Pharmacoeconomic evaluation of Simulect prophylaxis in renal transplant recipients

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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 (BAS) in conjunction with maintenance triple drug therapy with oral cyclosporin, corticosteroids and azathioprine, for the prophylaxis of acute rejection after renal transplantation. BAS was administered as a 20-mg intravenous bolus injection on day 0 and day 4 after transplantation.

Type of intervention
Secondary prevention.

Economic study type
Cost-effectiveness analysis.

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

Setting
The setting was a hospital and secondary care. The economic study was carried out in several countries.

Dates to which data relate
The dates when the effectiveness and resource use data were collected were not reported. The price year was 1996.

Source of effectiveness data
The effectiveness evidence was derived from a single study.

Link between effectiveness and cost data
The costing was carried out prospectively on the same sample of patients as that used in the effectiveness analysis.

Study sample
Limited information on the study sample was provided as the methods and results of the clinical study had been published already. An overall sample of 340 patients was enrolled in the trial. There were 168 patients in the BAS group and 172 patients in the placebo group. The overall sample was predominantly male and of Caucasian origin, and the mean age was 44 years.

Study design
This was a prospective, multi-centre, international, double-blind, placebo-controlled clinical trial that was carried out at 31 centres in 12 countries (Belgium, Finland, France, Israel, Italy, Mexico, Poland, South Africa, Turkey, UK,
Germany, and Spain). The patients were followed for 12 months but the outcomes were only reported for the first 6 months, so as to match the 6-month time horizon of the cost analysis. No patient appears to have been loss to the follow-up assessment.

**Analysis of effectiveness**
The analysis of the clinical study was conducted on an intention to treat basis. The primary outcome measures used were:

- the rate of deaths;
- the proportion of patients returning to regular dialysis;
- the rate of failed grafts;
- the proportion of patients who had a nephrectomy;
- the number of patients requiring retransplantation;
- the incidence of first confirmed acute rejection episode;
- the rate of biopsy-proven acute rejection episodes; and
- the rate of treatment failure (acute rejection, graft loss, or death).

All outcome measures referred to a 6-month post-transplantation period. The study groups were comparable at baseline in terms of their demographics and disease characteristics.

**Effectiveness results**
The rate of deaths in the whole cohort was 1.1%.

The proportion of patients returning to regular dialysis was 6.5% in the BAS group and 10.5% in the placebo group.

The rate of failed grafts was 6.5% in the BAS group and 11% in the placebo group.

The proportion of patients who had a nephrectomy was 4.2% in the BAS group and 9.4% in the placebo group.

There was only one retransplantation in the placebo group.

The incidence of first confirmed acute rejection episode was 20.8% in the BAS group and 34.9% in the placebo group, (p=0.005).

The rate of biopsy-proven acute rejection episodes was 18.5% in the BAS group and 29.1% in the placebo group, (p=0.023).

The rate of treatment failure was 25.6% in the BAS group and 39.5% in the placebo group, (p=0.008).

**Clinical conclusions**
The effectiveness analysis showed that BAS patients experienced significantly fewer cases of treatment failure, including rejection episodes and deaths, in comparison with placebo patients.

**Measure of benefits used in the economic analysis**
The summary benefit measure was the number of treatment failures. This was derived directly from the effectiveness analysis.
Direct costs
Discounting was not relevant since the costs were incurred during 6 months. The unit costs were not presented separately from the quantities of resources used. The health services included in the economic evaluation were grouped using the following categories:

- overnight hospitalisation, in the intensive care unit (ICU) and non-ICU;
- immunosuppressive therapies;
- procedures (ultrasound, magnetic resonance imaging or angiograms, computed tomography scan, and Doppler imaging);
- laboratory tests (biochemistry, haematology, and urinanalysis);
- outpatient visits (consultations, day admissions and emergency room visits, excluding dialysis and biopsies);
- postoperative dialysis;
- nephrectomy (marginal cost);
- renal biopsies;
- major concomitant medication use; and
- BAS.

The cost/resource boundary of the health service payer was adopted. Resource use was estimated using patient-level data derived from the sample of individuals included in the clinical trial. Since some resource use data were unavailable for some patients, their resource use was assumed to have been similar to the average of the patients with available data. Resource use data from individual countries were pooled for the analysis. Some quantities of resources used (i.e. BAS doses and patients requiring dialysis after graft loss) were based on authors' assumptions. The unit costs came from either local service providers or national data sources for each country involved in the study. Since cost data were not available for Israel, Turkey, South Africa, Poland and Mexico, simple median averages of the available cost data from other countries were used. The costs were valued at 1997-98 prices but were presented using 1996 values.

