An economic and quality-of-life assessment of basiliximab vs antithymocyte globulin immunoprophylaxis in renal transplantation

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
Two prophylaxis schemes against organ rejection in renal transplantation were compared in the study:

- basiliximab 20 mg i.v. bolus on days 0 and 4 in conjunction with cyclosporin A microemulsion (CsA ME) on day 0, mycophenolate mofetil (MMF) and steroids; and
- antithymocyte globulin (ATG) 15 mg/kg i.v. per day for up to 14 days in addition to CsA ME, MMF, and corticosteroids.

Variations in the baseline indications and administration were reported in the paper.

Type of intervention
Secondary prevention.

Economic study type
Cost-utility analysis.

Study population
The study population comprised unselected patients undergoing renal transplantation. Specific exclusion criteria were not reported.

Setting
The setting was a transplantation centre. The economic study was carried out in the USA.

Dates to which data relate
Data on effectiveness and resource use were gathered from November 1997 to March 1999. The price year appears to have been 1997, although not explicitly reported.

Source of effectiveness data
The effectiveness evidence came from a single study.

Link between effectiveness and cost data
The costing was performed prospectively on the same sample of patients as that used in the effectiveness study, but actual hospitalisation costs were derived from a sub-sample of 40 patients (please see below for details).
Study sample
Power calculations were not reported and no evidence was provided to show whether the initial sample size was appropriate for the study question. The method of sample selection was not stated. An overall sample of 138 patients was enrolled: 70 patients (mean age: 45 years; weight: 77.5 kg; 53% men) were included in the basiliximab group and 68 patients (mean age: 50 years; weight: 80.8 kg; 65% men) in the ATG group. However, three patients in the ATG group did not receive any therapy, thus the final group of ATG consisted of only 65 patients. Patients were grouped into high-risk subgroup (patients who were either African Americans, had panel-reactive antibodies (PRA) greater than 30% at baseline, or had a cold ischaemia time for more than 24 hours), and low-risk subgroup (all other patients). There were 24 high-risk patients and 41 low-risk patients in the ATG group and 24 high-risk patients and 46 low-risk patients in the basiliximab group.

Study design
This was an open-label phase IIIb clinical trial, carried out in six medical centres in the USA. The method of randomisation was not reported. Patients were followed for one year or until death, whichever was earlier, the one-year retention rate was 94% in both groups. No blinded assessment of outcome was performed.

Analysis of effectiveness
The basis of the analysis of the clinical study appears to have been treatment completers only as the three patients randomly allocated to the ATG group who did not receive any dose of drug were excluded from the effectiveness analysis. The primary health outcomes used in the analysis were health-related quality of life (estimated using the visual analogue scale (VAS) from the EuroQol instrument at baseline, day 4, and weeks 1, 2, 4, 12, 24, and 52) and the quality-adjusted survival curve (estimated for the year subsequent to treatment by multiplying survival probability by VAS score at each follow-up interview). Secondary outcomes were mortality, acute clinical rejection, biopsy-proven acute rejection, second transplants, delayed graft function, 6-month survival, and one-year survival (most of these results were presented in a previous abstract, but no paper was available). Study groups were shown to be comparable at baseline in terms of demographic and clinical characteristics of donors and patients receiving the organ. However, patients in the basiliximab group were significantly younger than those in the ATG group.

Effectiveness results
The mean VAS scores in the ATG group were as follows:

Baseline 68, day four 67.5, week one 72.2, week two 74.9, week four 81.2, week twelve 81.1, week twenty-four 81.7, and week fifty-two 82.4.

The mean VAS scores in the basiliximab group were as follows:

Baseline 66.9, day four 70.4, week one 74.2, week two 76.2, week four 80.2, week twelve 81.9, week twenty-four 80.2, and week fifty-two 83.8.

The total quality-adjusted life year 81.5 +/- 16.5 in the ATG group and 81.1 +/- 19.5 in the basiliximab group. The difference (0.45; 95% CI: -5.9 - 6.8) was not statistically significant.

As regards secondary outcome, the number of deaths was 4 (basiliximab) and 2 (ATG); the rate of acute clinical rejection was 33% (basiliximab) and 32%(ATG); the biopsy-proven acute rejection was 19% (basiliximab) and 18%(ATG); the rate of second transplants was 7% (basiliximab) and 9%(ATG); the rate of delayed graft function was 23% (basiliximab) and 34%(ATG); the 6-month survival was 94% (basiliximab) and 97%(ATG); and the one-year survival was 94% (basiliximab) and 98%(ATG).

None of the differences between groups in the primary and secondary outcomes were statistically significant. The subgroup analysis showed similar results.
Clinical conclusions
The effectiveness analysis showed that the two immunoprophylaxis therapies were similar in terms of clinical results and quality of life as perceived by the patients.

Measure of benefits used in the economic analysis
The effectiveness study showed that the two immunoprophylaxis approaches were similarly effective and led to comparable quality of life scores and, as a consequence of these results, a cost-minimisation analysis was conducted.

