A prospective economic evaluation of basiliximab (Simulect) therapy following 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
Basiliximab (Simulect), a chimeric anti-interleukin-2-receptor (anti-IL-2R) monoclonal antibody, plus dual immunosuppressive therapy (cyclosporine modified and corticosteroids) versus dual therapy alone (placebo plus cyclosporine modified and corticosteroids) to reduce kidney transplant rejection.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
Kidney transplant patients aged between 18 and 65 years.

Setting
21 US Transplant Centres.

Dates to which data relate
Both effectiveness and economic data were collected between June 1995 and May 1997. 1997 prices were used.

Source of effectiveness data
Effectiveness data were derived from a single study.

Link between effectiveness and cost data
The costing was undertaken prospectively on the same patient sample as that used in the effectiveness study.

Study sample
The study sample consisted of 346 kidney transplant patients (173 in each group) taken from 21 US transplant centres. Treatment groups were similar with respect to age (mean age 44.9 years in basiliximab group versus 46.2 years in placebo group), gender (64% male versus 62%), race (68% Caucasian versus 61%), donor source (69% cadaveric versus 71%) and HLA-antigen mismatches (mean 4.0 versus 3.9). No power calculations were provided. Data from all patients were included in the final analysis on an intention to treat basis.
The study was a randomised, double-blind, placebo-controlled clinical trial carried out in 21 transplant centres in USA. The duration of follow-up was one year. Patients were randomised to receive either basiliximab or placebo prior to transplantation. Neither the method of randomisation nor the blinding method was stated.

**Analysis of effectiveness**
Analysis was undertaken on an intention to treat basis. The primary health outcomes were the incidence of acute rejection and adverse events. The groups were shown to be comparable with respect to demographic variables, disease characteristics, and immunologic and donor parameters. There were no adjustments for confounding factors.

**Effectiveness results**
There was a significant reduction in the incidence of acute rejection (38% versus 55%; p<0.01) in the basiliximab arm of the trial, and this was accomplished without increasing the overall cost of care. Fewer basiliximab-treated patients (8% versus 15%; p=0.03) were hospitalised. This observation suggested less serious illness among basiliximab-treated patients because the overall incidence of infection was similar between the groups. In terms of serious adverse events, there were no clinical differences between the two groups (54% of basiliximab patients versus 61% of placebo patients).

**Clinical conclusions**
The study revealed that induction immunosuppression with basiliximab, combined with cyclosporine modified and corticosteroids, was therapeutically beneficial during the initial post-transplant year. There were significant reductions in the incidence of acute allograft rejection, without associated increases in rates of infections or other adverse events.

**Measure of benefits used in the economic analysis**
No summary benefit measure was used. Clinical outcomes were left disaggregated within a cost-consequences analysis.

**Direct costs**
Direct medical costs were determined for all hospitalisations, outpatient provider visits, procedures (excluding the initial transplant procedure), laboratory and diagnostic tests, and immunosuppressants. Charges for 1996 were used and converted to costs using the 1996 national average of rural and urban state-wide hospital operating cost-to-charge ratio. Cost values were adjusted to 1997 dollars on the basis of the annual hospital market basket report. Cost estimates were taken from a number of sources including the Health Care Investment Analysis, the Medicare Resource Based Relative Value Scale, the Red Book, the Medicare Fee Schedule, and a sample of local hospitals. Discounting was not relevant as the follow-up period was only one year. Costs and quantities were analysed separately (for example, resource utilisation data were collected at each patient contact using standardised case report forms completed by trained study co-ordinators) and were based on actual data. Costs associated with certain procedures such as organ procurement were not included in the analysis because these resources would not be expected to differ between the two treatment groups. Costs were analysed from the perspective of the payer.

**Statistical analysis of costs**
The statistical significance of differences in median costs per patient between groups was determined using the non-parametric Wilcoxon rank sum test and 95% confidence intervals were reported.

**Indirect Costs**
Indirect costs were not included.

**Currency**
US dollars ($).
Sensitivity analysis
Sensitivity analyses were conducted by varying the key cost elements in the model, hospital per diem and physician consultation costs, by plus or minus 25% and plus or minus 50%. Because the clinical outcomes and resource utilisation values included were based on primary data gathered from case report forms from patients in the clinical trial, and because no other data to test the ranges of the primary clinical outcomes or resource consumption were available, sensitivity analyses could not be carried out for these parameters.

Estimated benefits used in the economic analysis
No summary benefit measures were determined in the study and thus the reader is referred to the effectiveness results reported previously.

Cost results
Total first-year medical costs were lower for the basiliximab group than for the placebo group ($28,927 versus $32,300; not significant). First-year hospital costs for treating acute rejection were also lower for the basiliximab group ($9,328 versus $10,761; not significant). The significant reduction in the incidence of acute rejection was achieved without increasing the overall cost of care. The adverse event profile of patients receiving basiliximab was economically indistinguishable from that of those treated with placebo.

Synthesis of costs and benefits
The authors did not undertake a synthesis of costs and benefits. Although the authors did not specifically state why a synthesis was not undertaken, the most likely reason is that the intervention was in fact the dominant strategy in that clinical results were superior and costs were lower, although cost differences did not reach statistical significance.

Authors’ conclusions
Induction immunosuppression with basiliximab, combined with cyclosporine modified and corticosteroids, was therapeutically beneficial and contained medical costs during the initial post-transplant year. In particular, significant reductions occurred in the incidence of acute kidney transplant rejection, without associated increases in rates of infections or other adverse events. The length of hospitalisation was found to be the most important factor determining costs.

CRD COMMENTARY - Selection of comparators
The reason for the choice of comparator was clear with placebo being used to test the relative effectiveness and cost-effectiveness of the treatment drug in a trial setting as an addition to dual immunosuppressive therapy.

Validity of estimate of measure of effectiveness
The validity of the measure of effectiveness should be high due to randomisation and results being presented on an intention to treat basis. In addition, the two groups were comparable at baseline and thus confounding factors did not have to be taken into consideration. No power calculations were undertaken so it is not clear whether the sample size was sufficient.

Validity of estimate of measure of benefit
No summary measure of benefit was reported due to the cost-consequences approach used in the study.

Validity of estimate of costs
The sources of direct costs and resource utilisation data were clearly presented and accounted for and sensitivity analyses were used to test the robustness of the economic findings. Costs were reported separately from quantities and
this should improve the external validity of the findings. However, only direct costs were included in the analysis. Also, no power calculations were included to determine whether the sample size was sufficient to detect differences in the economic analysis. As with the validity of the clinical findings, the authors recognised the threat to validity of only using a one-year follow-up period for the analysis.

Other issues
The robustness of the findings was tested using sensitivity analyses. This should improve the generalisability of the findings to other settings although the authors did not explicitly address this.

Implications of the study
The use of the intervention drug had significant clinical benefits without increasing costs. However, before changes can be recommended, the authors advised that more detailed, prospectively powered analyses should be carried out to evaluate the economic impact of various therapeutic regimens over longer periods of time.

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