Cost-effectiveness of alemtuzumab for T-cell prolymphocytic leukemia
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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.

CRD summary
The study compared the cost-effectiveness of alemtuzumab with conventional chemotherapy in patients with the rare T-cell prolymphocytic leukaemia disease. The authors concluded that although there was substantial uncertainty around model findings, alemtuzumab was potentially cost-effective if used earlier in the course of the disease replacing the use of multiple alternative therapies. The analysis required the use of several assumptions, so although the authors’ conclusions appear valid, there is high uncertainty in the clinical parameters.

Type of economic evaluation
Cost-utility analysis

Study objective
The cost-effectiveness of alemtuzumab was compared with conventional chemotherapy for patients with T-cell prolymphocytic leukaemia who had completed at least one prior conventional therapy and were not suitable for stem cell transplantation.

Interventions
The monoclonal antibody alemtuzumab (administered as two-hour intravenous infusion three times a week) was compared with conventional chemotherapy (including pentostatin, cyclophosphamide plus vincristine plus prednisolone plus doxorubicin, fludarabine and cladribine) for patients with T-cell prolymphocytic leukaemia.

Location/setting
UK/Tertiary care.

Methods
Analytical approach:
The analysis was based on a decision tree with a lifetime horizon. The authors stated that the study was conducted from the perspective of the UK NHS.

Effectiveness data:
Some evidence for the model was taken from the literature, but the authors stated that many assumptions were required because of the limited published studies on the efficacy and safety of these treatments. Key evidence on the efficacy of alemtuzumab came from a case series of 39 patients with T-cell prolymphocytic leukaemia who were treated with alemtuzumab as a two-hour intravenous infusion, generally three times a week. Efficacy for conventional therapy came from another case series of patients receiving some of the conventional treatments assumed. Overall survival was the key outcome of the clinical analysis.

Monetary benefit and utility valuations:
Utility valuations were taken from a study of patients with chronic lymphocytic leukaemia for three conditions (time spent on treatment, in response, and in progressive disease).

Measure of benefit:
Quality-adjusted life-years (QALYs) were used as the summary benefit measure and were discounted at an annual rate of 3.5%.

Cost data:
Three main cost categories were included: drugs, drug administration, and management of opportunistic infections in the alemtuzumab group (particularly cytomegalovirus reactivation). Quantities of resources used were based on published sources and expert opinions. Unit costs were taken from NHS reference costs, the British National Formulary, and published studies. Costs were estimated in UK £ and were converted into Euros (EUR) at the exchange rate reported in January 2012. A 3.5% annual discount rate was applied.

Analysis of uncertainty:
Various deterministic and probabilistic sensitivity analyses were carried out. The expected value of perfect information (EVPI) was calculated for four different scenarios based on the combination of two key assumptions made in the model. The scenarios involved one or three lines of conventional therapy with alemtuzumab started at three or seven months after diagnosis.

Results
Given the uncertainty in the model assumptions, no base case was simulated. Four scenarios were considered.

When assuming one line of conventional therapies with alemtuzumab started seven months after diagnosis, the incremental cost was EUR 15,277 and the incremental QALYs were 0.1596, and the incremental cost per QALY gained (incremental cost-effectiveness ratio, ICER) was EUR 95,746.

When assuming one line of conventional therapies with alemtuzumab started three months after diagnosis, the incremental cost was EUR 15,909 and the incremental QALYs were 0.2449, and the ICER was EUR 64,973.

When assuming three lines of conventional therapies with alemtuzumab started seven months after diagnosis, the incremental cost was EUR 6,424 and the incremental QALYs were 0.1596, and the ICER was EUR 40,265.

When assuming three lines of conventional therapies with alemtuzumab started three months after diagnosis, the incremental cost was EUR 8,365 and the incremental QALYs were 0.2449, and the ICER was EUR 34,163.

Substantial changes in the cost-utility ratios were observed when changing the survival curves for patients treated with alemtuzumab based on the proportion of patients who were still alive at the end of month 53. Another influential input was the length of time in progressive disease for the two groups.

The probabilistic sensitivity analysis showed that the highest probability of alemtuzumab being cost-effective at a threshold of EUR 36,300 per QALY gained was 53% in the fourth scenario considered above (three lines of treatment and alemtuzumab given three months after diagnosis).

The expected value of perfect information analysis showed that resolving parameter uncertainty in this specific patient population would have considerable value, up to EUR 5.3 million.

Authors' conclusions
The authors concluded that there was substantial uncertainty around model findings, but in general alemtuzumab was potentially cost-effective if used earlier in the course of T-cell prolymphocytic leukaemia and where it replaced the use of multiple alternative therapies.

CRD commentary
Interventions:
The rationale for the selection of the comparators was clear as there were limited treatment options for this patient population.

Effectiveness/benefits:
Clinical data came from two case series with several potential drawbacks. First, the sample size of the two studies was relatively small. Second, there were some differences in the patient population of the two studies. Third, the use of a non-randomised study might have introduced some bias. The authors acknowledged that some bias in favour of alemtuzumab could not be excluded. Several sensitivity analyses were conducted and showed the strong impact of some assumptions.
The use of QALYs was appropriate given the impact of the disease on mortality and morbidity of this patient population. No utility weights for this rare disease were available; data from a similar condition were used, although no details were given on instruments used.

Costs:
The costs categories used in the model and the sources used to derive unit costs were consistent with the perspective of the NHS. A breakdown of cost items was provided. Most of the assumptions required were explicitly reported. Appropriate discounting was applied. The price year was reported, which would allow reflation exercises in other time periods. Cost estimates were varied in the sensitivity analyses.

Analysis and results:
No formal base case analysis was carried out due to the uncertainty around the model assumptions. Extensive sensitivity analyses were carried out. The results of all the simulations were clearly presented and discussed. The study results were clearly presented for each scenario. The authors acknowledged the limitations of the analysis mainly related to the lack of good clinical evidence. This study should be seen as an explanatory analysis of the potential cost-effectiveness of alemtuzumab. Future studies should corroborate these results that should be considered specific to the UK context.

Concluding remarks:
The analysis used a cost-effectiveness methodology that required the use of several assumptions. Although the authors’ conclusions appear valid, there is high uncertainty in the clinical parameters.

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