Economic impact of GPIIB/IIIA blockade after high-risk angioplasty: results from the RESTORE trial


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
Administration of platelet glycoprotein (GP) IIB/IIIA receptor blocker tirofiban after coronary intervention to prevent untoward complications.

Type of intervention
Secondary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
Patients were asked to participate if they were undergoing coronary intervention within 72 hours of presentation with an acute coronary syndrome (unstable angina pectoris or acute MI). All patients qualified as undergoing high-risk angioplasty.

Setting
The setting was secondary care. The economic study was carried out at Emory University, Atlanta, Georgia, USA.

Dates to which data relate
The dates for the effectiveness, and resource use data were January 1995 to November 1995. The price year was 1995.

Source of effectiveness data
The evidence/estimate for the final outcome was derived from a single study.

Link between effectiveness and cost data
The costing was undertaken prospectively on a subset of patients from the sample used in the effectiveness study.

Study sample
Information on the study sample was available for the total RESTORE study rather than for the US sample on which the economic analysis was based. This information was available in another published article and it should be noted that the final sample numbers differ slightly in the two papers. Patients were asked to participate if they were undergoing coronary intervention within 72 hours of presentation with an acute coronary syndrome (unstable angina pectoris or acute MI).

Patients were randomised to one of two arms of the study, namely tirofiban or placebo. The sample size was selected to
obtain 80% power in detecting a 30% reduction rate in the composite event rate. A total of 2,212 patients were randomised to the trial of whom 1,070 were allocated to the placebo treatment and 1,071 to the treatment arm. The method of randomisation was not discussed. The study was double-blinded. 71 patients were randomised but did not receive the study drug for technical or administrative reasons so that, in total, 2,141 patients were included in the analysis.

Patients were excluded from the study when presenting with certain clinical characteristics, such as that receiving thrombolytic therapy within 24 hours or contraindication to anticoagulation, or if they were over 80 years of age.

The economic study was based on the 1,920 patients enrolled in the USA, of whom 963 were randomised to the placebo treatment. The mean age was 59.2 years, 72.7% were males, 19.9% had diabetes risk factor, 57.3% presented with hypertension and 66.8% had a history of smoking. 39.3% had had a previous myocardial infarction, 20.5% had had a previous coronary angioplasty, 8.3% had had previous coronary surgery and 32.3% presented with acute myocardial infarction.

957 patients were randomised to the tirofiban treatment, the mean age was 59, 72% were males, 20.7% had a diabetes risk factor, 55.4% presented with hypertension and 64.1% had a history of smoking. 36.5% had had a previous myocardial infarction, 20.8% had had a previous coronary angioplasty, 6.9% had had previous coronary surgery and 32.1% presented with acute myocardial infarction. All patients qualified as undergoing high-risk angioplasty. The percentage of patients who did not complete the study in the USA was not stated.

**Study design**

The study was a multi-centred, randomised, controlled trial. 30 sites provided the cost data for the study. The total number of US sites was not specified. The duration of follow-up was 6 months, but the economic study focussed on the 2 day and 30 day intermediate results. Patients were blindly randomised to the study arms although the exact method was not specified. Randomisation was delayed until a guidewire was successfully passed across the lesion intended for dilation or atherectomy. No patients were lost to follow-up. Outcomes were independently assessed by blinded assessors.

**Analysis of effectiveness**

The study stated that the analyses were conducted on an intention to treat basis. However of the 2,212 patients randomised to the trial only the 2,141 of those to whom the drug infusion was administered, were actually included in the study. Consequently it would seem that the analysis was performed on the basis of treatment completers rather than on intention to treat. However it was not specified whether any of the 71 patients who were randomised, but who did not complete the treatment, belonged to the US sample. The primary health outcome used in the analysis was a composite measure including death from all causes, myocardial infarction, repeat angioplasty, coronary surgery and stent placement, such that each patient was only counted once in the composite end point. Patients in the US sample, and patients for whom the cost substudy was conducted, were shown to have comparable baseline characteristics in both arms of the study.

**Effectiveness results**

The effectiveness results for all US patients indicated that at two days the composite event rate was 36% lower for tirofiban compared with placebo, (8% versus 12%, p=0.0002). At 30 days, the risk reduction was 16% for patients on tirofiban compared to patients on placebo, (14.4% versus 17.1%, p=0.10). For the US patients included in the cost sub-study, the composite event rate at two days was 46% lower for tirofiban compared with placebo, (7% versus 12.9%, p=0.005). At thirty days, the risk reduction was 28% for patients on tirofiban compared to patients on placebo, (12.7% versus 17.7%, p=0.049).

**Clinical conclusions**

Tirofiban has been shown to decrease in-hospital, and possibly 30 day events after high-risk angioplasty.
Modelling
A linear regression was used to estimate costs for all US patients. Primary data for 820 US patients were used to run the regression. In-hospital cost data were predicted by the following independent variables: initial hospital length of stay, coronary surgery during initial hospitalisation, additional coronary angioplasty, stent for bailout or inadequate result, myocardial infarction at presentation, congestive failure and myocardial infarction as a complication.

Measure of benefits used in the economic analysis
The measure of benefits used in the economic analysis was a composite measure of events including death from all causes, myocardial infarction, repeat angioplasty, coronary surgery and stent placement. Individual components of the composite measure were also reported. A valuation of health outcomes was not performed.

