New protease inhibitors for the treatment of chronic hepatitis C: a cost-effectiveness analysis
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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 new protease inhibitors, added to standard therapy, and an interleukin-28B genotyping assay to select patients for standard or triple therapy, for the treatment of chronic hepatitis C virus. The authors concluded that triple therapy was most cost-effective for patients with advanced fibrosis. For patients with mild fibrosis, triple therapy was not cost-effective, but testing could be cost-effective. The methods were appropriate and the authors' conclusions appear to be valid.

Type of economic evaluation
Cost-utility analysis

Study objective
This study examined the cost-effectiveness of new protease inhibitors, added to standard therapy, and of an interleukin-28B genotyping assay to select patients for standard or triple therapy, for the treatment of chronic hepatitis C virus.

Interventions
Three strategies were examined: standard therapy; triple therapy of standard therapy and a new protease inhibitor; and interleukin-28B genotyping to assign patients to treatment, with those with non-CC genotypes given triple therapy and those with CC genotypes given standard therapy.

Standard therapy was 150 micrograms once weekly of pegylated interferon alpha-2b (or 180 micrograms of pegylated interferon alpha-2a) plus 1g daily of ribavirin. Triple therapy included boceprevir as the protease inhibitor.

Location/setting
USA/secondary care.

Methods
Analytical approach:
The analysis was based on a Markov model, with a lifetime horizon. The interleukin-28B genotype (CC or non-CC) was a key factor to define the patient cohort. Two main scenarios were considered (for mild and advanced fibrosis). The authors stated that the study took the perspective of society.

Effectiveness data:
The treatment effect was the rate of sustained virological response (SVR) and this was the key input for the model. It was from two pivotal phase III trials for the new protease inhibitor and from an intention-to-treat analysis of cohorts for standard therapy. Race- and gender-specific data were used. Some estimates on mortality were from official life tables. Assumptions were made for treatment adherence.

Monetary benefit and utility valuations:
Most of the health-related quality-of-life weights were from the Medical Expenditure Panel Survey; some were from other published studies.

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

Cost data:
The economic analysis included the costs of drugs (including for adverse events), interleukin-28B testing, and annual health care depending on the stage of disease (including liver transplantation). Age-specific baseline health care costs included patients’ out-of-pocket expenses. Drug costs were based on average wholesale prices, which were converted to best prices using a specific conversion factor consistent with Congressional Budget Office estimates. Annual medical care costs were based on medical claims data for chronic hepatitis C. All costs were in US $ and an annual discount rate of 3% was used. The price year was 2010.

Analysis of uncertainty:
Both deterministic and probabilistic sensitivity analyses were performed to investigate uncertainty around all the inputs to the model, using published and assumed ranges of values. An alternative protease inhibitor, telaprevir, was considered in a scenario analysis.

Results
In patients with mild fibrosis, the expected lifetime costs were $160,456 with standard therapy, $177,152 with testing, and $183,257 with triple therapy. The QALYs were 10.97 with standard therapy, 11.24 with testing, and 11.30 with triple therapy.

The incremental cost per QALY gained was $62,900 with testing, compared with standard therapy, and $102,600 with triple therapy, compared with testing. These figures fell to $32,800 with testing and $51,500 with triple therapy for patients with advanced fibrosis. Excluding the testing strategy, the incremental cost per QALY gained with triple therapy over standard therapy was $70,100 in mild fibrosis patients and $36,300 in patients with advanced fibrosis.

An increase in the price of protease inhibitors increased the incremental cost-utility ratios, for example when using telaprevir instead of boceprevir. Variations in the side-effects did not substantially change the findings.

The probabilistic analysis showed that, for patients with advanced fibrosis, the likelihood of testing or triple therapy being cost-effective was 98% at a threshold of $50,000 per QALY or 100% at a threshold of $100,000 per QALY. For patients with mild fibrosis, the likelihood was 18% at $50,000 and 95% at $100,000 per QALY.

Authors' conclusions
The authors concluded that triple therapy was most cost-effective for patients with chronic hepatitis C virus and advanced fibrosis, compared with standard therapy or testing. For patients with mild fibrosis, triple therapy was not cost-effective, but testing could be cost-effective.

CRD commentary
Interventions:
The comparators were appropriately selected to include the possible treatments for patients with chronic hepatitis C. The authors pointed out that in the main analysis, a general protease inhibitor was considered as no randomised trial directly compared new protease inhibitors and their reported efficacies were similar.

Effectiveness/benefits:
The clinical inputs were from several sources that appear to have been appropriate. For example, the treatment effect was mainly from clinical trials, and the epidemiological and behavioural data were from local sources. Some assumptions were needed and were extensively tested in the sensitivity analysis, showing that the findings were robust. Hepatitis C virus affects both survival and quality of life, so QALYs were an appropriate benefit measure. Most of the data for the utility estimates were from a US database.

Costs:
The analysis adopted a broad perspective and included a wide range of costs, most of which were relevant to the health care system. Most of the costs were presented as category totals because their sources did not report itemised data. In general, US sources were used. The drug costs were the main driver of the analysis, and an alternative, more expensive,
A protease inhibitor was considered in a secondary analysis. The price year was reported, and reflation exercises will be possible. The sensitivity analyses considered appropriate variations in the economic inputs.

Analysis and results:
The results were clearly presented. The costs and benefits were appropriately synthesised, using an incremental approach. The uncertainty was satisfactorily investigated and the results of the sensitivity analyses were discussed and illustrated. The structure and assumptions of the model were explicitly presented. The authors acknowledged some limitations to their analysis, such as the lack of evidence for the predictive value of interleukin-28B. They stated that these findings were relevant to patients with hepatitis C virus only and not for those who also had hepatitis B virus or HIV. The findings also appear to be relevant only to the USA.

Concluding remarks:
The methods were appropriate and well described and the authors’ conclusions appear to be valid.

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