Economic analysis of Neoral in de novo renal transplant patients in Canada

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
Drug treatment. The study compared a new microemulsion oral formulation of cyclosporine A (CsA) (Neoral) with the oral cyclosporine (Sandimmune SGC) in de novo renal transplant patients.

Type of intervention
Treatment and secondary prevention.

Economic study type
Cost-effectiveness analysis (cost-minimisation analysis).

Study population
The study population was de novo renal transplant patients recruited from five centres. Male and female recruits between the ages of 18 and 65 receiving a first or second renal transplant were included. Patients were predominantly male (>61.1%), Caucasian (>88.8%) and married (>65.0%) with a mean age of 41.6 years.

Setting
The study was carried out in institutions; five centres in Quebec and Ontario, Canada.

Dates to which data relate
Data for the effectiveness analysis were collected between February and November 1993. Retrospective health care resource utilisation data were collected on patient charts between March and July 1994.

Source of effectiveness data
Evidence for the outcomes was derived from a single study although some reference was made to journal articles published in 1994.

Link between effectiveness and cost data
The cost data were derived from the same patient sample (less dropouts) which took part in the clinical trial.

Study sample
41 de novo renal transplant patients were recruited from 5 centres to participate in the Canadian arm of OLM-105 clinical trial. Subjects were randomly assigned to two groups in a 1:1 ratio (Neoral n=20, SGC n=21). Of the 41 patients who were enrolled in the clinical study five were discontinued from the clinical trial (3 from SGC and 2 from Neoral). Those who, during the previous 2 week period, had received any drug that would interfere with CsA pharmacokinetics were excluded.
Study design
A randomised controlled double blind clinical trial (OLM-105) was carried out. Loss to follow up was 5/41 (12%).

Analysis of effectiveness
The analysis of the clinical study was based on treatment completers only. The primary health outcomes were the safety and tolerability of the new microemulsion oral formulation of cyclosporine. The groups were comparable in terms of age and sex and there were no significant differences noted between the groups.

Effectiveness results
10 (50%) of the Neoral patients had no rejection while 8 (40%) had 1 rejection and 2 (10%) had two rejections or more. 8 (44.4%) of the SGC patients had no rejections, 7 (38.9%) had one rejection and 3 (16.7%) had two or more rejections. No significant difference was seen between groups. The mean number of hospitalisations and their duration, inpatient and outpatient consultations were all lower for patients treated with Neoral. The length of time immunosuppressive drugs were administered was less for Neoral patients.

Clinical conclusions
The proportion of patients experiencing rejection episodes was comparable in both groups as rejections were evenly distributed across groups. The daily CsA starting dose ranged from 300 to 1800mg in the Neoral group and from 100 to 1400 mg in the SGC group. Although CLTs were slightly higher in the Neoral group the difference was not significant.

Measure of benefits used in the economic analysis
Since the analysis showed no significant difference in effectiveness between the intervention and the comparator, the economic analysis was based on the difference in costs.

Direct costs
Costs were looked at from two main perspectives, namely the Ministry of Health (MoH) and hospitals. MOH costs included: hospitalisation (per diem), physician fees that were composed of inpatient consultations, outpatient consultations and inpatient and outpatient procedures, and outpatient drugs (based on provincial formularies). Hospital costs included hospitalisations (75% of MoH per diem), inpatient and outpatient procedures, and inpatient drugs. MoH costs were basically average costs whereas some of the hospital costs considered were marginal costs as they had data on the patient utilisation of drugs.

Statistical analysis of costs
Two tailed statistical tests were performed with 0.05 as the upper limit of significance.

Indirect Costs
Indirect costs were not considered as the study focused on the provider perspective.

Currency
Canadian dollars (Can$).

Sensitivity analysis
Sensitivity analysis was performed to test the robustness of results by varying cost scenarios according to the ranges reported by each hospital.
Estimated benefits used in the economic analysis
The benefits used in the economic analysis were the savings in costs as the study was a provider-based study.

Cost results
In the MoH analysis total direct costs per patient for the twelve week period averaged Can$15,475 in the SGC group and Can$13,621 in the Neoral group (12% less). The cost difference of Can$1,854 was primarily due to lower hospitalisation costs (Can$1,250) and 2.1 times lower physician fees for inpatient and outpatient procedures in the Neoral group compared to the SGC group. A 10% hospitalisation cost reduction was observed for the Neoral group with both the highest and lowest hypotheses. Total cost reductions of 12-12.5% were also observed for the highest and lowest hypothesis respectively, both in favour of Neoral. From the hospital perspective the fixed hospitalisation cost was 9.6% lower in the Neoral group compared to the SGC group. The mean cost for inpatient drugs (excluding CsA) was 33.9% higher for the Neoral group. Total mean costs show a cost reduction for the Neoral group of Can$988 (6.8%). The cost reduction is 1.9 times lower than that calculated from MOH perspective.

Synthesis of costs and benefits
Costs and benefits were not combined due to the nature of the study.

Authors' conclusions
The results of the study indicate a trend towards a reduction in health care resource consumption and a concomitant decrease in direct health care costs associated with the use of Neoral in de novo transplant recipients. The higher cost of care for the SGC group compared to Neoral group could be attributable to the greater intensity of health care received. The difference could be explained by longer duration of hospitalisation and higher professional fees for the SGC group than for the Neoral group.

CRD COMMENTARY - Selection of comparators
The reason for the choice of comparators is clear. Use of SGC is limited by its variability and hence the poor absorption of CsA. CsA drug levels must be monitored at repeated intervals and the doses adjusted for satisfactory maintenance of a defined therapeutic window to avoid both toxicity and organ rejection from either too high or low CsA exposure.

Validity of estimate of measure of benefit
The study was based on the provider perspective and focused mainly on cost minimisation no benefits were mentioned. The benefits were assumed as (indicated by the clinical trial) to be equivalent.

Validity of estimate of costs
Prices were clearly indicated for the 12 week period under consideration. The authors noted that statistical difference was lacking due to the small sample size.

Other issues
The authors' conclusions are likely to be justified but, as they pointed out, the results are preliminary. The issue of generalisability was mentioned as an issue that could be addressed in future studies. Such a study would increase the external validity for Canadian settings initially.

Implications of the study
The study is basically a baseline study as it only focuses on the provider perspective. As the authors mentioned, the data should be seen as indicative of a trend and preliminary to further investigations. The study provides a benchmark for future studies.

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