Cost-effectiveness analysis of lopinavir/ritonavir and atazanavir+ritonavir regimens in the CASTLE study

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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
This study examined the cost-effectiveness of lopinavir with ritonavir versus atazanavir plus ritonavir for antiretroviral-naive patients with an average-to-moderately elevated coronary heart disease (CHD) risk. Atazanavir plus ritonavir was not cost-effective as it provided a small improvement in survival at a very high cost compared with the lopinavir with ritonavir regimen. A more detailed reporting of the clinical sources would have been useful, but the methods were valid and the authors’ conclusions appear to be robust.

Type of economic evaluation
Cost-utility analysis

Study objective
This study examined the cost-effectiveness of lopinavir with ritonavir versus atazanavir plus ritonavir for antiretroviral-naive patients with an average-to-moderately elevated coronary heart disease (CHD) risk.

Interventions
Twice daily lopinavir with ritonavir was compared with once-daily atazanavir plus ritonavir.

Location/setting
USA/secondary care.

Methods
Analytical approach:
The analysis used a published Markov model of human immunodeficiency virus (HIV) disease that incorporated CHD. A lifetime horizon was considered and the authors stated that the perspective of the medical care system was adopted.

Effectiveness data:
The clinical data came from a selection of relevant studies. The evidence for the treatment effect for the two regimens was based on the 48-week results of an international, multicentre, open-label, randomised controlled trial, namely the CASTLE study (Molina, et al. 2008, see ‘Other Publications of Related Interest’ below for bibliographic details). The key endpoint of the trial for this study was the proportion of patients with an elevated total cholesterol level. Other inputs were from the published model, which used Framingham equations to estimate the long-term risk of CHD.

Monetary benefit and utility valuations:
The utility values were from the original model. They were elicited from patients, who received highly active antiretroviral therapy (HAART), using the European Quality of life (EQ-5D) questionnaire.

Measure of benefit:
Quality-adjusted life-years (QALYs) were the benefit measure and they were discounted at an annual rate of 3%.

Cost data:
The economic analysis included the costs of acquired immune deficiency syndrome (AIDS) events treated in both in-patient and out-patient settings, CHD events (myocardial infarctions), lipid-lowering therapy, and antiviral therapy. AIDS-related costs were based on Medicaid out-patient data and on all-payer discharge data for in-patients. The latter
source was also used for CHD hospitalisation costs. The drug costs were based on average wholesale prices. All costs were in US dollars ($) and the price year was 2007. A 3% annual discount rate was applied.

Analysis of uncertainty:
A series of one-way sensitivity analyses was undertaken on three groups of selected inputs. The first group was the cost of the ritonavir needed for boosting atazanavir, the cost of statins to manage total cholesterol elevation, the cost of AIDS events resulting from disease progression, and the prices of the two protease inhibitor drugs used in the first antiviral regimen. The second group was the effect of differences in the baseline CHD risk due to smoking and elevated systolic blood pressure. The third group was the effects of the assumption of the cost of drugs used in the second and third antiviral regimens.

Results
Without discounting, compared with lopinavir with ritonavir, atazanavir plus ritonavir led to an additional cost of $38,490 and a gain of 0.031 QALYs (11 quality-adjusted days), resulting in a lifetime discounted incremental cost per QALY gained with atazanavir plus ritonavir of $1,409,734.

The most influential input was the cohort's baseline risk of CHD, but even assuming that all patients were smokers (50% in the base case), the incremental cost per QALY gained remained above the commonly used cost-effectiveness thresholds of $50,000 to $100,000 per QALY.

Authors’ conclusions
The authors concluded that the regimen of atazanavir plus ritonavir was not cost-effective as it provided a small improvement in survival at a very high cost compared with the lopinavir with ritonavir regimen.

CRD commentary
Interventions:
No formal justification for the selection of the comparators was provided, but they appear to have been widely used treatments for antiretroviral-naïve patients. The doses and patterns of administration were not reported.

Effectiveness/benefits:
The relevant sources of data appear to have been selected, without a literature review. The bulk of the evidence was either data already incorporated in the model or the results of the CASTLE study and the methods of this new study should have ensured the validity of these estimates. More details would have allowed a more comprehensive assessment of the clinical data. The instrument used to elicit the patient preferences for health conditions (EQ-5D) was appropriate and has been validated. The authors justified their use of UK data for US estimates. QALYs were a valid benefit measure. They capture the impact of the interventions on a patient's health and can be compared with the benefits of other health care interventions.

Costs:
The costs and their sources were consistent with the perspective of the health care payer. Limited information on the unit costs and resource quantities was provided. Some unit costs for the regimens were reported, but generally total categories were presented, limiting the transparency of the economic analysis. The cost estimates were treated deterministically. Reflation exercises will be possible as the price year was reported.

Analysis and results:
The expected costs and benefits of the two interventions were clearly reported, without discounting. An incremental analysis was appropriately carried out to combine the discounted costs and benefits. The issue of uncertainty was only partially investigated, using a deterministic approach on selected inputs. The study results should be considered to be specific to the patient population included in the CASTLE study and not generalisable to patients at different CHD risks or with different baseline cluster of differentiation (CD) 4-cell counts. The Markov model was described in detail and appears to have correctly represented the progression of disease.

Concluding remarks:
A more detailed reporting of the clinical sources would have been useful, but the methods were valid and the authors’
conclusions appear to be robust.

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