Cost-effectiveness analysis of the early conversion of tacrolimus to mammalian target of rapamycin inhibitors in patients with 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.

CRD summary
The study assessed the cost-effectiveness of early conversion from the immunosuppressant tacrolimus to sirolimus versus continuous treatment with tacrolimus in patients after kidney transplantation. The authors concluded that a strategy of early replacement of tacrolimus with sirolimus was the most cost-effective from the perspective of the third-party payer. The study used transparent methods from valid sources of data that enhanced the robustness of the authors’ conclusions.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
The study assessed the cost-effectiveness of early conversion from tacrolimus to sirolimus (a mammalian target of rapamycin inhibitor, mTORi) versus continuous treatment with tacrolimus in renal (kidney) transplant patients.

Interventions
The two treatment strategies were examined. Both strategies included induction with basiliximab (20mg/day 0 and day 4) plus extended-release tacrolimus (therapeutic range, 5 to 10ng/mL) plus mycophenolate mofetil (1g every 12 hours) plus corticosteroids. One strategy included early replacement of tacrolimus by sirolimus (therapeutic range 5 to 10ng/mL).

Location/setting
Colombia/secondary care and hospital.

Methods
Analytical approach:
The analysis was based on a Markov model with a lifetime horizon. The authors stated that the perspective of the Colombian Health Care System was adopted.

Effectiveness data:
Clinical inputs were derived from published sources and some assumptions. In particular, a literature review was carried out to identify relevant sources of the clinical effectiveness and safety of the immunosuppressive therapy for adult renal transplant patients with schemes to replace tacrolimus with sirolimus or everolimus. Sources searched were The Cochrane Library, MEDLINE and LILACS. Only randomised clinical trials were considered for this specific key input of the clinical analysis. The quality of retrieved trials was assessed using the deviation risk scale of the Cochrane collaboration. Additional information came from observational studies and cost-effectiveness studies.

Monetary benefit and utility valuations:
Not considered.

Measure of benefit:
Life-years (LYs) were used as the summary benefit measure and were discounted at an annual rate of 5%. The life years free from renal loss was used as an alternative benefit measure.
Cost data:
The economic analysis included the typical costs incurred by kidney transplantation such as routine management, adverse events, rejection episodes, and graft loss. The prices of induction therapies, tacrolimus and sirolimus were reported in detail at monthly intervals. Other costs were reported including those for diagnosis, follow-up and hospitalisation. Unit costs were based on official Colombian prices set by the Colombian Ministry of Health. Resource quantities were validated by expert consensus. Costs were in Colombian dollars (COL$) and were discounted at an annual rate of 5%.

Analysis of uncertainty:
One-way sensitivity analyses were carried out to assess the impact of variations in model inputs on cost-effectiveness ratios. Probabilistic sensitivity analyses were conducted using a Monte Carlo simulation to generate cost-effectiveness acceptability curves.

Results
For patients continuously treated with tacrolimus, the expected cost per patient was COL$ 589,929,906, projected life years gained with treatment were 9.48, with 7.08 life years free from renal loss.

For patients who had early conversion from tacrolimus to sirolimus, the expected cost per patient was COL$ 591,809,608, projected life years gained with treatment were 10.25, with 7.54 life years free from renal loss.

The incremental cost per life year gained with sirolimus over tacrolimus was COL$ 2,441,171.43.

The incremental cost per life years free from renal loss gained with sirolimus over tacrolimus was COL$ 4,104,152.84.

Both ratios were below the cost-effectiveness threshold based on the criterion of more than three times the Colombian gross domestic product (GDP) per capita (COL$ 11,065,393 in 2009).

The deterministic analysis showed that tacrolimus became the preferred strategy only when the risk of death due to cancer was not increased. Otherwise, sirolimus was the most cost-effective option, as confirmed in the sensitivity analyses.

Authors' conclusions
The authors concluded that a strategy of early replacement of tacrolimus with sirolimus was the most cost-effective from the perspective of the third-party payer.

CRD commentary
Interventions:
The selection of the comparators was appropriate as the available treatments for this patient population were considered. The authors did not include the mammalian target of rapamycin inhibitor everolimus as a possible alternative as no clinical trials were found that evaluated the effects of changing immunosuppressive therapy from tacrolimus to everolimus.

Effectiveness/benefits:
A systematic review of the literature was undertaken to select sources for clinical parameters. Only randomised clinical trials were used for data of efficacy and safety of the two options compared; the quality of these trials was analysed. This was a strength of the analysis. The authors provided some details on the key references used. Other data were taken from observational studies and cost-effectiveness analyses, when no clinical trial was available. Some assumptions were needed, but the clinical analysis was conducted satisfactorily in general. Life years were an appropriate benefit measure, which captured the impact of the disease on patients’ health. Survival was the key outcome for transplant patients, although the use of quality weights would have been interesting because of the effect of disease on the quality of life in this population.

Costs:
The cost categories included in the analysis appeared to be consistent with the perspective of the public payer. Unit costs and resource quantities were not presented separately, but a detailed breakdown of costs was given. Monthly costs...
were provided for each strategy considered. Patterns of resource consumption were based on expert opinions; country-specific sources were used to estimate unit costs. The price year was not explicitly stated, so reflation exercises in other time periods could be difficult. The impact of variations in the cost estimates was tested in the sensitivity analyses.

Analysis and results:
Key assumptions and the structure of the decision model were appropriately presented. Methods used for sensitivity analyses to investigate uncertainty were valid and their findings were clearly reported. However, the methods use for the probabilistic sensitivity analyses were not extensively reported. The study results were presented in detail. The expected costs and benefits were synthesised using an incremental approach. The transferability of the study results was not explicitly addressed; these results appear to be specific to the Colombian setting.

Concluding remarks:
The study used transparent methods from valid sources of data that enhanced the robustness of the authors’ conclusions.

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