Direct costs
Discounting was not relevant as costs were incurred over a period of one year. A detailed breakdown of costs was provided, but unit costs were not reported separately from quantities of resources used. Only drug unit costs were reported. The health service costs included in the economic evaluation were hospitalisation, subsequent transplant-related hospitalisation, outpatient visits, and medication use in both inpatient and outpatient settings. Hospitalisation data included length of hospital stay, days in the intensive care unit (ICU), and procedures. Organ acquisition costs were not included in the analysis because they were incurred prior to randomisation. The cost/resource boundary adopted in the study was not stated. Resource use was based on actual data collected alongside the trial. The estimation of hospital costs was derived from the bills of 40 patients (hospitalised in one centre). The costs incurred by the remaining 95 patients (in the other five centres) were estimated using a linear regression imputation technique. Charges were converted to costs using the hospital-wide Medicare cost to charge ratio. Physician fees were estimated from Medicare reimbursement rates, while drug expenses were based on average wholesale prices. Other costs were based on reimbursement rates. The price year appears to have been 1997.

Statistical analysis of costs
Univariate and multivariate statistical analyses were conducted to analyse costs, mainly due to the skewed distribution of costs. The same subgroup analysis as that conducted in the effectiveness analysis was carried out with costs.

Indirect Costs
Indirect costs were not included.

Currency
US dollars ($).

Sensitivity analysis
No sensitivity analyses were performed.

Estimated benefits used in the economic analysis
Please refer to the effectiveness results reported earlier.

Cost results
Total initial costs were $54,729 in the ATG group and $45,857 in the basiliximab group and the difference favoured the basiliximab group ($8,872; 95% CI: $1,169 - $16,573), mainly due to lower initial hospitalisation costs and lower drug costs.

Post-discharge costs were similar: $19,183 in the ATG group and $19,213 in the basiliximab group, with a difference of only $30 (95% CI: -$4,757 - $4,697). The multivariate regression analyses led to similar results.
Synthesis of costs and benefits
This was not relevant as a cost-minimisation analysis was conducted.

Authors' conclusions
The authors concluded that the immunoprophylaxis treatment based on basiliximab and early CsA ME reduced the costs of care without reducing the quality of care as perceived by the patients in comparison with the therapy consisting of ATG with delayed CsA ME.

CRD COMMENTARY - Selection of comparators
The authors discussed the choice of the comparators and in the present analysis focused on the differences in terms of administration times and doses between basiliximab and ATG, but did not state whether other therapies were available. You, as a user of this database, should decide whether they represent widely used immunosuppressive therapies in your own setting.

Validity of estimate of measure of effectiveness
The analysis of effectiveness was based on a randomised controlled trial, which appears to have been appropriate for the study question. However, the method of randomisation was not reported. Study groups were shown to be comparable at baseline, with the exception of patient age. The effect, if any, this difference would have on the results was not discussed within the paper. Subgroup analyses were also performed. The study sample appears to have been representative of the study population, although the method of patient selection was not reported. The study was conducted in six large centres in the USA. No blinded outcome assessment was performed, thus assessment bias may have occurred. Furthermore, the basis of the analysis was treatment completers only. The major limitations to the internal validity of the analysis were the lack of power calculations and the fact that no evidence was provided about whether the initial sample size was appropriate to detect statistically significant differences between the groups.

Validity of estimate of measure of benefit
No summary benefit measure was used in the economic analysis as no statistically significant differences were found in any of the clinical outcomes used in the effectiveness study. The analysis was therefore categorised as a cost-minimisation study (see validity of effectiveness comments above).

Validity of estimate of costs
The perspective adopted in the study was not explicitly reported, although it could have been that of the third party payer as cost data were mainly derived from Medicare reimbursement rates. If this is the case, it appears that all relevant categories of costs were included in the analysis. The costs of the organ were not included in the analysis as they were incurred before data collection, which began with randomisation. Several statistical analyses of costs and quantities were performed, but no sensitivity analyses were reported. The cost estimates were quite specific to one study hospital; this could limit the generalisability of the study results. Unit costs and quantities of resources used were not reported separately. The price year was not explicitly reported, although it appears to have been 1999. Reporting the price year facilitates reflation exercises in other settings. The sources of cost data were clearly reported.

Other issues
The authors compared their findings with those from other published studies only for the effectiveness side of the analysis. The issue of the generalisability of the study results to other settings was not addressed and no sensitivity analyses were performed. As a consequence, the external validity of the analysis was low. The study enrolled unselected patients undergoing renal transplantation and the study results apply to both high- and low-risk patients. The authors discussed the impact of different drug administration procedures and stated that cost data were collected only from one hospital and, as such, these data may not have been representative of the costs incurred in the remaining five centres included in the study.
Implications of the study
The study suggests that patients receiving basiliximab for immunosuppressive therapy after renal transplantation had lower fist-year costs compared to patients receiving ATG, but quality of life was similar. The authors suggested that future research should further assess the economic and clinical benefits of the basiliximab treatment on low-risk patients.

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