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Title **Clinical and Cost Effectiveness of Newer Immunosuppressive Regimens in Renal Transplantation: A Systematic Review and Modeling Study**

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Aim

To examine the clinical and cost effectiveness of the newer immunosuppressive drugs for renal transplantation: basiliximab, daclizumab, tacrolimus, mycophenolate (mofetil and sodium), and sirolimus.

Conclusions and results

The newer immunosuppressant drugs (basiliximab, daclizumab, tacrolimus and MMF) consistently reduced the incidence of short-term (1-year) acute rejection compared with conventional immunosuppressive therapy. The independent use of basiliximab, daclizumab, tacrolimus and MMF was associated with a similar absolute reduction in 1-year acute rejection rate (approximately 15%). However, the effects of these drugs did not appear to be additive. Thus, the addition of one of these drugs to a baseline immunosuppressant regimen was likely to affect adversely the incremental cost effectiveness of the addition of another. The trials did not assess how the improvement in short-term outcomes, together with the side-effect profile associated with each drug, translated into changes in patient-related quality of life. The impact of the newer immunosuppressants on long-term graft loss and patient survival remains uncertain.

The absence of both long-term outcome and quality of life from trial data makes assessment of the clinical and cost effectiveness on the newer immunosuppressants contingent on modeling based on extrapolations from short-term trial outcomes. The choice of the most appropriate short-term outcome (eg, acute rejection rate or measures of graft function) for such modeling remains a matter of clinical and scientific debate. The decision to use acute rejection in the meta-model in this report was based on the findings of a systematic review of the literature of predictors of long-term graft outcome.

See the full report for a detailed description of the results from randomized controlled trials (RCTs) included in this systematic review and modeling study.

Recommendations

Only a small proportion of the RCTs identified in this review assessed patient-focused outcomes, eg, quality of life. Since immunosuppressive drugs have both clinical benefits and specific side effects, the balance of these harms and benefits could best be quantified through future trials using quality of life measures.

Methods

The review of clinical effectiveness followed explicit quality standards. Several sources were used to search for reviews and primary studies. Inclusion was based on predefined criteria. Data were extracted and quality-assessed. Each of the 5 company submissions to NICE contained cost-effectiveness models. A 3-stage critique of the company models was undertaken and included model checking, model description, and model rerunning.

Further research/reviews required

Most trials have been designed solely with drug licensing in mind, and are powered to examine short-term changes in clinical outcome (eg, acute rejection rate). Future trials need to include quality-of-life measures, examine effects in high-risk patients and children, and improve their reporting. Several issues in this area make RCTs potentially difficult to design and undertake (eg, comparing multiple therapies). Consideration should be given to collecting prospective observational outcome data on immunosuppressant regimens, possibly via a national registry.

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