Direct costs
Costs were not discounted since the study period for which costs were collected was one month. Quantities and costs were not reported separately. Direct costs included hospital costs, physician costs and drug costs. The cost boundary adopted was that of the provider, i.e. the hospital. The estimation of hospital costs for 820 patients was based on the hospital charges to payers (available on UB92 forms) that were then transformed into hospital costs using the hospital's global cost-to-charge ratio (published in the Medicare Cost Report for each hospital). Physician costs were derived using a model based on data available at Emory University for patients undergoing coronary intervention. Again, charges were converted to costs. The cost of the drug was based on a catalogue price. Hospital and physician costs for US patients for whom costs were not measured, were imputed using a linear regression model. Costs were measured during the trial period from January to November 1995. The price date was 1995.

Statistical analysis of costs
Costs were analysed using the t test, or Wilcoxon rank sum test where the assumption of normality was violated.

Indirect Costs
Indirect costs were not included in the analysis.

Currency
US dollars ($).

Sensitivity analysis
Sensitivity analysis was not conducted.

Estimated benefits used in the economic analysis
The effectiveness results for all US patients indicated that at two days the composite event rate was 36% lower for tirofiban compared with placebo, (8% versus 12%, p=0.0002). At 30 days, the risk reduction was 16% for patients on tirofiban compared to patients on placebo, (14.4% versus 17.1%, p=0.10). For the US patients included in the cost sub-study, the composite event rate at two days was 46% lower for tirofiban compared with placebo, (7% versus 12.9%, p=0.005). At thirty days, the risk reduction was 28% for patients on tirofiban compared to patients on placebo, (12.7% versus 17.7%, p=0.049). An incremental analysis was not performed.

Cost results
For the 820 patients for whom costs were available the measured initial hospital cost was $10,289 (+/- 6,241) for the placebo group and $10,551 (+/- 5,388) for the tirofiban group, (p=0.52). The 30 day hospital costs were $10,717 (+/- 6,615) for the placebo group and $10,914 (+/- 5,909) for the tirofiban group, (p=0.65). For all US patients the estimated initial costs were $12,145 (+/- 5,882) for the placebo group and $12,230 (+/- 5,527) for the tirofiban group.
The 30 day hospital costs were $12,402 (+/- 6,147) for the placebo group and $12,446 (+/- 5,814) for the tirofiban group, (p=0.87). An incremental analysis was not performed.

Synthesis of costs and benefits
A synthesis of costs and benefits was not performed as both the treatment and the comparator was similar in costs.

Authors' conclusions
The authors concluded that the GPIIB/IIIA blocker, tirofiban, can reduce complications in patients with acute coronary syndromes after angioplasty at no increase in cost.

CRD COMMENTARY - Selection of comparators
The choice of a placebo as comparator to the treatment was justified, since the tirofiban administration constituted an additional treatment to usual practice.

Validity of estimate of measure of benefit
In terms of the effectiveness results, the study constituted a well-designed, double blind, randomised controlled trial. However, a slight confusion arises from the difference in sample numbers reported in the effectiveness article and the economic study article. Furthermore, it did appear that the results were analysed on the basis of treatment completers rather than intention to treat. An analysis based on the former method could introduce bias in the results, since the patients could have been excluded on a basis that was not random. It was not possible to impute whether any of the patients who had not completed the protocol were actually part of the US sample of patients on which the economic analysis was based.

Validity of estimate of costs
All relevant categories of cost seem to have been included, although more information on the exact content of three cost categories (drugs, physician costs and hospital costs) would have been useful. It would also have been helpful to have a breakdown by resource use, which would facilitate transposing the study to another setting. The authors also pointed out that the validity of their estimate of costs was dependent on the accuracy on the hospital cost reports that are filed annually with the Health Care Financing Agency. A sensitivity analysis of costs was not performed.

Other issues
Comparisons of the results were made with another study, although the methods for searching the literature were not documented. The issue of generalisability was addressed with respect to costs. The authors pointed out that the costs used in the study were dependent on their setting and specific accounting system.

Implications of the study
Further research is required for different population groups, in particular to determine whether lower risk patients would also benefit from the intervention. Furthermore, the development of different methods of administering the treatment (such as oral or transdermal GPIIB/IIIA or other antiplatelet agents) should also be investigated since this could improve the cost-effectiveness of the treatment.

Source of funding
None stated.

Bibliographic details
GPIIB/IIIA blockade after high-risk angioplasty: results from the RESTORE trial. Journal of the American College of Cardiology 1999; 34(4): 1061-1066

PubMedID
10520791

Other publications of related interest

Indexing Status
Subject indexing assigned by NLM

MeSH
Adult; Aged; Angioplasty, Balloon, Coronary /economics; Cohort Studies; Combined Modality Therapy; Coronary Disease /economics /mortality /therapy; Cost-Benefit Analysis; Double-Blind Method; Female; Hospital Mortality; Humans; Male; Middle Aged; Myocardial Infarction /economics /mortality /therapy; Platelet Aggregation Inhibitors /economics /therapeutic use; Platelet Glycoprotein GPIIb-IIIa Complex /antagonists & inhibitors; Recurrence; Retreatment; Risk Factors; Tyrosine /analogs & derivatives /economics /therapeutic use; United States

AccessionNumber
21999001894

Date bibliographic record published
31/03/2001

Date abstract record published
31/03/2001