Cost-effectiveness of tipranavir in treatment-experienced HIV patients in the United States
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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 tipranavir plus ritonavir (TPVr) in comparison with one of a selection of protease inhibitors plus ritonavir (CPIr) for the treatment of human immunodeficiency virus (HIV)-1-infected patients, who had received extensive treatment. The authors concluded that TPVr was a cost-effective alternative to CPIr from the perspective of the US payer. The study was based on valid methodology which enhances the validity of the authors’ conclusions.

Type of economic evaluation
Cost-effectiveness analysis, cost-utility analysis

Study objective
This study examined the cost-effectiveness of tipranavir plus ritonavir (TPVr) in comparison with one of a selection of protease inhibitors plus ritonavir (CPIr) for the treatment of human immunodeficiency virus (HIV)-1-infected patients, who had already received extensive treatment.

Interventions
The two treatments were TPVr and CPIr. The comparator protease inhibitors were amprenavir, fosamprenavir, indinavir, lopinavir, or saquinavir.

Location/setting
USA/secondary care.

Methods
Analytical approach:
A previously published Markov model was updated with recently available data to simulate the management of a hypothetical cohort of treatment-experienced HIV patients over their lifetime. The authors stated that the perspective of the US public payer was adopted.

Effectiveness data:
The clinical data were derived from a selection of known, relevant studies. The first stages of the model (short-term data) were populated with data derived from two open-label, multi-country, randomised controlled trials (RCTs); the Randomized Evaluation of Strategic Intervention in Multi-Drug Resistant Patients with Tipranavir (RESIST)-1 and -2. These enrolled a total of 1,483 patients, whose data were pooled, given the baseline comparability of patients and treatments. The clinical data, beyond the 48-week follow-up period of the two trials, were derived from 1,456 patients treated in the Infectious Disease Clinics of the Medical University of South Carolina or at one of its 54 community medical practices. Other data were already incorporated in the model and derived from published sources which were not described.

Monetary benefit and utility valuations:
The utility values were derived from a previous study which included European quality of life (EQ-5D) data from 20,901 observations of HIV or acquired immune deficiency syndrome (AIDS) patients in different stages of health. The same utility weights were applied to both treatments.

Measure of benefit:
Quality-adjusted life-years (QALYs) and life-years (LYs) were used as the summary benefit measures. A 3% annual
The analysis considered the costs of drugs (those under examination and others used for patients who experienced a failure), physician visits, and diagnostic and laboratory tests. The drug costs were average wholesale prices, while drug resource consumption was based on data from the two RCTs. Other costs and quantities of resources came from HIV-infected Medicaid patients in South Carolina. The costs were associated with each model health state. The price year was 2007. All costs were in US dollars ($) and were discounted at an annual rate of 3%.

**Analysis of uncertainty:**
Several one-way sensitivity analyses were carried out on the key model inputs, using ranges or alternative assumptions defined by the authors. Two probabilistic analyses were also undertaken; a second-order Monte Carlo simulation and a bootstrap analysis, based on individual patient data from the two RCTs. In an alternative scenario, patients on enfuvirtide (ENF) were excluded from both treatment arms.

**Results**
The lifetime discounted costs were $310,379 with TPVr and $274,209 with CPIr. The discounted expected QALYs were 5.69 with TPVr and 5.04 with CPIr. The discounted LYs were 6.74 with TPVr and 6.06 with CPIr. The incremental cost per QALY gained with TPVr over CPIr was $56,517, while the incremental cost per LY gained was $53,987.

Excluding patients on ENF, from both treatment arms, led to an incremental cost per QALY gained of $46,147.

The deterministic sensitivity analysis showed that the incremental cost per QALY gained was in the range $51,106 to $65,000. On the whole, the base-case findings were robust, although they were slightly sensitive to changes in the drug costs and utility weights.

The probabilistic sensitivity analysis indicated that, at a willingness to pay threshold of $100,000 per QALY, the probability that TPVr was cost-effective was 100%.

**Authors' conclusions**
The authors concluded that TPVr was a cost-effective alternative to CPIr from the perspective of the US payer.

**CRD commentary**
**Interventions:**
The selection of the comparators was appropriate and was extensively discussed. They were also likely to be relevant in other health care systems.

**Effectiveness/benefits:**
The selection of the sources for data was based on an attempt to update a previous model with the most recently available and relevant data. The use of evidence from the RESIST-1 and -2 trials represents a strong point of the analysis given the robust and valid design of RCTs. These data were supplemented with clinical inputs from an administrative database, the validity of which was unclear given the lack of information on its main characteristics. The other data used in the previous model (estimates, sources, types of treatments) were not fully described. The two benefit measures were appropriately selected in order to capture the impact of the treatments on both survival and quality of life, which are two relevant dimensions of health for patients with HIV.

**Costs:**
The analysis of costs appears to have been consistent with the perspective. However, a detailed breakdown of cost items was not provided, with the costs being presented as macro-categories. This might reduce the transparency of the economic evaluation, but represents a common approach in Markov models for HIV and AIDS. Other aspects of the analysis, such as the sources of data, price year, use of discounting, and stochastic distributions of cost estimates, were reported.
Analysis and results:
The incremental approach used to combine the costs and benefits of the two strategies was appropriate. The study findings were clearly presented. The issue of uncertainty was satisfactorily addressed in the sensitivity analysis, which used a comprehensive approach, but also focused on specific inputs. An extensive description and discussion of the decision model were provided. The authors reported the findings from other studies, which showed similar results to those from the current evaluation. The authors pointed a potential limitation of their study, which was the uncertainty surrounding the future mix of treatments following the treatment with TPVr and CPIr. This analysis used average wholesale prices while large payers might receive discounts.

Concluding remarks:
The study was based on valid methodology which enhances the validity of the authors’ conclusions.

Funding
Funding received from Boehringer Ingelheim GmbH, Germany.

Bibliographic details

PubMedID
18753117

DOI
10.1310/hct0904-225

Other publications of related interest


Indexing Status
Subject indexing assigned by NLM

MeSH
Adolescent; Adult; Aged; Aged, 80 and over; Clinical Trials as Topic; Cost-Benefit Analysis; Drug Therapy, Combination; Female; HIV Infections /drug therapy /economics; HIV Protease Inhibitors /therapeutic use; Humans; Male; Markov Chains; Middle Aged; Pyridines /therapeutic use; Pyrones /therapeutic use; Quality-Adjusted Life Years; Ritonavir /therapeutic use; United States

AccessionNumber
22008101771

Date bibliographic record published
01/12/2008
Date abstract record published
13/05/2009