Cost utility analysis based on a head-to-head phase 3 trial comparing ustekinumab and etanercept in patients with moderate-to-severe plaque psoriasis: a Canadian perspective

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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 evaluated the cost-effectiveness of ustekinumab compared with etanercept among adults with moderate to severe plaque psoriasis who had an inadequate response or had contraindications to at least one conventional systemic therapy or phototherapy. The authors concluded that ustekinumab was more cost-effective than etanercept for patients with moderate to severe plaque psoriasis. The study methodology seemed appropriate and the methods and results were presented adequately. The authors’ conclusions appear appropriate.

Type of economic evaluation
Cost-utility analysis

Study objective
The aim of the study was to evaluate the cost-effectiveness of ustekinumab compared with etanercept among adults with moderate to severe plaque psoriasis who had an inadequate response or contraindications to at least one conventional systemic therapy or phototherapy (such as ultraviolet B rays).

Interventions
Ustekinumab administered at a dose of 45mg at week zero and week four was compared with etanercept administered at a dose of 50mg biweekly for 12 weeks. Both interventions were given by subcutaneous injection.

Location/setting
Canada/secondary care.

Methods

Analytical approach:
A Markov model was used to combine data from a single study with data from published evidence. This model followed the psoriasis assumptions from the health technology assessment (HTA) report undertaken by the Centre for Reviews and Dissemination (CRD), University of York, UK. The time horizon of the study was 10 years. The perspective was that of the Ontario Ministry of Health, Canada.

Effectiveness data:
Effectiveness data was from the 12-week Active Comparator Psoriasis Trial (ACCEPT). This was a phase three multicentre randomised controlled trial. The study included 903 adult patients who were randomised between etanercept (347 patients), ustekinumab 45mg (209 patients) and ustekinumab 90mg (347 patients). Only the ustekinumab 45mg group was used in the model. The study had a follow-up period of 12 weeks. The main clinical effectiveness estimate was the Psoriasis Area and Severity Index (PASI) 75 score collected from patients at week 12.

The trial results were extrapolated for the model using published literature and a Delphi panel of Canadian experts.

Monetary benefit and utility valuations:
Utility gains were applied to patients regardless of treatment arm in accordance with the PASI change from baseline achieved in the ACCEPT study. PASI data did not provide utility scores, so the Dermatology Life Quality Index (DLQI) index was transformed to utility values through linear regression. The regression analysis used data from the Health Outcomes Data Repository where both EuroQol-5D (EQ-5D) and DLQI were collected from patients. ACCEPT
did not collect DLQI data, so the scores were obtained from the two pivotal Phase 3 randomised double-blind placebo-controlled trials of ustekinumab in similar patients (PHOENIX 1 and PHOENIX 2) to provide patient-level data for the regression analysis.

Measure of benefit:
The benefit measure was Quality Adjusted Life Years (QALYs) discounted at an annual rate of 5%.

Cost data:
The main cost categories in the study were outpatient visits (dermatology visit), monitoring (lab tests for full blood count, liver functioning and urea and electrolyte test) and drugs. Costs came from the Ontario Health Insurance Plan. Resource use was estimated by a panel of experts and validated using a previous study. Costs were presented in Canadian dollars (CAD) and discounted at an annual rate of 5%.

Analysis of uncertainty:
One-way sensitivity analyses were conducted to examine the influence of uncertainty on the incremental cost-effectiveness ratio. Probabilistic sensitivity analysis was conducted by varying model parameters across their potential distributions over 10,000 iterations. A scatter plot was used to present the results.

Results
Over the 10-year time horizon mean annual costs were $16,807 for ustekinumab (45mg) and $19,525 for etanercept (50mg).

Average duration of therapy was 2.77 years for ustekinumab and 2.35 years for etanercept.

Etanercept was dominated by ustekinumab (etanercept was more costly and less effective).

The results proved to be robust to changes made in the sensitivity analysis.

Authors’ conclusions
The authors concluded that ustekinumab was more cost-effective than etanercept for patients with moderate to severe plaque psoriasis.

CRD commentary
Interventions:
The interventions were adequately described and appeared to be appropriate comparators. The practice in Canada was appropriately included in the study. Other doses and interventions could have been included in this study but were excluded as they were not relevant to the study setting, so the comparators may not be generalisable to other study settings.

Effectiveness/benefits:
Effectiveness data were derived from a good-quality study and this ensured the validity of the estimates. Appropriate details of this study were provided. Extrapolation of effectiveness data from 12 weeks to 10 years was a concern. However, the time horizon was reduced in the sensitivity analysis and the extrapolation was validated by experts and previous studies, which should reduce the uncertainty of the estimates.

The benefit measure was appropriate to capture both morbidity and mortality of patients. The methods used to estimate the utilities were quite complex, given that no direct data were available. However, techniques that map lesser used utility values to the EQ-5D measure are an accepted method when EQ-5D values are not available. Adequate details of this complex method were provided, but more detailed information would have been helpful to fully assess the appropriateness of the methods used.

Costs:
The study perspective was clearly stated. It appeared that all the relevant cost categories were included. The cost data sources seemed appropriate. Resource use was estimated by experts, which was not ideal, but the estimates were validated by previous studies. Costs were appropriately discounted. No mention was made of a price year and it was
unclear whether costs were adjusted for inflation.

Analysis and results:
The analytical approach seemed appropriate. A graph of the model flow was provided. The model was validated by clinical experts outside of the study. Uncertainty in the model was appropriately assessed using both one-way and probabilistic sensitivity analysis. Both these techniques should provide an indication of the individual parameter uncertainty as well as the overall model uncertainty. However, additional reporting of the sensitivity analysis results would have been useful. The results were reported adequately. The authors discussed several limitations to their study.

Concluding remarks:
The study methodology seemed appropriate and the methods and results were presented adequately. The authors’ conclusions appear appropriate.

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