Cost-effectiveness of interferon alfa in chronic myelogenous leukemia
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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.

Health technology
Interferon alfa (IFN alpha) as a treatment for chronic myelogenous leukemia was compared with conventional chemotherapy (CT). Two treatment strategies for using IFN alpha were compared with chemotherapy, but they were not compared explicitly with each other. Strategy A was to give prolonged treatment (IFN alpha 5MU/M2) for patients who responded to the induction phase and tolerated the drug (this is the current protocol reported in published clinical trials), and strategy B was to shift patients to chemotherapy if they did not achieve cytogenetic remission within 18 months after the induction phase. The comparator strategy was to give chemotherapy throughout using hydroxyurea 1.5g/d or, for patients who failed to respond to this, busulfan 4 mg/d.

Type of intervention
Treatment.

Economic study type
Cost-utility analysis.

Study population
Patients, over 15 years of age, with chronic myelogenous leukemia in the early chronic phase (diagnosis < 12 months) who had not had extensive chemotherapy during this period. Their cytogenetic response fulfilled criteria based on those reported by Talpaz et al.

Setting
Hospital. The economic study was carried out in Pavia, Italy.

Dates to which data relate
Clinical studies used were published between 1992 and 1995. Direct costs were based on retail prices in 1995 or were derived from the literature.

Source of effectiveness data
Effectiveness data were based on a synthesis of previously completed studies and on assumptions based on mortality rates.

Modelling
A decision tree incorporating a Markov model was used to model both outcomes and costs.

Outcomes assessed in the review
The outcomes assessed in the review were the probabilities of responding to treatment and being in various health states.
after induction: cytogenetic remission, complete hematologic remission, partial hematologic remission, or blastic crisis. The probabilities of moving from one of these health states to another during treatment were calculated from results in the review. Details of the results were not given.

**Study designs and other criteria for inclusion in the review**

Four criteria were given:

1. Patients with chronic myelogenous leukemia in the early chronic phase (diagnosis < 12 months);
2. Patients who had not had extensive chemotherapy during this period;
3. Patients who were aged over 15 at diagnosis;
4. Patients' cytogenetic response fulfilled criteria based on those reported by Talpaz et al.

Criteria relating to study design were not mentioned.

**Sources searched to identify primary studies**

The authors used a MEDLINE search and review of the selected references to identify primary studies.

**Criteria used to ensure the validity of primary studies**

Not stated.

**Methods used to judge relevance and validity, and for extracting data**

Not stated.

**Number of primary studies included**

Nine studies were used including 5 multicentre randomised controlled trials.

**Methods of combining primary studies**

A meta-analysis was carried out. Results were pooled by adding the numbers of patients in the health states in question in each study. Data points from different studies were weighted according to sample size. In one study (where some patients were beyond the early chronic phase of the disease) only results from patients who fulfilled all 4 criteria listed above were included in the pooling.

**Investigation of differences between primary studies**

Differences in method and doses were described. In one trial patients not responding well to IFN alpha also received chemotherapy. It is stated that this produced a bias in favour of IFN alpha but differences in results were not described. In another two trials, doses of IFN alpha were lower than the standard.

**Results of the review**

In the induction phase, of patients given IFN alpha, the probability of a patient being a non-responder was 12.3%, of being intolerant to the drug 15%, of achieving cytogenetic remission 27%, complete hematologic remission 39.5%, partial hematologic remission 28%, and blastic crisis 5.5%. Of patients given chemotherapy the probability of a patient being a non-responder was 0.7%, of being in cytogenetic remission 2%, hematologic remission 92.5% and blastic crisis 5.5%. When in cytogenetic remission (both for IFN alpha and CT patients) the probability of staying in that state in the next Markov cycle (6 months) was 95%, of moving to complete hematologic remission was 2.3%, of moving to the
chronic phase was 1.7%, and of moving to blastic crisis was 1%. When in complete hematologic remission (IFN alpha patients) the probability of staying in that state was 92%, of moving to secondary chronic phase was 5%, and of moving to blastic crisis was 3%. When in partial hematologic remission (IFN alpha patients) the probability of remaining in that state was 80%, of moving to the chronic phase was 10% and of moving to blastic crisis was 10%. When in hematologic remission (CT patients) the probability of remaining in that state was 85%, of moving to the chronic phase was 6.55% and of moving to blastic crisis was 8.5%. When in the chronic phase (both cohorts) the probability of remaining in that state was 90% and of moving to blastic crisis was 10%.

Methods used to derive estimates of effectiveness
Probability of death was estimated from Italian life table and disease related mortality rates. Other estimates were based on opinion with reference to "the literature".

