations have been identified.

[a] Expert opinion.

Ongoing or related research

SILVA (Survival in an International Phase III Prospective Randomised Limited Disease SCLC Vaccination Study – EORTC protocol) is an ongoing randomised trial of BEC-2 with BCG compared with standard care in 500 patients newly diagnosed with small cell lung cancer and limited disease who have responded to prior treatment with a standard therapy.[5] Four or five induction chemotherapy cycles of cisplatin/etoposide, carboplatin/etoposide or cyclophosphamide/doxorubicin/etoposide with concomitant or sequential chest radiotherapy are planned. Prophylactic cranial radiotherapy is recommended but not mandatory. Enrolment began in 1998. The trial is expected to have a 2-year follow-up and to be complete in autumn 2003. The trial will include a quality of life and an economic evaluation.

Phase II trials in small cell lung cancer extensive disease are reportedly ongoing.

Cost impact and projected diffusion

If 50% of patients with limited small cell lung cancer complete and respond to initial chemotherapy and radiotherapy we estimate that between 670 – 1,665 patients may be eligible to receive BEC-2 if it is licensed in England and Wales. We cannot estimate the cost impact because this is one of the first cancer vaccines and we do not know how expensive or cheap these products will be.

References

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