Lung cancer: the effectiveness of paclitaxel, docetaxel, gemcitabine and vinorelbine

Rapid review

A rapid and systematic review of the clinical effectiveness and cost-effectiveness of paclitaxel, docetaxel, gemcitabine and vinorelbine in non-small-cell lung cancer

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Executive summary

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Executive summary

Background

The incidence of lung cancer is declining following a drop in smoking rates, but it is still the leading cause of death from cancer in England and Wales, with about 30,000 deaths a year. Survival rates for lung cancer are poor everywhere, but they appear to be better in the rest of the European Community and the USA than in the UK. Only about 5% of people with lung cancer survive for 5 years, and nearly all of these are cured by surgery after fortuitously early diagnosis. At present, only a small proportion of patients (probably about 5%) with non-small-cell lung cancer are being given chemotherapy. Some centres treat a greater proportion.

Objectives

This review examines the clinical effectiveness and cost-effectiveness of four of the newer drugs – vinorelbine, gemcitabine, paclitaxel and docetaxel – used for treating the most common type of lung cancer (non-small-cell lung cancer). The first three drugs are used for first-line treatment, but at present docetaxel is used only after first-line chemotherapy has failed.

Methods

This report was based on a systematic literature review and economic modelling, supplemented by cost data.

Results

Number and quality of studies

A reasonable number of randomised trials were found – three for docetaxel, six for gemcitabine, five for paclitaxel and 13 for vinorelbine. The quality of the trials was variable but good overall. There was a wide range of comparators. Some trials compared chemotherapy with best supportive care (BSC), which involves care that aims to control symptoms, with palliative radiotherapy if needed, but not to prolong life. Others compared the newer drugs against previous drugs or combinations.

Summary of benefits

The gains in duration of survival with the new drugs are modest – a few months – but worthwhile in a condition for which the untreated survival is only about 5 months. There are also gains in quality of life compared with BSC, because on balance the side-effects of some forms of chemotherapy have less effect on quality of life than the effects of uncontrolled spread of cancer.

Costs

The total cost to the NHS of using these new drugs in England and Wales might be about £10 million per annum, but is subject to a number of factors. There would be non-financial constraints on any increase in chemotherapy for the next few years, such as staffing; the number of patients choosing to have the newer forms of chemotherapy is not yet known; and the costs of the drugs may fall, for example, as generic forms appear.

Cost per life-year gained

The available data did not provide an entirely satisfactory basis for cost-effectiveness calculations. The main problem was the lack of direct comparisons of the new drugs. In order to strengthen the analysis, three different modelling approaches were used: pairwise comparisons using trial data; cost-minimisation analysis, as if all the new regimens were of equal efficacy; and cost-effectiveness analysis pooling the results of several trials with different comparators, giving indirect comparisons of the new drugs by using BSC as the common comparator. A number of different scenarios were explored through extensive sensitivity analysis in each model. Outcomes were expressed in incremental cost per life-year saved or incremental cost, versus BSC. There was insufficient evidence from which to derive cost per quality-adjusted life-year.

In first-line treatment, vinorelbine, gemcitabine, and the lower-dose paclitaxel plus cisplatin combinations generally performed well against BSC under a range of different scenarios and especially when given as a maximum of 3 cycles. Incremental cost per life-year gained (LYG) versus BSC varied depending on scenario, but baseline figures based on trial data and protocols were: single-agent vinorelbine, £2194 per LYG; vinorelbine plus cisplatin, £5206; single-agent

gemcitabine, £5690; gemcitabine plus cisplatin, £10,041; and paclitaxel plus cisplatin, £8537. In second-line chemotherapy, docetaxel gave a cost per LYG of £17,546, again well within the range usually accepted as cost-effective.

However, in routine care, the impact of therapy would be regularly reviewed, and continuation would depend on response, side-effects, patient choice and clinical judgement. Chemotherapy would be stopped in non-responders, making chemotherapy more cost-effective. A 'real-life' scenario in which 60% of patients receive only 1 or 2 cycles of chemotherapy gives much lower costs per LYG, with single-agent gemcitabine, single-agent vinorelbine, and paclitaxel plus platinum appearing to be cost-saving compared with BSC; the incremental cost of gemcitabine plus cisplatin would be £2478 per LYG, and of vinorelbine plus cisplatin, £2808.

At the very least, gains in duration of survival were achieved without diminution of quality of life (at best, they improved quality) and with relatively low incremental cost.

Comparisons among the individual drugs should be viewed with caution because they have had to be based on indirect comparisons.

Limitations of the analysis

Each of the three models had limitations. The cost-effectiveness estimates from the pairwise comparisons were based on single studies. The cost-minimisation analysis assumed that the regimens have equal efficacy in practice. The cost-effectiveness analysis had to be based on pooling data from individual trials.

The costs of BSC, inpatient stay and outpatient visits were from Scottish data. Median rather than mean data on duration of survival have been used in the analysis, because most of the trials reported only median data. Median survival and number of drug cycles were calculated by averaging across a number of studies, rather than being reliant on one particular study. The costs of the less expensive antiemetics cited in the trials were omitted. The use of more modern and costly antiemetics would have a modest detrimental effect on cost-effectiveness. In the absence of published data, an estimate was made of the cost of side-effects of chemotherapy, in particular hospital admissions, and applied to all the new regimens. In practice, admissions related to side-effects and their respective costs are likely to vary by regimen.

Conclusions

The new drugs for non-small-cell lung cancer extend life by only a few months compared with BSC, but appear to do so without net loss in quality of life and at a cost per LYG that is much lower than for many other NHS activities. Depending on assumptions used, these new drugs range from being cost-effective, as conventionally accepted, to being cost-saving.

Implications of the newer drugs

One of the present constraints on chemotherapy is availability of inpatient beds. The advent of newer and gentler forms of chemotherapy given on an outpatient basis would not only overcome this, but it would allow more patients to be treated. This might apply particularly to older patients. The treatment of more patients would increase workload for oncologists, cancer nurses and pharmacists. The Government has already announced increased expenditure on staff for cancer care. The previously pessimistic attitudes to chemotherapy in non-small-cell lung cancer are changing in the wake of the newer agents, and this shift is likely to increase referral.

Need for further research

Recent advances in chemotherapy are welcome, but their effects remain small for patients with non-small-cell lung cancer. Much more research is needed into better drugs, better combinations, new ways of assessing the likelihood of response and especially direct comparisons between the new regimens. This research would be aided by having a greater proportion of patients involved in trials, but there will be infrastructure implications of increased participation.

Publication

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