Statistical analysis of costs
Standard statistical analyses of the costs were carried out to test the statistical significance of differences in the total costs. The validity of using pooled data for resource use was confirmed by an analysis of variance.

Indirect Costs
The indirect costs were not considered in the economic evaluation.

Currency
US dollars ($). Health care-specific purchasing power parity (PPP) United States (US) dollar exchange rates were obtained for each country.

Sensitivity analysis
Univariate sensitivity analyses were performed to examine the impact of changing resource use assumptions on total costs. Such analyses excluded the costs of nephrectomy, excluded the marginal cost of a nephrectomy, and excluded the hospital costs of nephrectomy for 10 patients with missing data.
Estimated benefits used in the economic analysis
See the 'Effectiveness Results' section.

Cost results
None of the differences between groups in resource use data reached statistical significance.

The total estimated 6-month costs per patient in 1996 PPP US dollars were $34,821 (+/- 18,387) (range: 13,601 - 122,827) in the BAS group and $34,172 (+/- 22,927) (range: 3,827 - 184,595) in the placebo group. The difference was $649 (95% confidence interval, CI: -3,480 - 5,078).

None of the differences in total costs and in sub-groups of costs reached statistical significance.

The sensitivity analysis showed that the changes in the cost assumptions did not significantly affect the magnitude of cost-differences.

At 12 months, the estimated costs were $37,113 (+/- 23,840) with BAS and $37,070 (+/- 26,949) with placebo. The difference in costs of $43 (95% CI: -5,382 - 5,468) did not reach statistical significance.

Synthesis of costs and benefits
An incremental cost-effectiveness ratio was calculated to combine the costs and benefits of BAS over placebo.

The incremental cost per treatment failure avoided with BAS over placebo was $4,669. The number-needed-to-treat for benefit (i.e. no benefit failure) was 7.2 (95% CI: 4.3 - 25.2), that is, 8 patients needed to be treated with BAS rather than placebo in order for one additional patient to benefit (i.e. have no treatment failure in the 6 months post-transplantation).

Authors' conclusions
Basiliximab (BAS) in combination with triple immunosuppressive therapy led to better clinical outcomes without significantly increasing resources use or costs over a 6-month period. The cost-saving potential of BAS could increase over time.

CRD COMMENTARY - Selection of comparators
The selection of the comparator reflected the typical prophylactic treatment for renal transplant recipients. You should decide whether this is a valid comparator in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness evidence was based on a well-conducted clinical trial. The use of random assignment of patients, double-blinding, and multiple centres enhanced the internal validity of the analysis. However, limited information on the design and methods of analysis was provided because the primary study had been published already.

Validity of estimate of measure of benefit
The summary benefit measure was specific to the disease considered in the study and, as such, is hardly comparable with the benefits of other health care interventions. It was derived directly from the effectiveness analysis.

Validity of estimate of costs
The authors stated explicitly the perspective adopted in the study. All the relevant categories of costs were included. The unit costs were not presented separately from the quantities of resources used, which reduces the possibility of
replicating the study. The resource use data came from local sources, which were then pooled. The validity of such pooling was confirmed using statistical tests. The authors made some assumptions to derive missing values. Resource use assumptions were varied in the sensitivity analysis. The costs came from local sources and PPP was used to express the total costs under a common currency. The price year was reported, which makes reflation exercises in other settings easy. The authors noted that the inclusion of indirect and non-medical costs could have resulted in cost-savings associated with BAS.

Other issues
The authors stated that their findings confirmed those from a published economic evaluation of BAS. The evidence and costs came from multiple countries, which ensure a high generalisability of the results. Some sensitivity analyses were also performed, which further enhanced the external validity of the study. The study referred to renal transplant recipients and this was reflected in the authors' conclusions.

Implications of the study
The study results supported the use of BAS in conjunction with triple immunosuppressive therapy for the prevention of acute rejection in renal transplant recipients.

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None stated.

Bibliographic details

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11750367

Other publications of related interest


Indexing Status
Subject indexing assigned by NLM

MeSH
Antibodies, Monoclonal /economics /pharmacokinetics /therapeutic use; Biopsy; Costs and Cost Analysis; Double-Blind Method; England; Humans; Kidney Transplantation /economics /immunology /mortality; Length of Stay; Placebos; Postoperative Complications /classification /epidemiology; Recombinant Fusion Proteins /economics /pharmacokinetics /therapeutic use; Survival Rate; Treatment Failure; Treatment Outcome

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