Cost-effectiveness of adding an agent that improves immune responses to initial antiretroviral therapy (ART) in HIV-infected patients: guidance for drug development

Morris BL, Scott CA, Wilkin TJ, Sax PE, Galick RM, Freedberg KA, Schackman BR

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 assess the cost-effectiveness of immune-enhancement of antiretroviral therapy to improve response in patients with low cluster of differentiation (CD)4 cell counts before treatment. Immune enhancement had to increase CD4 cell counts more than observed or have lower costs, to be considered cost-effective. The methods were adequate, but the limitations of the study and the lack of information on the clinical and utility evidence, mean that the conclusions should be treated with caution.

Type of economic evaluation
Cost-utility analysis

Study objective
The objective was to assess the cost-effectiveness of adding an immune-enhancing drug to initial antiretroviral therapy (ART) to achieve the best response in patients with a low cluster of differentiation (CD)4 cell count before treatment. A second objective was to define the thresholds for effectiveness and costs, at which therapy becomes cost-effective, to guide drug development and the design of clinical trials.

Interventions
The three interventions were a first-line ART regimen, consisting of efavirenz, tenofovir, and emtricitabine, with the addition of an immune-enhancing agent, for six months; first-line ART, without the immune-enhancing agent; and no ART.

Location/setting
USA/secondary care.

Methods
Analytical approach:
The Cost-effectiveness of Preventing AIDS Complications (CEPAC) model of HIV disease progression and treatment (Schackman, et al. 2007, see ‘Other Publications of Related Interest’ below for bibliographic details) was used. The time horizon was the lifetime of the patient. The authors stated that their analysis was from the health system perspective.

Effectiveness data:
The clinical and effectiveness data were mainly those used in the original CEPAC model, with some data from published studies. The main effectiveness estimates were the percentage of HIV ribonucleic acid (RNA) suppression at 24 weeks, and the mean increase in CD4 cell count at 48 weeks. These estimates were from published studies. It was assumed that enhancement increased the CD4 cell count by five to 100 cells per microlitre.

Monetary benefit and utility valuations:
Not reported.

Measure of benefit:
Quality-adjusted life-years (QALYs) gained were the measure of benefit and life-years were assessed. Future benefits were discounted at an annual rate of 3%.
Cost data:
The direct costs included those of the drug treatments; routine care for AIDS; tests; treatment of acute opportunistic infections, including pneumonia, toxoplasmosis, cytomegalovirus and fungal infections; and death. The costs were from published studies, hospitals, and reports. The price year was 2009 and all costs were presented in US $. Future costs were discounted at an annual rate of 3%.

Analysis of uncertainty:
One-way sensitivity analyses were undertaken by varying the effectiveness of the immune-enhancing agent and the costs of the drugs.

Results
Assuming an increase of 40 cells per microlitre with enhanced ART, the discounted QALYs gained per patient were 2.29 with no ART, 8.97 with ART, and 9.08 with ART plus an immune-enhancing agent. The discounted costs per patient were $125,140 with no ART, $345,990 with ART, and $357,220 with enhanced ART.

Compared with no ART, ART had an incremental cost-utility ratio (ICUR) of $33,100 per QALY gained. Compared with ART, enhanced ART had an ICUR of $107,600 per QALY gained.

If the addition of an immune-enhancing agent increased the CD4 cell count response by an additional five cells per microlitre, the ICUR of enhanced ART was $854,100 per QALY gained, compared with ART. If it increased the response by an additional 100 cells per microlitre, the ICUR was $54,800 per QALY gained.

Authors’ conclusions
The authors concluded that immune enhancement agents had to increase patients’ CD4 cell counts more than have done or have lower costs, to be considered cost-effective in the USA.

CRD commentary
Interventions:
The interventions were described sufficiently.

Effectiveness/benefits:
The clinical and effectiveness data were from a published model, with some additional data from two published studies. The authors did not report the methods used to identify these studies, nor a systematic review of the literature to identify them, making it impossible to determine if all the relevant data were analysed. The authors did not provide any details of the sources for the utility data, which were probably those used in the published model.

Costs:
For the health care system perspective, all the major relevant costs appear to have been included. The resource use and unit costs were not presented separately, which would have allowed the replication of the study for other settings. The references for the costs were reported. The price year, time horizon, and discount rate were reported.

Analysis and results:
The clinical and outcome information was synthesised in a Markov model. A limited one-way sensitivity analysis was used to assess the impact of changes in the key variables on the results. This type of analysis goes some way towards evaluating the impact of uncertainty, but a probabilistic sensitivity analysis could have evaluated the overall model uncertainty. As a main limitation to their study, the authors reported that favourable assumptions on the efficacy of immune-based therapy were made, even though previous studies had not found any clinical benefit.

Concluding remarks:
The methods were adequate, but the limitations of the study and the lack of information on how the clinical and utility evidence was identified, mean that the authors’ conclusions should be treated with caution.

Funding
Funded by the National Institute for Allergy and Infectious Diseases, USA.
Bibliographic details

PubMedID
22306583

DOI
10.1310/hct1301-1

Original Paper URL
http://thomasland.metapress.com/content/k4x7528017n0rp33/?p=1945499515d74f75a07306c789016ecb&amp;pi=0

Other publications of related interest

Indexing Status
Subject indexing assigned by NLM

MeSH
Adult; Anti-HIV Agents /therapeutic use; CD4 Lymphocyte Count; Cost-Benefit Analysis; Drug Discovery; Female; HIV Infections /drug therapy /immunology; Humans; Male; Middle Aged; Models, Theoretical; Quality-Adjusted Life Years

AccessionNumber
22012012006

Date bibliographic record published
09/06/2012

Date abstract record published
17/12/2012