Economic analysis of basiliximab in renal transplantation
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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
The use of basiliximab (20 mg intravenously daily on day 0 and day 4 after the transplant) for the prevention of renal allograft rejection. Basiliximab is a chimeric alpha-chain of the interleukin-2 receptor, which is important in activating the immune response. The patients were assessed at predetermined intervals during the first 12 months after transplant.

Type of intervention
Secondary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients who had just undergone renal transplant.

Setting
The setting was a hospital. The economic analysis was conducted as part of a multi-centre trial that took place in Canada, UK, Germany, France, Belgium, Switzerland and Norway.

Dates to which data relate
The dates during which the effectiveness evidence and cost evidence were gathered were not given. Canadian 1999 prices were used.

Source of effectiveness data
The effectiveness data were derived from a single study and from the authors' assumptions.

Link between effectiveness and cost data
The effectiveness data were derived from a different source from the cost data. The cost data were derived from published Canadian studies, whereas the effectiveness data were derived from a multinational trial.

Study sample
No power calculations to determine the sample size were reported. No information was given on how the patients had been recruited and whether some had refused to participate. The paper gave conflicting information on the size of the sample, either 376 or 380 patients. There was also conflicting information on the size of the placebo group, either 180 or 176 patients. The basiliximab group comprised 190 patients. The data were published elsewhere (see Other Publications of Related Interest no.1).
Study design
This was a multi-centre (21 centres) randomised controlled trial in which the patients were randomised within each centre. The follow-up was carried out for 12 months after the transplant.

Analysis of effectiveness
The analysis was conducted on an intention to treat basis. The primary health outcome used to assess the effectiveness was the percentage of patients who experienced acute rejection.

The patients were shown to be comparable in terms of their age. The mean age was 47.2 years, 47.0 years in the placebo group versus 47.4 years in the basiliximab group, (p=0.726). The proportion of Caucasians was 96.2% in the placebo group and 94.2% in the basiliximab, (p=0.710). The proportion of males was 63.4% in the placebo group and 66.3% in the basiliximab group.

Effectiveness results
Six months after the transplant, 34.8% of the basiliximab group and 52.2% of the placebo group had experienced acute rejection, (p<0.001).

Twelve months after the transplant, 37.9% of the basiliximab group and 54.8% of the placebo group had experienced acute rejection, (p=0.002). This gave an absolute risk reduction of 16.8%.

The incidence of steroid-resistant first rejection episodes was 10% in the basiliximab group and 23% in the placebo group, (p<0.001).

It was stated that there was no difference between the groups in the incidence of important adverse events such as infection and malignancy.

Clinical conclusions
The rate of acute rejection was reduced when renal transplant patients who were receiving Neoral and steroids were also given basiliximab.

Modelling
A model was used to estimate the effects and costs of basiliximab for 5 years after transplantation.

Methods used to derive estimates of effectiveness
The authors assumed that the absolute risk reduction for rejection for 5 years would be the same as that for 1 year.

Estimates of effectiveness and key assumptions
The 5-year absolute risk reduction for rejection was 16.8%.

Measure of benefits used in the economic analysis
No summary benefit measure was used in the economic analysis. A cost-consequences analysis was therefore performed. The health benefits are associated with the effectiveness results.

Direct costs
The costs were calculated for initial hospitalisation, treatment of acute rejection, graft function, graft loss and dialysis, maintenance of immunosuppressive drugs, and follow-up hospitalisation.
The costs and the resource quantities were not reported separately.

The drug costs were obtained from a Canadian multi-centre study which used acquisition data from hospital pharmacies in Canada (see Other Publications of Related Interest below). The cost of basiliximab (Simulect, Novartis) was taken as zero in the initial cost calculation as it was not yet available on the open market. The cost of dialysis was taken from a study in British Columbia. The cost of other resources was taken from the Canadian multi-centre study.

Discounting to take account of time differences between the costs and the benefits was not carried out. The authors state that they used the Canadian price index to discount the costs in order to take inflation into account. They used a rate of 1.49% per year to adjust the costs so that they would be expressed in 1999 Canadian dollars.

**Statistical analysis of costs**
No statistical analysis of the costs was reported.

**Indirect Costs**
The indirect costs were not included in the analysis.

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

**Sensitivity analysis**
A one-way sensitivity analysis was carried out identify those variables that influenced the costs. The sensitivity analysis was conducted in two stages. First, the parameter associated with the control group was varied, keeping the difference between the two therapies constant. Then, the parameter of the experimental therapy was varied. The following variables were investigated:

- the duration of initial hospital stay;
- the risk of acute rejection in first year;
- the percentage of patients who experience graft loss and then survive;
- the days of hospitalisation excluding acute rejection events (AREs);
- the percentage of steroid-sensitive AREs requiring hospitalisation;
- the percentage of steroid-resistant AREs requiring hospitalisation; and
- the percentage of days of OKT3 therapy as inpatient.

