An estimate of the cost effectiveness of gemcitabine in stage IV non-small cell lung cancer

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Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
Gemcitabine (nucleoside analog with a broad spectrum of antitumour activity) in stage IV non-small cell lung cancer (NSCLC).

Type of intervention
Treatment; palliative care.

Economic study type
Cost-effectiveness analysis.

Study population
A hypothetical cohort of stage IV NSCLC patients.

Setting
Hospital. The economic study was carried out in Ontario, Canada.

Dates to which data relate
The main effectiveness data were taken from studies published in 1996 and 1988. Resource use data were derived partly from experts' opinion and partly from data published in 1988, 1996 and 1990. The price date was 1993.

Source of effectiveness data
Effectiveness data were derived from a review of previously completed studies.

Link between effectiveness and cost data
The resource use data associated with the comparator, and some of the data for the intervention, were obtained from the studies which provided their respective survival (effectiveness) data. Some data were collected retrospectively from different patient samples/sources.

Modelling
A population health model (POHEM) was used to evaluate the costs of gemcitabine and to estimate the nation-wide costs associated with treating stage IV NSCLC with the intervention as opposed to the standard. The model assumed that the intervention would be associated with cycles (3.3 on average) each of which would consist of weekly x 3 drug injections followed by a 1 week rest. It was also assumed that test results would not be duplicated during the patient's course through the health care system.
Outcomes assessed in the review
The outcome assessed in the review was the median survival of patients with stage IV NSCLC.

Study designs and other criteria for inclusion in the review
Randomised controlled trials were included in the review.

Sources searched to identify primary studies
Not stated.

Criteria used to ensure the validity of primary studies
Not stated.

Methods used to judge relevance and validity, and for extracting data
Not stated.

Number of primary studies included
One study was included for the comparator's estimate of survival benefit and another one for the intervention's.

Methods of combining primary studies
Not combined.

Investigation of differences between primary studies
Not stated. The authors did mention that the patient sample in the study providing the estimate of survival of patients under the standard therapy was a select group of stage IV patients with good performance status and little weight loss. They then went on to use comparable data from the general population of two regions in Canada to support the validity of results arising from the data of that select group.

Results of the review
Gemcitabine was found to gain an additional 0.42 years, on average, relative to the standard best supporting care for patients with stage IV NSCLC.

Methods used to derive estimates of effectiveness
Complication rates associated with gemcitabine were based on the authors' assumptions.

Estimates of effectiveness and key assumptions
Gemcitabine was assumed to be administered without complications being present.

Measure of benefits used in the economic analysis
The measure of benefits was life years gained. These benefits were estimated from actual clinical data from two separate studies each of which included one of the strategies being compared by the economic study.

Direct costs
Costs were not reported as discounted. The cost implications of diagnosis, treatment, and terminal care were included in
the analysis. Major quantities of resource use were analysed separately from the costs. The major sources of these quantities were the two studies which in turn served as sources for the effectiveness data of the study. However, it is worth noting that major resource data for the intervention (i.e. terminal care hospitalisation) were assumed to be similar to that for the chemotherapeutic option in the clinical study which provided the survival data associated with the comparator in the effectiveness study. Original cost data for 1984 and 1988 were inflated using the Canadian Consumer Price Index (by 41.1% and 20.1%, respectively) to obtain the final estimates in 1993 prices. Total costs were estimated using a model, which also gave Canadian estimates of the implications of a potential nation-wide intervention.

**Currency**
Canadian dollars (Can$).

**Sensitivity analysis**
A two-way sensitivity analysis was performed on the estimate of effectiveness and the cost per treatment cycle of gemcitabine.

**Estimated benefits used in the economic analysis**
The life years gained by the intervention (Gemcitabine) relative to the comparator (best supportive care) was 0.42 years.

**Cost results**
The total per patient cost of the supportive care arm was Can$20,914, and Can$22,172 (assuming a cost of Can$1,000 per cycle for the latter). The total cost to the Canadian health care system of managing all stage IV patients with gemcitabine was estimated to be Can$91.4 million.

**Synthesis of costs and benefits**
The cost per life-year gained (at 1993 prices without discounting being mentioned) was estimated to be Can$3,193 for the intervention (given a Can$1,000 per cycle cost of gemcitabine). Such a cost-effectiveness ratio was found to range from Can$1,609 to Can$16,230 depending on the cost per treatment cycle (range: Can$800 - Can$1,800) and the estimate of effectiveness (reduced up to 50% from that of the base case).

**Authors' conclusions**
Gemcitabine appears to be a cost-effective intervention for advanced NSCLC.

**CRD COMMENTARY - Selection of comparators**
The reason for the choice of comparator is clear. 'Best supportive care' was defined as a standard of practice (as opposed to chemotherapy treatment) based on survey data of Canadian oncologists in 1985.

**Validity of estimate of measure of benefit**
The estimate of measure of benefit used in the economic analysis may not be internally valid due to the fact that the effectiveness data associated with the intervention and comparator were not derived from the same study. The survival estimates derived from the corresponding patient groups of two different RCTs may be showing the effects of factors other than the different treatment options used. In principle, differences in other medical care service delivery, practice or technology (due to non-concurrent controls) are some of the possible explanations.

**Validity of estimate of costs**
Although the major resource use quantities were reported separately from the costs, these were not adjusted for by
applying annual discount rates taking into account the difference in the timing of the resource use consumption implied by the strategies being compared. It seems that no important cost items apart from indirect costs and costs incurred by patients were omitted from the analysis. The inclusion of those two components seems unlikely to change the conclusions of the study, as is the case with the fact that the estimate of cost of terminal hospitalised care associated with the intervention was based on data associated with a different chemotherapy. The authors justified such assumption on the grounds of similar observed effects of both strategies in terms of response rate and median survival time. The sensitivity analysis showed that each additional day of hospitalisation for terminal care under the intervention would add Can$1,000 to the base case cost-effectiveness ratio reported above.

Other issues
The authors’ conclusions were justified in terms of their sensitivity analysis. However, their conclusions rely to a crucial degree upon the assumption of a health gain in terms of survival, which is based on data of questionable quality. The issue of generalisability should wait to be addressed until after the more compelling issue of the validity of the estimate of benefits is resolved.

Implications of the study
Further studies are warranted to reduce the critical uncertainty in the estimate of effectiveness attached to the intervention. A prospective study with concurrent, comparable controls is needed to provide clearer evidence of the benefit claimed for the use of gemcitabine in advanced non-small cell lung cancer patients. Only after the improved survival outcomes associated with such an intervention are well established, can its low incremental costs be linked to a potentially efficient result in the allocation of the corresponding scarce medical resources.

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