Cost-effectiveness of atazanavir/ritonavir compared with lopinavir/ritonavir in treatment-naive human immunodeficiency virus-1 patients in Sweden
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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 objective was to examine the cost-effectiveness of atazanavir with ritonavir, compared with lopinavir with ritonavir, for treatment-naive patients with human immunodeficiency virus (HIV)-1, for whom efavirenz was not suitable. The authors concluded that atazanavir with ritonavir was more effective and cost-saving compared with lopinavir. The analytic approach and the sources of clinical data were valid. The authors’ conclusions appear to be robust.

Type of economic evaluation
Cost-utility analysis

Study objective
The objective was to examine the cost-effectiveness of atazanavir combined with ritonavir, compared with lopinavir combined with ritonavir, for treatment-naive patients with human immunodeficiency virus (HIV)-1, for whom efavirenz was not suitable.

Interventions
Atazanavir 300mg was compared with lopinavir 400mg, both combined with ritonavir 100mg, in treatment-naive patients with HIV-1, for whom efavirenz was not suitable. Darunavir 1,200mg with ritonavir 100mg was the second-line treatment, except for those who discontinued lopinavir due to adverse events. These patients switched to atazanavir with ritonavir. Several third-line options were considered.

Location/setting
Sweden/secondary care.

Methods
Analytical approach:
The analysis was based on a Markov model, with a lifetime horizon. The authors stated that it was carried out from the perspective of society, except in the abstract, which stated a payer perspective.

Effectiveness data:
The clinical data appear to have been from a selection of relevant studies, which included pivotal clinical trials, such as the Comparison of Atazanavir/ritonavir in naive Subjects in combination with Tenofovir-emtricitabine versus Lopinavir/ritonavir in combination with tenofovir-emtricitabine to assess safety and Efficacy (CASTLE), ARTEMIS, and TITAN studies. The efficacy and safety of atazanavir and lopinavir, in combination with ritonavir, was from the CASTLE trial that directly compared the two options over 96 months. Additional data were from country-specific statistics and databases. The incidence of cardiovascular events was a key input for the model and was estimated using the Framingham study, as recommended in the guidelines by the British HIV Association.

Monetary benefit and utility valuations:
The utility values were derived from published studies.

Measure of benefit:
Quality-adjusted life-years (QALYs) were the summary benefit measure and were discounted at an annual rate of 3%.
Cost data:
The economic analysis included the costs of drugs, loss of productivity, and treatment of cardiovascular events. Both the direct and indirect costs were considered. These costs were from official Swedish sources. The patterns of resource use were from other countries, especially for the indirect costs, which required some assumptions. These costs and those of added life-years were included in scenario analyses. All costs were in Swedish kronor (SEK) and were discounted at an annual rate of 3%. The price year was 2007.

Analysis of uncertainty:
Scenario analyses were used to assess the impact of variations in individual inputs to the model. A multivariate sensitivity analysis was carried out, in which important inputs were varied simultaneously using published and assumed ranges of values. A Monte Carlo simulation was performed and cost-effectiveness acceptability curves were generated.

Results
In the base case, atazanavir gained 0.16 QALYs (95% CI 0.00 to 0.33) and saved SEK 202,896 (95% CI 81,644 to 332,156), compared with lopinavir, over a lifetime. Improvements in QALYs and saved costs were observed from the beginning of treatment (a five-year time horizon) and increased consistently over time.

The dominance of atazanavir (saved costs and improved QALYs) held in the scenario analyses, except when assuming that second- and third-line treatment cost the same as lopinavir with ritonavir. In this scenario, atazanavir had an incremental cost per QALY gained of SEK 149,092.

At a societal willingness-to-pay threshold of SEK 200,000 per QALY, the probability of atazanavir being cost-effective was approximately 100%.

Authors' conclusions
The authors concluded that atazanavir with ritonavir was more effective and cost-saving compared with lopinavir with ritonavir.

CRD commentary
Interventions:
The authors provided a justification for their selection of the comparators, which were those examined in the pivotal CASTLE study. Boosted lopinavir was the most commonly prescribed protease inhibitor in Sweden at the time of the study.

Effectiveness/benefits:
The clinical data were from selected studies that generally appear to have been appropriate and valid. The treatment effect and adverse events for the two options were from a large head-to-head clinical trial that should have had high internal validity. The data on further treatment lines were from clinical trials, while the long-term disease progression was from validated and recommended algorithms. These clinical data were varied in the sensitivity analyses. The use of QALYs as the benefit measure was appropriate as the disease affects both expected survival and quality of life, but little information was given on the sources for the utility weights.

Costs:
The cost categories were consistent with the societal perspective. The authors stated that the estimation of productivity losses was complicated, due to the lack of statistics for unemployment of people with HIV in Sweden. Thus, a number of assumptions, based on studies not carried out in Sweden were required, and Italian resource use data were used in scenario analyses. The costs were presented as category totals and not broken down into single items. The sources for the unit costs and resource quantities were given, but these data were not reported separately. The discount rate and the price year were clearly stated.

Analysis and results:
The results were selectively presented, as only the incremental findings were reported. Various sensitivity analyses were carried out to examine the impact of variations in the clinical and economic inputs on the model results. The results of the analysis of uncertainty were clearly illustrated and discussed; in general, the base-case findings were robust.
Concluding remarks:
The analytic approach and the sources of clinical data were valid. The authors’ conclusions appear to be robust.

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