The following parameters were varied:

- the number of days on dialysis given graft loss and death;
- the number of days with a functioning graft for patients who die with a functioning graft, die with a failed graft, and survive with a failed graft; and
- the number of hospitalisation days as a result of graft loss.

It was stated that the ranges were chosen by reference to the literature, through clinical experience and from expert opinion.
Estimated benefits used in the economic analysis
See the 'Effectiveness Results' section.

Cost results
The total 1-year cost per transplant patient was Can$55,393 in the control group and Can$50,839 in the basiliximab group.

When the model was applied to the following 4 years, the projected 5-year total cost per transplant patient was Can$141,690 in the control group and Can$130,592 in the basiliximab group.

The cost of adverse events was dealt with in the costing.

Synthesis of costs and benefits
The effectiveness results showed that basiliximab therapy improved health outcomes. The cost analysis showed that, when priced at zero, basiliximab therapy reduced the costs by Can$4,554 per patient. Therefore, as long as basiliximab costs less than this amount it is a dominant treatment.

When the costs were calculated for an additional 4 years, the costs of basiliximab therapy per patient were Can$11,908 less than for a control group patient. Thus, provided that basiliximab therapy costs less than this, it is the dominant treatment.

The authors categorised parameters as sensitive if they led to a cost difference of more than Can$600. The most sensitive parameters, in order of their sensitivity (most sensitive given first), were:

the number of follow-up days in hospital for a basiliximab patient (excluding AREs), which could change the cost per patient by Can$4,262;

the initial length of stay in hospital for the basiliximab patient, which could change the cost per patient by Can$2,212;

the risk of ARE in the basiliximab patient, leading to a possible cost difference of Can$1,249;

the risk of graft loss in the basiliximab patient, which could change the cost per patient by Can$1,223; and

the length of hospital stay for the control group patient, which could change the cost per patient by Can$680.

Authors' conclusions
At a possible price of Can$3,000 per patient for basiliximab therapy, basiliximab is dominant and it achieves better clinical outcomes and reduces costs.

CRD COMMENTARY - Selection of comparators
The comparison group was valid as the drug treatment received represents standard practice for renal transplant patients.

Validity of estimate of measure of effectiveness
The analysis was partly based on a randomised controlled trial, which was an appropriate study design. The authors did not show whether the study population was representative of all kidney transplant patients. The patient groups were shown to be comparable at analysis for very few parameters. The authors pointed out that the different centres did not give identical treatment, in particular the length of hospitalisation following the transplant. They also made assumptions in order to extrapolate the results to 5 years. The authors did not present the results in terms of survival or adverse events, assuming that they were equal.
Validity of estimate of measure of benefit
The estimate of benefit was derived directly from the effectiveness evidence.

Validity of estimate of costs
The cost data covered the correct categories necessary to cost the treatment, but there were weaknesses in the way it was conducted. The cost data were derived from different Canadian sources, whereas the effectiveness data was derived from a multinational study. When the authors estimated the costs over a 5-year period, they did not discount for the fact that the costs were spread over several years. In addition, they only adjusted for inflation in the health care sector. The costs and the resource quantities were not reported separately, thus reducing transparency and generalisability.

The authors pointed out several times the crucial role of hospital stay in determining the overall costs. However, they did not include the indirect costs for the patient's family when patients spend less time in hospital. The price data were derived from published sources. The data relating to quantities were derived from the study and published sources. No statistical analysis of these data was carried out. No statistical analysis was performed of the cost estimates. Finally, the ranges of the parameters for the sensitivity analysis were justified, although without precise reference to the sources.

Other issues
The authors made appropriate comparisons of their findings with those from other studies. However, the issue of generalisability to other settings was only partially addressed by the sensitivity analysis. It would have been helpful if the price and quantity data had been reported separately. This would have both aided transparency and demonstrated whether the Canadian cost findings would be replicated in other countries. The authors acknowledged that extending the results for an additional 4 years was speculative.

Implications of the study
The authors realised the usefulness of gathering the effectiveness results for another 4 years to assess the long-term effect of basiliximab. It would have been useful if the cost data had been derived directly from the patients participating in the trial.

Source of funding
Funded by Novartis Pharmaceuticals (Canada) Inc. (manufacturers of basiliximab).

Bibliographic details

PubMedID
11435967

Original Paper URL
http://www.transplantjournal.com/

Other publications of related interest


**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
Antibodies, Monoclonal /economics /therapeutic use; Azathioprine /therapeutic use; Cost Control; Cyclosporine /therapeutic use; Double-Blind Method; Drug Costs; Drug Therapy, Combination; Female; Humans; Immunosuppressive Agents /economics /therapeutic use; Kidney Transplantation; Male; Middle Aged; Prednisone /therapeutic use; Prospective Studies; Recombinant Fusion Proteins

**AccessionNumber**
22001006420

**Date bibliographic record published**
30/11/2002

**Date abstract record published**
30/11/2002