Economics of switching to second-line antiretroviral therapy with Lopinavir/ritonavir in Africa: estimates based on DART trial results and costs for Uganda and Kenya

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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 switching to a second-line protease inhibitor (protease inhibitor) regimen of lopinavir plus ritonavir for patients who failed a first-line treatment in sub-Saharan Africa. The authors concluded that the switch to a second-line therapy with lopinavir plus ritonavir was cost-effective in both Kenya and Uganda. The study used a conventional cost-effectiveness framework and the authors’ conclusions appear robust.

Type of economic evaluation
Cost-utility analysis

Study objective
The study assessed the cost-effectiveness of switching to a second-line protease inhibitor regimen of lopinavir plus ritonavir for HIV-infected patients who failed a first-line treatment in sub-Saharan Africa.

Interventions
The intervention under examination was a switch from the initial non-nucleoside reverse transcriptase inhibitor (NNRTI) regimen to a boosted protease inhibitor regimen of lopinavir plus ritonavir (LPV/r) plus zidovudine (ZDV) and lamivudine (3TC). The comparator was remaining on a failing first-line NNRTI regimen. A do-nothing option was considered. Prophylaxis with cotrimoxazole was assumed.

Location/setting
Uganda and Kenya. Primary and secondary care.

Methods
Analytical approach:
The analysis was based on a published Markov model with a lifetime horizon. The authors stated that the perspective was of the health system.

Effectiveness data:
Clinical inputs for the model were derived from a selection of known relevant studies. Evidence on short-term efficacy of LPV/r and patients’ characteristics were retrieved from an open-label clinical trial that enrolled a sample of 447 antiretroviral-naive patients in Uganda and Zimbabwe in whom first-line regimen failed. Data on long-term progression of the disease was based on a published cost-effectiveness analysis. Rates of clinical events associated with the disease represented key inputs of the model.

Monetary benefit and utility valuations:
Utility valuations associated with World Health Organisation) WHO health states were derived from a published study that referred to Ugandan patients.

Measure of benefit:
Quality-adjusted life-years (QALYs) were used as the summary benefit measure and were discounted at an annual rate of 3%. Life-years saved were reported.

Cost data:
The economic analysis included the costs of antiretroviral therapy, cotrimoxazole prophylaxis, treatment of events and monitoring. All economic data were derived from a published cost study conducted in resource-limited settings and from the Medecins Sans Frontieres database. Some unit costs were reported. Costs were in US dollars ($) and were discounted at a rate of 3% per annum. The price year was 2007.

Analysis of uncertainty:
Various alternative scenarios were considered in the sensitivity analyses. Model selected assumptions were varied one at a time. A probabilistic sensitivity analysis was carried out using conventional distributions for model inputs.

Results
In Uganda, lifetime QALYs and costs (per 100 patients) were 314 and $473,542 with LPV/r and 142 and $185,656 with NNRTI. The incremental cost per QALY gained with LPV/r over NNRTI was $1,673.

In Kenya, lifetime QALYs and costs (per 100 patients) were 314 and $366,422 with LPV/r and 142 and $111,202 with NNRTI. The incremental cost per QALY gained with LPV/r over NNRTI was $1,483.

The sensitivity analysis showed the robustness of base case results. When no use of cotrimoxazole was assumed for either group, the greatest change in cost-utility ratios was observed: $1,328 in Uganda and $1,329 in Kenya.

Considering the criterion of gross domestic product (GDP) per capita, the switch to LPV/r-based regimen appeared likely to be cost-effective in either country. A budget impact analysis showed a clinic should expect to increase the cotrimoxazole budget by $25.42 per year and the antiretroviral budget by $361 per year.

Authors’ conclusions
The authors concluded that the switch to a second-line therapy with LPV/r was cost-effective in both Kenya and Uganda.

CRD commentary
Interventions:
The selection of comparators appeared appropriate within the setting of sub-Saharan Africa.

Effectiveness/benefits:
Clinical inputs for the short-term were taken from an open-label clinical trial conducted in the authors’ setting. Little information on this study was given as it was unpublished at the time of the analysis. Similarly few details were given on other sources of clinical data, which made it difficult to fully judge its validity. Extensive sensitivity analysis was conducted on key clinical parameters that showed the robustness of the base case findings. Life-years saved and QALYs were used as measures of benefits (costs were only combined with QALYs) and both represented valid options given the disease considered. Utility weights were taken from sources appropriate to the study context and justified by the authors.

Costs:
The economic analysis appeared consistent with the perspective of the health care system. Limited information on economic inputs was provided as most economic data for the model were derived from a published study and supplemented with estimates by Medecins Sans Frontieres. Both sources are relevant for sub-Saharan countries but more details on these studies would have been useful. Most costs were presented as macro-categories and only some were considered in the sensitivity analyses. Price year and discount rate were clearly stated. Variations in some cost inputs were considered.

Analysis and results:
Expected costs and benefits were reported for both strategies and were combined using an incremental approach. Conventional cost-effectiveness benchmarks based on WHO estimates of GDP were used to identify the optimal strategy. The issue of uncertainty was investigated by means of both deterministic and probabilistic sensitivity analyses, but the methods and results were selectively reported. The model adopted was well described and referred to a previous publication. The authors acknowledged some limitations of their analysis mostly related to the poor quality of some published sources. It was stated that results might be different in other settings.
Concluding remarks:
The study used a conventional cost-effectiveness framework and the authors’ conclusions appear robust.

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