The cost-effectiveness of mycophenolate mofetil as first-line therapy in active lupus nephritis

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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 study compared two alternative induction therapy strategies for patients with lupus nephritis (LN). These were prednisolone plus intravenous cyclophosphamide (IVC) and prednisolone plus oral mycophenolate mofetil (MMF).

Type of intervention
Treatment.

Economic study type
Cost-utility analysis.

Study population
The study population comprised a hypothetical cohort of active LN patients.

Setting
The setting was secondary care. The economic study was carried out in the UK.

Dates to which data relate
The effectiveness data were derived from studies and reviews published between 1991 and 2006. The costs were derived from national references and from studies published between 1996 and 2006. The price year was 2005.

Source of effectiveness data
The clinical and epidemiological data included in the model were:

- the treatment effectiveness at inducing remission;
- the risk of developing minor and major infections after treatment; and
- the probability of suffering an adverse event leading to discontinuation.

Modelling
A patient level simulation was conducted in order to simulate the costs and outcomes for each treatment. Average costs and outcomes for each treatment were estimated by means of a patient level simulation with 10,000 repetitions. The time horizon of the model was 24 weeks.

Sources searched to identify primary studies
Treatment effectiveness was derived from a published systematic review of the literature (Moore and Deny 2006, see 'Other Publications of Related Interest' for bibliographic details), which identified two published clinical trials. The risks of developing an infection were derived from published studies, a Cochrane review, and the authors' clinical
Methods used to judge relevance and validity, and for extracting data
The majority of the model parameters were populated using the results of systematic reviews of the literature that had been published between 2004 and 2006. Consequently, the need to undertake a new systematic review of the literature to identify new studies was diminished.

Measure of benefits used in the economic analysis
The measure of benefits used was the quality-adjusted life-years (QALYs) gained. Disutility values associated with adverse events were derived from the Harvard Cost-effectiveness Analysis Registry.

Direct costs
The direct costs to the health care system were included in the analysis. These comprised the costs of drug acquisition and administration, concomitant medications, and the treatment of minor and major infections. The costs were derived from the British National Formulary, national references and published studies. Since the costs were incurred during less than 1 year, discounting was not relevant and was not performed. The price year was 2005. The average costs were reported. The authors reported that costs incurred by both groups (e.g. concomitant medications) were not included in the analysis.

Statistical analysis of costs
The costs were reported as point estimates (i.e. the data were deterministic).

Indirect Costs
The productivity costs were not included.

Currency
UK pounds sterling ()

Sensitivity analysis
The authors presented uncertainty within the analysis using a cost effectiveness acceptability curve.

Estimated benefits used in the economic analysis
The average QALYs gained were 0.262 with prednisolone plus MMF compared with 0.223 for prednisolone plus IVC.

Cost results
The average cost was 1,388 when using prednisolone plus MMF compared with 2,994 for prednisolone plus IVC.

Synthesis of costs and benefits
The costs and benefits were combined using an incremental cost-utility ratio (i.e. the additional cost per QALY gained). However, this was not required as prednisolone in combination with MMF was found to be dominant over prednisolone plus IVC (i.e. it was both less costly and more effective).

The results of the sensitivity analysis suggested that, at a willingness-to-pay threshold of between 25,000 and 35,000 per QALY gained, the probability of prednisolone plus MMF being cost-effective was 81%.

Authors' conclusions
Mycophenolate mofetil (MMF) was more likely to result in better quality of life and to be less costly than intravenous cyclophosphamide (IVC) as induction therapy for lupus nephritis (LN).

CRD COMMENTARY - Selection of comparators
The authors used prednisolone in combination with IVC as the comparator. This intervention would not appear to be current practice, as it was not licensed for induction therapy in LN. However, subsequent correspondence with the authors has informed us that IVC was recommended by clinical experts as the most commonly used treatment, despite not being license for LN. You should decide if IVC is current practice in your own settings.

Validity of estimate of measure of effectiveness
The parameters were derived mainly from published research (studies identified in published systematic reviews and meta-analyses). When authors’ assumptions were necessary, these were supported by evidence from the literature. Although systematic reviews were used to identify relevant data on effectiveness and adverse events, the clinical data were scant. For example, one systematic review only identified two eligible studies.

Validity of estimate of measure of benefit
The estimation of health benefit was derived appropriately using a model. Since the QALYs were gained over a short time period, discounting was not relevant and was therefore not performed. The utilities were derived from a published database and included all utility estimates included in published economic evaluations.

Validity of estimate of costs
The analysis of the costs was performed from the perspective of the NHS paying for the treatments. All the relevant categories of costs appear to have been included in the analysis. Some relevant costs (e.g. concomitant medications) were not included as the authors reported they were incurred equally by the two treatment groups. The costs were derived from national references and published studies. Since the costs were incurred during a short time, discounting was not performed. The price year was reported, which will aid any future inflation exercises.

Other issues
The authors reported that their study was the first cost utility analysis comparing MMF with IVC for induction therapy in patients with LN. The issue of generalisability to other settings was not addressed. The authors do not appear to have reported their results selectively. The authors' conclusions reflected the scope of their analysis. The authors acknowledged a number of further limitations to their study. First, the model did not account for the fact that infections could lead to reductions in medication dosage, thus decreasing the effectiveness of treatment. Second, the time horizon was very short and, as a result, the long term cost effectiveness of the interventions is unknown. Finally, the model did not consider critical outcomes such as renal failure and death.

Implications of the study
The authors reported that further research was underway to evaluate the long-term consequences of treatments in maintenance of disease remission for LN patients.

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Other publications of related interest
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MeSH
Acute Disease; Computer Simulation; Cost-Benefit Analysis; Cyclophosphamide /administration & dosage /economics /therapeutic use; Day Care, Medical /economics; Drug Costs; Humans; Immunosuppressive Agents /economics /therapeutic use; Infusions, Intravenous; Lupus Erythematosus, Systemic /drug therapy; Lupus Nephritis /drug therapy; Models, Economic; Mycophenolic Acid /analogs & derivatives /economics /therapeutic use; Prednisolone /economics /therapeutic use; Quality-Adjusted Life Years; State Medicine /economics

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