Estimates of effectiveness and key assumptions
Death follows once a patient has entered the blastic phase and remained there for 1 Markov cycle. All cytogenetic remissions occurred within the first 2 years of IFN alpha treatment. CT patients who achieved cytogenetic remission followed the same progression as IFN alpha patients. IFN alpha therapy withdrawals were assumed to take place during the induction period. Patients who discontinued IFN alpha followed the same progression as those in the CT cohort. Patients' age at diagnosis was 45.

Measure of benefits used in the economic analysis
Quality adjusted life years (QALYs) gained. Health states and treatment utilities were assessed by 10 physicians using a 0-1 scale and using the mean scores. Thus side effects were included in the quality of life estimates. One year in IFN alpha treatment was estimated to equal 0.875 years in full health, hydroxyurea treatment equalled 0.98 years in full health, busulfan equalled 0.94 years and blastic crisis equalled 0.5 years. Benefits were discounted at 5%.

Direct costs
Prices and quantities of drugs only were included except for treatment during blastic crisis where a global estimate was given based on "the literature". Costs were stated to be based on retail drug prices in 1995 and quantities were not stated but were based on a mean monthly dose. Costs were discounted at 5%.

Indirect Costs
Indirect costs were based on time lost from work with each patient having an annual income of $25,000. Each IFN alpha patient continuing with the drug was assumed to lose 1 week's work in each Markov cycle due to side effects and any patient entering blastic crisis was assumed to retire with a production loss of half the annual income. These estimates were based on the expert panel judgement. Costs were discounted at 5%.

Currency
US dollars ($).

Sensitivity analysis
One-way sensitivity analyses were carried out to investigate the effects of variability of data, on the quality of life during IFN alpha treatment, the percentage cytogenetic remissions with IFN alpha, the cost per month of IFN alpha treatment and the discount rate.

Estimated benefits used in the economic analysis
The quality adjusted life expectancy was:
for treatment with CT, 42.5 months,
treatment with IFN alpha used in strategy A, 58 months
treatment with IFN alpha used in strategy B, 55 months.

The marginal gain of strategy A over chemotherapy was 15.5 quality adjusted months and the marginal gain of strategy B over chemotherapy was 12.5 quality adjusted months.

**Cost results**
The average lifetime costs of chemotherapy were $46,500 made up of treatment of the chronic phase ($1,000), treatment of blastic crisis ($36,400) and indirect costs ($9,100). The average lifetime costs of IFN alpha in strategy A were $162,100 made up of treatment of the chronic phase ($123,000), treatment of blastic crisis ($28,100) and indirect costs ($11,000). The average lifetime costs of chemotherapy were $112,600 made up of treatment of the chronic phase ($75,900), treatment of blastic crisis ($28,200) and indirect costs ($8,500). The incremental cost of strategy A over C was $115,600 and the incremental cost of strategy B over C was $75,600.

**Synthesis of costs and benefits**
Incremental cost-effectiveness for strategy A was $89,500 per QALY gained and for strategy B $63,500 per QALY gained. The discount rate of 5% was used for costs and benefits.

**Authors’ conclusions**
IFN alpha produced substantial gains in QALYs using both strategies but the costs were high particularly using the current protocol (strategy A). Marginal cost-effectiveness ranged from $50,000-100,000 under most assumptions. Sensitivity analysis showed cost-effectiveness results to be most sensitive to the cost of IFN Alpha. Reducing doses to the level of one of the studies reviewed could have brought the cost per QALY down to $20,000. Price changes would also have an effect, for example in the USA monthly treatment with IFN alpha costs less than in Italy ($1,500 versus $2,500) while treatment with hydroxyurea costs more ($20 versus $163).

**CRD COMMENTARY - Selection of comparators**
The selection of comparators is clear although the two strategies were compared with the comparator but not with each other. You, as a database user, should consider if this applies to your own setting.

**Validity of estimate of measure of benefit**
QALY values were produced by a panel of physicians and might not be as valid as those produced by a survey of the general public.

**Validity of estimate of costs**
It is not clear whether some important costs were omitted. The inclusion of indirect costs, and the methods by which they were calculated, make comparisons with other health programmes difficult.

**Other issues**
In the description of strategies the dose of IFN alpha is given as 5MU/M2/d but in the description of costs a mean dose of 8 MU/M2/d is assumed. Results might not be generalisable to other settings or countries.

**Source of funding**
None stated.
Bibliographic details

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9215840

Other publications of related interest

Indexing Status
Subject indexing assigned by NLM

MeSH
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