Cost effectiveness of peginterferon alpha-2a plus ribavirin versus interferon alpha-2b plus ribavirin as initial therapy for treatment-naive chronic hepatitis C


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.

Health technology
Peginterferon alpha-2a plus ribavirin was compared with interferon alpha-2b plus ribavirin for either 48 or 24 weeks. Peginterferon was given as a 180-microg once weekly injection with ribavirin (1,000 or 1,200 mg/day) (PI-alpha-2a). Interferon alpha-2b was given at a dose of 3 MIU three times weekly with ribavirin (1,000 or 1,200 mg/day). (I-alpha-2b).

Type of intervention
Treatment.

Economic study type
Cost-utility analysis.

Study population
The study population comprised a hypothetical cohort of reference patients defined as "45 years of age, male, with chronic hepatitis C (CHC), and without pre-existing cirrhosis".

Setting
The setting was secondary care. The economic study was carried out in the USA.

Dates to which data relate
The effectiveness data were taken from studies published between 1993 and 2002. The cost data were taken from a study published in 1996 and Italian NHS prices. The price year was 2002.

Source of effectiveness data
The effectiveness data were derived from a review and synthesis of completed studies, supplemented with some assumptions.

Modelling
A deterministic Markov state transition model of CHC disease progression was used to compare the clinical outcomes and costs. The model was necessary to extrapolate outcomes over the expected lifetimes of the patients. The model used annual transition intervals.

Outcomes assessed in the review
The review sought parameter estimates for input into the model. The following were assessed:
the SVR for PI-alpha-2a and I-alpha-2b and the duration of treatment; 
the week at which the predictive test for PI-alpha-2a and I-alpha-2b was performed; and 
patients discontinuing treatment after the predictive test for PI-alpha-2a and I-alpha-2b. 
The following disease progressions (annual rates) were also estimated: 
CHC to compensated cirrhosis; 
compensated cirrhosis to decompensated cirrhosis; 
compensated cirrhosis to hepatocellular carcinoma; 
decompensated cirrhosis to hepatocellular carcinoma; 
decompensated cirrhosis to liver transplantation; 
decompensated cirrhosis to death; 
hepatocellular carcinoma to death; 
liver transplantation (year 1) to death; 
liver transplantation (year 2+) to death. 

**Study designs and other criteria for inclusion in the review** 
The SVR data were taken from a large multi-centre, randomised trial of 1,121 treatment-naive patients with CHC. 
Several other studies were used to derive the disease progression probabilities. 

**Sources searched to identify primary studies** 
Not reported. 

**Criteria used to ensure the validity of primary studies** 
Not reported. 

**Methods used to judge relevance and validity, and for extracting data** 
Not reported. 

**Number of primary studies included** 
Ten primary studies were included in the review. 

**Methods of combining primary studies** 
Generally, the authors did not combine the primary estimates. Nevertheless, the annual progression rates from liver 
transplant (1 years and 2+ years) were the result of combining primary estimates. The methods used were not reported. 

**Investigation of differences between primary studies** 
Not reported.
Results of the review
The SVR for PI-alpha-2a was 46% for hepatitis C virus (HCV) genotype 1 and 76% for HVC genotype non-1.

The SVR for I-alpha-2b was 36% for HCV genotype 1 and 61% for HVC genotype non-1.

The duration of treatment was 48 weeks for HCV genotype 1 and 24 weeks for HVC genotype non-1.

The predictive test was performed at week 12 for PI-alpha-2a and week 24 for I-alpha-2b.

The proportion of patients discontinuing treatment after the predictive test was 20.9% for PI-alpha-2a and 47.8% for I-alpha-2b.

The disease progressions (annual rates) were:
for CHC to compensated cirrhosis, 0.073;
for compensated cirrhosis to decompensated cirrhosis, 0.039;
for compensated cirrhosis to hepatocellular carcinoma, 0.014;
for decompensated cirrhosis to hepatocellular carcinoma, 0.014;
for decompensated cirrhosis to liver transplantation, 0.031;
for decompensated cirrhosis to death, 0.129;
for hepatocellular carcinoma to death, 0.427;
for liver transplantation (year 1) to death, 0.210; and
for liver transplantation (year 2+) to death, 0.057.

Methods used to derive estimates of effectiveness
The effectiveness estimates were supplemented with some authors' assumptions and expert opinion.

Estimates of effectiveness and key assumptions
The authors made assumptions about the reference patients. They also assumed constant annual rates of progression. The variation of the parameters in the sensitivity analysis was determined by expert opinion.

Measure of benefits used in the economic analysis
The summary measures of health benefit were the life-years gained and quality-adjusted life-years (QALYs). Valuations were taken from published, actual patient estimates derived from the Health Utility Index (HUI - Mark III).

