Economic assessment of tirofiban in the management of acute coronary syndromes in the hospital setting: an analysis based on the PRISM PLUS trial

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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
Use of tirofiban plus heparin and aspirin in the treatment of patients with acute coronary ischaemic syndromes.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
Patients with acute coronary ischaemic syndromes.

Setting
Secondary care. The economic study was conducted in Zurich, Switzerland.

Dates to which data relate
Effectiveness data were taken from the PRISM PLUS trial, carried out between November 1994 and September 1996. Cost and resource use data relate to 1997 and 1998.

Source of effectiveness data
Effectiveness data were derived from a single study.

Link between effectiveness and cost data
Costing was undertaken retrospectively on a hypothetical cohort of 100 patients, therefore there is no direct link between effectiveness and cost data.

Study sample
The intervention group (tirofiban plus heparin) consisted of 773 patients, while the comparator group (heparin alone) had 797 patients. For the group receiving tirofiban alone, the study had to be discontinued after seven days because of excess mortality. A sample size of 1,260 patients (420 per treatment group) was initially planned, in order to detect 30 percent reduction from an estimated 35 percent event rate with heparin, with 90% power and a two-tailed significance level of 0.05. To account for the two primary comparisons, tirofiban versus heparin and the combination of tirofiban and heparin versus heparin, the nominal P value set for two-sided statistical significance was 0.025 and it was maintained despite the discontinuation of the study in the tirofiban group. The protocol specified one sample-size adjustment by the data and safety monitoring board on the basis of the event rate in the heparin-only group at the first
interim efficacy analysis, without consideration of the effect of treatment. The data and safety monitoring board recommended following this rule, an increase in the sample size to 735 patients per group.

**Study design**
The study was an international, multicentre, randomised, double-blind controlled clinical trial, carried out in 72 hospitals in 14 countries. Randomisation was performed locally by means of sealed envelopes. The duration of follow-up was 7 days. There was no loss to follow up.

**Analysis of effectiveness**
Analysis of effectiveness was based on intention to treat. The main health outcome considered in the analysis was defined as a composite end-point of death, myocardial infarction and refractory conditions at 7 days after randomisation. Groups were reported to be comparable in their baseline characteristics.

**Effectiveness results**
The composite end-point results at 7 days, taken from the PRISM PLUS trial were 17.9% for heparin and 12.9% for tirofiban plus heparin, (p=0.004, odds ratio=0.66).

The components of composite end-point results at 7 days for the intervention group were refractory ischaemic condition 9.3%, myocardial infarction (MI) 3.9%, death 1.9% and MI/death 4.9%.

Outcomes for the comparator at 7 days were refractory ischaemic condition 12.7% (p= 0.022, odds ratio= 0.685), myocardial infarction (MI) 7.0% (p= 0.006, odds ratio= 0.528), death 1.9% (p= 0.98 odds ratio= 1.011) and MI/death 8.3% (p= 0.007, odds ratio= 0.565).

**Clinical conclusions**
Tirofiban is a reversible, highly selective non-peptide inhibitor of platelet glycoprotein (GP) IIb/IIIa receptors. The potential advantages of such drugs include immediate onset of action, rapid reversal of antiplatelet activity after drug discontinuation, suitability for multiple repeat administrations and high specificity for the GP IIb/IIIa receptor.

**Measure of benefits used in the economic analysis**
The authors did not provide any measure of benefits.

**Direct costs**
The cost analysis was performed strictly from the admitting hospitals' point of view. The determination of costs was based on the additional hospital days required to treat complications (refractory ischaemic conditions and myocardial infarctions) during the first 7 days. The need for additional days in ICU and revascularisation procedures for each complication was also considered. In order to quantify the costs of these complications, typical clinical practice patterns in Swiss hospitals were analysed. Using a structured questionnaire, data were obtained from 6 cardiologists, representing larger university teaching hospitals and smaller hospitals, on the probability and quantity of additional days on the normal ward and ICU, including the probability of revascularisation procedures. The additional days were weighted in accordance with the average cost per day, published by the association of Swiss hospitals. The costs of the revascularisation procedures were obtained from a study published in 1997 (Influence of lipid lowering therapy on resource utilisation in health care - relevance of the Scandinavian 4S study on reducing costs in Swiss health care setting). The drug costs were based on a loading dose and a maintenance dose. Discounting was not required due to the short duration of follow-up. The cost date appears to be 1998. All calculations were standardised to 100 treated patients.

**Indirect Costs**
Not considered.
Currency
Swiss francs (SFr) and European currency units (ECU). Exchange rate 1 ECU = SFr1.6428 (April 1998).

Sensitivity analysis
Three types of sensitivity analyses were conducted:

- univariate analysis covering a broad range of plausible values between -50% and +50% for the unit resource costs,
- threshold analysis to obtain the drug cost at which the results change from net savings to net investments between the treatment groups,
- analysis considering 95% confidence intervals of the absolute risk reduction between the two treatment groups.

Estimated benefits used in the economic analysis
Not applicable.

Cost results
The additional use of tirofiban resulted in net savings of SFr54,899 (ECU33,418) per 100 patients, achieved through a reduction in the cost of treating refractory ischaemic conditions (SFr79,306, ECU48,275) and myocardial infarctions (SFr57,658, ECU35,097).

Synthesis of costs and benefits
Not applicable.

Authors' conclusions
Tirofiban is cost-saving in acute coronary ischaemic syndromes and improves the economics of managing these patients during the initial hospitalisation.

CRD COMMENTARY - Selection of comparators
The reason for the choice of the comparators (tirofiban plus heparin plus aspirin versus heparin plus aspirin) is clear, as both drug combinations are used in Swiss health care for the management of acute coronary syndromes in a hospital setting. You, as a database user, should consider whether this applies to your own setting.

Validity of estimate of measure of benefit
The effectiveness evidence comes from a randomized double-blind controlled trial with comparable patient groups and a sufficient sample size. The authors acknowledged, unlike the Platelet Receptor Inhibition in Ischaemic Syndrome Management (PRISM) trial, that the study group receiving tirofiban only was discontinued because of excess mortality compared with heparin alone at seven days. As only separate clinical outcomes were used in the analysis, it should be considered as a cost-consequence analysis.

Validity of estimate of costs
As acknowledged by the authors, the study is a retrospective analysis and the cost structure is principally determined by expert opinion. The costs relate only to the 7 days after treatment onset, leaving out potential additional costs that might become evident later. Extensive cost comparisons with studies dealing with glycoprotein inhibitors IIb/IIIa were performed.
**Other issues**
The authors acknowledge the following limitations of the study:

- a potential limitation of the PRISM PLUS study on which this study is based is that patients' quality of life during the extended survival period associated with therapy was not assessed;

- caution should be exercised when extrapolating the results of this study to other countries and healthcare settings without taking into account local practice patterns and technology availability.

**Implications of the study**
According to the authors "primary therapy with tirofiban is an economically justified intervention in the initial management of patients with acute coronary ischaemic syndrome in the Swiss hospital setting”.

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