Cost-effectiveness of raltegravir in HIV/AIDS
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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 investigated the cost-effectiveness of raltegravir plus optimised background therapy compared with optimised background therapy alone in six European countries and Australia. The authors concluded that raltegravir was cost-effective under most scenarios and in all countries in both treatment-naïve and treatment-experienced patients. The model inputs, analyses and results were not fully transparent and there appeared to be considerable uncertainty around the study findings. The findings should be interpreted with caution.

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

Study objective
The aim of the study was to examine the costs and health benefits of raltegravir for treatment of HIV/AIDS. The study population was a hypothetical cohort of HIV-infected adults who were either treatment-naïve or treatment-experienced (with HIV multidrug resistance).

Interventions
Raltegravir plus optimised background therapy (OBT) was compared with OBT alone in countries for which pharmacoeconomic data were available. Background therapy and raltegravir's place of therapy was dependent on country-specific regimens and treatment algorithms. Raltegravir was administered orally at a dose of 400mg twice daily.

Location/setting
Six European countries (UK, Hungary, Portugal, Spain, Switzerland and Sweden) and Australia/Primary care.

Methods
Analytical approach:
Two health state transition Markov models were used (one each for treatment-naïve and treatment-experienced patients) to synthesise evidence from published studies, epidemiological data and key clinical trials (Steigbigel RT et al. 2008 & 2010, Lederberger B et al. 2010, Martinez E et al. 2010 & Eron J et al. 2010 see Other Publications of Related Interest). The base case analysis time horizon was 30 years (UK) and 50 years/lifetime (Spain, Switzerland, Hungary, Portugal, Sweden and Australia). The authors’ stated the study perspective was that of the respective health system in each country. Country-specific data was used for data inputs when available.

Effectiveness data:
Clinical outcomes included indicators of virologic response (CD4 counts), disease progression, primary and recurrent opportunistic infections. Results of randomised trials of raltegravir plus OBT versus OBT alone were used to derive data inputs to the model (Steigbigel RT et al. 2010, Lederberger B et al. 2010, Druyts E et al. 2009, see Other Publications of Related Interest). Risk of opportunistic infections and AIDS-related complications were based on those reported in the Multicenter AIDS Cohort Study. Assumptions were made on the duration of immunologic failure rates.

Monetary benefit and utility valuations:
Utility estimates were derived from a previous published HIV cost-effectiveness study (Simpson KN et al. 2004, see Other Publications of Related Interest).

Measure of benefit:
Undiscounted life expectancy and quality-adjusted life-years (QALYs) discounted annually according to national recommended discount rates (%).

Cost data:
Direct medical costs included antiretroviral pharmaceuticals, drug administration and monitoring, opportunistic infection prophylaxis treatment, all hospital costs, laboratory tests, clinical examinations, treatment of adverse events and other service costs. Resource use quantities were determined from analyses of patient-level data with patients with HIV at the British Columbia Center of Excellence for HIV/AIDS and published literature. The unit costs were country-specific and derived from the respective country sources. Prices were presented in 2007 Euros (€) and 2010 exchange rates were applied.

Analysis of uncertainty:
The model input parameters were examined with one-way sensitivity analyses. Parameters tested included time horizon, discount rate, utilities, incidence of opportunistic infections, drug price, treatment duration and treatment failure rates.

Results
For a five-year treatment duration in treatment-experienced patients, raltegravir plus OBT resulted in QALYs in the range 11.90-14.63 (UK, Spain and Switzerland) compared with 9.07-12.43 QALYs for OBT alone. Incremental cost per QALY ratios were €19,117 for the UK, €31,431 for Spain and €33,107 for Switzerland. Results for treatment-naïve patients were €14,830 for Hungary, €4,016 for Portugal and €8,929 for Sweden and €18,678 for Australia.

The authors stated that the results of the one-way sensitivity analyses showed the base case findings were most sensitive to treatment duration, time horizon, utility values and raltegravir costs.

Authors’ conclusions
The authors’ concluded that five years of raltegravir was cost-effective under most scenarios and in all countries included in the analysis. They suggested that raltegravir used as first-line in treatment-naïve patients and not used as salvage therapy was cost-effective.

CRD commentary
Interventions:
The therapeutic agents for OBT appeared to be different for each country and raltegravir did not belong to the same therapeutic drug class as other antiretroviral HIV drugs. Readers should decide which country’s treatment algorithm was closest to their own setting and assess the relative prices of the comparator agents.

Effectiveness/benefits:
The clinical effectiveness of the agents was based on clinical trials that were not described in the article. The quality of these trials was unknown as was whether they were suitable for the analysis and how they were combined for input into the model. Utility values were measured directly on the intended patient groups (by CD4 counts) but no further details were provided. Readers should view the original trial reports to assess their quality.

Costs:
The included costs appeared to be relevant to the perspective stated by the authors. Methods and measurement of resource quantities were clearly presented in the report along with their unit costs. The measurement of these resources appeared comprehensive and reasonable. Unit costs were appropriately based on publicly available and country-specific sources.

Analysis and results:
The authors discussed their findings with other pharmacoeconomic studies that found similar conclusions of raltegravir being a cost-effective approach. Specific values used in the one-way sensitivity analyses were not reported. The results from which the extent of variation in changes to key variables could be assessed were not reported. Limitations were acknowledged in the report and included omission of adherence to medications, simplification of real-life complex treatment pathways, unknown likely treatment duration of raltegravir and the need for post-marketing data to further assess clinical and economic benefits over the long-term. These limitations introduced considerable uncertainty to the results presented.
Concluding remarks:
The model structure and evidence used appeared comprehensive and well-developed but the model values, analyses and results were not entirely clear and there appeared to be considerable uncertainty around the study findings.

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