Direct costs
The costing was carried out from the perspective of the Italian NHS. The authors reported that the costs and benefits were discounted at a rate of 3%. Resource use was derived from the model. The authors used the official NHS tariff schedule to value inpatient, outpatient, diagnostic and procedural costs. Public prices were used to value drug treatment costs at the cost to the NHS. All the costs were converted into 2002 prices. The unit costs were reported separately.

Statistical analysis of costs
The costs were treated deterministically.
Indirect Costs
The indirect costs were not estimated, as they were not relevant to the perspective of the study.

Currency
Euros (Euro).

Sensitivity analysis
One-way sensitivity analyses were used to explore the impact of treatment effectiveness, progression probabilities, discount rates, medical care costs and the price of PI-alpha-2a. These were carried out to evaluate uncertainty in the model.

Estimated benefits used in the economic analysis
PI-alpha-2a increased the life-years by 0.78 years and the QALYs by 0.67 years compared with I-alpha-2b.

Cost results
The total costs of treatment were not reported.

The annual cost of CHC was Euro 246.

The annual cost of compensated cirrhosis was Euro 347.

The annual cost of decompensated cirrhosis was Euro 5,105.

The annual cost of hepatocellular carcinoma was Euro 4,123.

The annual cost of liver transplantation was Euro 57,283 (year 1) and Euro 4,729 (year 2+).

The drug costs were Euro 392.14 per week for PI-alpha-2a and Euro 195.32 per week for I-alpha-2a.

Synthesis of costs and benefits
The incremental cost was Euro 9,433 per life-year gained and Euro 10,894 per QALY gained.

The weighted, average, incremental cost-effectiveness ratio was Euro 6,811 per life-year gained and Euro 7,865 per QALY gained.

The authors reported that, in all sensitivity analyses, the incremental cost-effectiveness ratio remained below Euro 25,000 per QALY gained.

Authors' conclusions
Peginterferon alpha-2a (PI-alpha-2a) plus ribavirin is cost-effective when compared with interferon alpha-2b (I-alpha-2b) plus ribavirin for treatment naive adults with chronic hepatitis C (CHC), regardless of genotype. The cost-effectiveness ratio is comparable to that of many well-accepted clinical interventions.

CRD COMMENTARY - Selection of comparators
The authors compared PI-alpha-2a plus ribavirin with the best, proven available alternative, I-alpha-2b, for the treatment of CHC. It was unclear which alternative the authors were currently using in their own setting.
Validity of estimate of measure of effectiveness
The authors did not state that a systematic review of the literature was carried out. As a Markov model was used to estimate the costs and effects, the authors selected published evidence relevant to the parameters of the model. The majority of the effectiveness estimates from the primary studies were not combined, except in the case of liver transplant. The authors did not discuss how these estimates were combined to give a single estimate. The authors did not discuss actual differences between the primary studies and the impact these might have had on the effectiveness estimates, although extensive sensitivity analyses were carried out around treatment effectiveness to assess the robustness of the results.

Validity of estimate of measure of benefit
The life-years gained and QALYs were used as the summary measures of health benefit. Although the authors used actual patient estimates to obtain quality of life estimates, these were taken from the Health Utility Index (HUI - Mark III). It was unclear whether CHC patients provided these estimates, or whether they related specifically to patients with CHC.

Validity of estimate of costs
The costing was carried out from the perspective of the Italian NHS. The analysis appropriately included costs relevant to this perspective, although it was unclear whether an estimate for hospital overheads and clinician time was incorporated. The sources and justifications for the estimates were appropriately reported. Confidence intervals were not presented for the incremental cost-effectiveness ratios. It is therefore not possible to surmise whether assuming a different perspective, and thereby including different cost estimates, would alter the principal results and conclusions reported. The analysis, and the reader's understanding and interpretation, would have been further improved by a summary of the total treatment costs of treating individuals with either PI-alpha-2a or I alpha-2b, separate from the cost-effectiveness ratios.

Other issues
The authors made some comparisons of their findings with other published results, citing authors who found similar cost-effectiveness from the US perspective. The issue of generalisability to other settings was not addressed, although it was greatly improved by the sensitivity analyses. Due to the perspective adopted, the results are most likely comparable to other settings with a National Health Service. The authors did not report their results selectively and, in fact, reported extensively on the sensitivity analyses. The conclusions drawn accurately reflected the scope of the study in referring strictly to the reference patient assumed within the study. The limitations of the study centred on the assumptions made by the authors. For example, assuming that a patient remains free of HCV infection once an SVR is achieved. However, the authors explained how these assumptions generally led to conservative results, suggesting that cost-effectiveness would improve further if these assumptions were altered.

Implications of the study
The authors did not make any recommendations for policy or practice as a result of their study, although their support for PI-alpha-2a was clear. Further research, in the form of updating the model with new information, was suggested. In particular, when trials of two pegylated interferon products report.

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Other publications of related interest


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