Postmarketing evaluation of mycophenolate mofetil-based triple therapy immunosuppression compared with a conventional azathioprine-based regimen reveals enhanced efficacy and early pharmacoeconomic benefit after 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 intervention was mycophenolate mofetil (MMF) triple therapy immunosuppression regimen (MMF, cyclosporin A, steroids) after kidney transplantation. The comparator was standard triple therapy regimen of azathioprine (AZA), cyclosporin A and steroids.

Type of intervention
Secondary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised people who had undergone renal allograft transplantation and who required immunosuppression therapy to prevent acute rejection in the first 3 months.

Setting
The setting was tertiary care.

Dates to which data relate
The authors did not report the dates of the effectiveness and resource data and did not report the price year.

Source of effectiveness data
The effectiveness data were collected from a single study

Link between effectiveness and cost data
The costing was undertaken on the same patient sample as that used in the effectiveness study. The authors did not report whether the data were collected prospectively or retrospectively.

Study sample
A total of 22 consecutive patients receiving the MMF-based triple therapy regimen after kidney transplantation were compared with 22 consecutive patients who underwent transplantation before the change in immunosuppressant regimen. The authors did not report whether the sample size was sufficient to detect statistically significant differences where they existed, the methods of selecting patients, inclusion or exclusion criteria or details about the patients who were not included. The authors did not report whether the study sample was defined prospectively or retrospectively.
Study design
The study was a before-and-after study conducted at a single centre. Patients in the study and comparator groups were followed up for 3 months. No patients selected for the study were lost to follow-up.

Analysis of effectiveness
The analysis of the clinical study was based on all patients selected for inclusion in the study. If one of the inclusion criteria used by the authors was that patients had a complete record of care then the analysis equates to that of treatment completers only. The primary health outcomes were: patient survival, graft survival, rejection rate, serum creatinine, and cyclosporine levels. The study and comparator groups were similar in terms of age, sex, cause of end stage renal disease and degree of sensitisation. Donor characteristics were also similar for the two groups. The degree of donor-recipient HLA mismatching, and the D+/R- cytomegalovirus risk constellation, also did not differ between the two groups.

Effectiveness results
Outcomes were analysed after 3 months for the MMF and AZA based regimens respectively:

- patient survival was not significantly different: 100% versus 86%;
- graft survival was not significantly different: 91% versus 82%;
- rejection rate was significantly reduced in the MMF-based treatment group: 13.6% versus 63.6%;
- serum creatinine (micromol/ml) was not significantly different: 1400 (+/- 45) versus 144 (+/- 88); and
- cyclosporine level was not significantly different (ng/ml): 212 (+/- 73) versus 204 (+/- 52).

Clinical conclusions
The author concluded that the MMF-based regimen was superior to the AZA-based regimen in the early stages after kidney transplantation.

Measure of benefits used in the economic analysis
The outcomes were reported in a disaggregated fashion and, as such, a cost-consequences analysis was conducted.

Direct costs
Discounting was not relevant due to the short time frame of this study (3 months). Quantities and costs were not reported separately. The costs were calculated on the basis of average treatment dosing per patient. The costs measured were rejection treatment, maintenance immunosuppression, induction treatment, hospitalisation for rejection treatment and transplant biopsies. Estimation of quantity and costs was based on actual data. The authors did not report the price year. The authors did not report the source or nature of the unit cost data.

Statistical analysis of costs
There was no statistical analysis of costs.

Indirect Costs
Indirect costs were not reported.
Currency
The currency was Swiss francs (Sfr). No currency conversions were reported.

Sensitivity analysis
A sensitivity analysis was not performed.

Estimated benefits used in the economic analysis
The reader is referred to the effectiveness results reported previously.

Cost results
The total costs per patient over the 3-month treatment period were Sfr8,767 for MMF based treatment and Sfr7,604 for AZA based treatment.

Synthesis of costs and benefits
In this cost-consequences analysis, the estimated costs were not combined with benefits.

Authors' conclusions
The MMF-based regimen was superior to the AZA-based regimen in terms of the major beneficial effect of reducing the incidence of acute rejection episodes. The MMF-based regimen was more cost-effective than the AZA-based regimen.

CRD COMMENTARY - Selection of comparators
The selection of the AZA-based regimen as comparator was reported to represent conventional triple therapy immunosuppression. The authors did not report whether triple therapy immunosuppression is itself standard practice. You as a user of this database should consider whether this is a widely used health technology in your own setting.

Validity of estimate of measure of effectiveness
The estimates of effectiveness were derived from a before-and-after study, a study design which can introduce bias through the selection of patients for inclusion in the study, through physicians', patients' and investigators' knowledge of treatment allocation and through changes in other variables that may influence outcomes over time. The authors did not report any power calculations to suggest that the sample size used was sufficient to detect statistically significant differences in any of the outcomes measured. The authors reported that the patients were comparable at baseline. The authors report that the time frame was short and that a longer term study is required.

Validity of estimate of measure of benefit
In this cost-consequences study, no summary measure of benefit was used. This means that it is not possible to quantify the overall value of changes in patient survival and health status.

Validity of estimate of costs
The authors did not provide full details of resource use and costs. The source and nature of the unit costs used was not defined. The authors used a before-and-after study design, which does not control for the impact of changes over time in other variables that are determinants of costs. The authors did not conduct a statistical or sensitivity analysis to test the robustness of the cost results to uncertainty or chance variation in the data or to control for the influence of confounding variables or changes over time. These factors mean that it is not possible to assess the validity of the estimate of costs.
Other issues
The authors did not compare the results of their study with other published literature or discuss the extent to which the results were transferable to other settings. The authors did not provide sufficient information about the derivation of costs to enable the reader to substitute local data and assess the relevance of the study to their own setting.

Implications of the study
Three months after transplantation, the MMF-based regimen was more cost-effective than the AZA-based regimen. However, long-term maintenance immunosuppression with MMF could be more expensive compared with AZA-based treatment. Further research is required to assess the pharmacoeconomic and patient benefits over the long term.

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