Dr Rossi Ticagrelor versus genotype-driven antiplatelet therapy for secondary prevention after acute coronary syndrome: 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
The study assessed the cost-effectiveness of universal ticagrelor treatment compared with genotype-driven antiplatelet therapy in patients with acute coronary syndrome. The authors concluded that prescribing ticagrelor universally was cost-effective given typically accepted thresholds. The quality of the study methods was adequate. Although more details could have been reported about how clinical and effectiveness data were identified, the authors’ conclusions appear to be appropriate.

Type of economic evaluation
Cost-utility analysis

Study objective
The study determined the cost-effectiveness of ticagrelor treatment compared with a genotype-driven selection antiplatelet agents in patients (66 years or older) hospitalised for acute coronary syndrome.

Interventions
The two treatments compared were genotype-driven treatment (where the patient was tested for CYP2C19*2 mutations and prescribed clopidogrel in their absence or ticagrelor in the presence of any CYP2C19*2 mutations) versus universal ticagrelor without genetic testing.

Location/setting
USA/Outpatient secondary care.

Methods
Analytical approach:
A hybrid decision tree/Markov model was used to simulate the likelihood of a gene mutation and the ongoing risk of myocardial infarction, bleeding, dyspnoea (shortness of breath) and death. It was based on a population of 100,000 Medicare beneficiaries, aged 66 or older, hospitalised for acute coronary syndrome. The time horizon was five years. The authors reported that the perspective adopted was that of Medicare, which was reported as the primary health insurance provider for virtually all US citizens aged 65 years or older.

Effectiveness data:
The effectiveness estimates came from two previously published studies (Yusuf, et al. 2001 and Wallentin, et al. 2009, see 'Other Publications of Related Interest' below for bibliographic details). The main effectiveness parameters used in the model were rate ratios of mortality, myocardial infarction bleeding and dyspnoea for clopidogrel versus placebo and ticagrelor versus clopidogrel. The probability of gene mutation was also included. There were no test accuracy data in the model. It was assumed that ticagrelor response was independent of all genotypes.

Data comparing the clinical performance of ticagrelor and clopidogrel came from the PLATO (Platelet Inhibition and Patient Outcomes) trial (James, et al. 2009, see 'Other Publications of Related Interest' below for bibliographic details). Since the hazard rate for clopidogrel in the PLATO trial was based on patients with or without mutated genes, the authors adjusted the rate using a placebo versus clopidogrel hazard ratio from a different population to obtain effectiveness based on patients without a mutated gene.
Monetary benefit and utility valuations:
Utility values for patients hospitalised with acute coronary syndrome were obtained from a nationally representative
survey of non-institutionalised Americans using the EQ-5D (European Quality of Life at 5 Dimensions) questionnaire.
For other health states, cost-effectiveness analysis registries were searched to locate utility weightings, limiting results
to reports on American patient populations published since 1998.

Measure of benefit:
The measure of benefit was quality-adjusted life-years (QALYs) gained. As benefits could be generated over a five-
year time period, future benefits were discounted at an annual rate of 3%.

Cost data:
The direct costs included were: genotype test; ticagrelor; clopidogrel; fatal and non-fatal myocardial infarction
treatment; treatment for bleeding; and follow-up treatment for acute coronary syndrome. Myocardial infarction event
costs were estimated from Medicare-related group hospital payments. Drug costs were estimated from manufacturers’
list prices and published studies. Other costs came from previously published studies. All costs were inflated to 2009
prices using the Medical Care Component of the Consumer Price Index. As costs could be incurred over a five-year
time period, future costs were discounted at an annual rate of 3%. All costs were reported in US $.

Analysis of uncertainty:
One-way sensitivity analyses were conducted by varying parameters individually. A probabilistic sensitivity analysis was
also conducted using 1,000 Monte Carlo simulations; for this analysis, probability distributions were fitted alongside
each model parameter. The results were presented in a cost-effectiveness acceptability curve.

Results
For 100,000 Medicare patients given genotype-driven treatment, the total QALYs gained were 217,711 and the total
costs incurred were $794,382,109.

For 100,000 Medicare patients given universal ticagrelor treatment, the total QALYs gained were 228,049 and the total
costs incurred were $794,382,109.

Costs and benefits were combined using an incremental cost-utility ratio (the additional cost per QALY gained). When
compared with the genotype-driven intervention, universal ticagrelor treatment was associated with an incremental cost
per QALY gained of $10,059.

The results of the probabilistic sensitivity analysis showed that for 977 of the 1,000 simulations, the estimated
incremental cost-utility ratio for universal ticagrelor versus genotype-driven treatment was less than the $50,000 per
QALY threshold.

Authors’ conclusions
The authors concluded that prescribing ticagrelor universally was cost-effective given typically accepted thresholds
compared with genotype-driven therapy.

CRD commentary
Interventions:
The interventions were reported adequately and justified as likely strategies. The current practice was unclear.

Effectiveness/benefits:
Clinical and effectiveness data primarily from came published studies. For each parameter in the model, the authors
adequately reported the base case value, range of values for the sensitivity analysis, and the source. However, the
authors did not report how published studies were identified or whether they were identified through a systematic
review of the literature. As a result, it was not possible to determine if the best available evidence was used in the
model. The authors had to adjust the clopidogrel effectiveness estimate from one trial because the population was a
mixture of patients with and without a mutated gene, so this estimate was uncertain. However, the range of
effectiveness values varied in sensitivity analysis suggested that the estimate would need to be significantly wrong for
ticagrelor to cease being cost-effective.
Costs:
The perspective adopted was explicitly reported to be that of Medicare. For this perspective it would appear that all relevant major costs were included in the analysis. The authors adequately reported the sources from which costs were derived. The time horizon, discount rate, price year and currency details were all adequately reported.

Analysis and results:
Cost and outcome information were synthesised using a hybrid decision tree/Markov model. Adequate details of the model structure were provided including a diagram. The impact of uncertainty on the results was appropriately tested using one-way and probabilistic sensitivity analyses. As a main limitation to their study, the authors reported that their analysis was based on the efficacy of treatment in clinical trials with short follow-up durations.

Concluding remarks:
The quality of the study methods was adequate. Although more details could have been reported about how clinical and effectiveness data were identified, the authors' conclusions appear to be appropriate.

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