Rosuvastatin is cost-effective in treating patients to low-density lipoprotein-cholesterol goals compared with atorvastatin, pravastatin and simvastatin: analysis of the STELLAR 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
The use of rosuvastatin (10 - 40 mg/day), atorvastatin (10 - 80 mg/day), pravastatin (10 - 40 mg/day), and both branded and generic simvastatin (10 - 80 mg/day) in the treatment of hypercholesterolaemia.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients with hypercholesterolaemia (LDL-C \( \geq 160 \text{ mg/dL} \) and \( < 250 \text{ mg/dL} \), triglyceride concentration \( < 400 \text{ mg/dL} \) aged 18 years or older.

Setting
The study setting was secondary care. The economic analysis was conducted in the UK.

Dates to which data relate
The dates to which the effectiveness data related were not reported. The price year was 2003.

Source of effectiveness data
The effectiveness data were derived from the Statin Therapies for Elevated Lipid Levels compared across doses to Rosuvastatin ( STELLAR ) randomised controlled trial (RCT).

Link between effectiveness and cost data
The costing was undertaken retrospectively on the same patient sample as that used in the effectiveness study.

Study sample
The authors only reported limited information on the methods and conduct of the effectiveness trial. Further information is provided in Jones et al. 2003 (see 'Other Publications of Related Interest' below for bibliographic details). A total of 2,268 patients were recruited in the study. Of these:

- 473 patients received rosuvastatin (156 received a 10-mg dose, 160 a 20-mg dose, and 157 a 40-mg dose);
- 633 patients received atorvastatin (158 received a 10-mg dose, 154 a 20-mg dose, 156 a 40-mg dose and 165 an 80-mg...
485 patients received pravastatin (160 received a 10-mg dose, 164 a 20-mg dose, and 161 a 40-mg dose); 648 patients received branded simvastatin (165 received a 10-mg dose, 162 a 20-mg dose, 158 a 40-mg dose and 163 an 80-mg dose); and 648 patients received generic simvastatin (165 received a 10-mg dose, 162 a 20-mg dose, 158 a 40-mg dose and 163 an 80-mg dose).

The authors did not report the age or gender distribution of these patients.

**Study design**
The authors reported that the study was a parallel-group, open-label, multi-centre RCT. The patients were followed up for 6 weeks.

**Analysis of effectiveness**
The authors did not report whether the analysis of effectiveness was conducted on an intention to treat basis or for treatment completers only. The primary end point of the trial was the change in plasma LDL-C from baseline. The authors reported that the treatment groups were well balanced in the distribution of patients across the Third Joint European Task Force CVD categories and, hence, in terms of the target LDL-C levels to be achieved.

**Effectiveness results**
The authors reported that in the STELLAR trial, treatment with rosuvastatin (10 - 40 mg) achieved mean reductions in plasma LDL-C levels of 46 to 55%, compared with 37 to 51% for atorvastatin (10 - 80 mg), 20 to 30% for pravastatin (10 - 40 mg) and 28 to 46% for simvastatin (10 - 80 mg).

The STELLAR trial also showed that rosuvastatin 10 - 40 mg reduced LDL-C to a significantly greater extent than the milligram-equivalent doses of atorvastatin, pravastatin and simvastatin, (p<0.001).

More results from the STELLAR trial were published by Jones et al. (2003).

**Clinical conclusions**
The authors concluded that rosuvastatin 10 - 40 mg reduced LDL-C to a significantly greater extent than the milligram-equivalent doses of atorvastatin, pravastatin and simvastatin.

**Measure of benefits used in the economic analysis**
The measures of benefits used were the percentage reduction in LDL-C levels and the proportion of patients achieving the European guideline LDL-C goals. The authors assumed that the efficacy of the different treatment options at 6 weeks was equivalent to that after one year.

**Direct costs**
The costs included in the analysis were those relevant to the UK NHS. The authors only included annual drug acquisition costs. These costs were based on prices for the branded products taken from the British National Formulary, September 2003. The prices for generic simvastatin were taken from the Drug Tariff, November 2003. Discounting was not necessary, as the costs were incurred during one year, and was therefore not performed. The study reported the annual mean costs per patient. The price year was 2003.

**Statistical analysis of costs**
The costs were reported as point estimates (i.e. the data were deterministic).

**Indirect Costs**
The indirect costs were not included.

**Currency**
UK pounds sterling (€).

**Sensitivity analysis**
Sensitivity analyses on efficacy parameters were undertaken using the lower and upper 95% confidence intervals (CIs) for the percentage reduction in LDL-C and the proportion of patients treated to LDL-C goals. A further sensitivity analysis allowed the relative prices of statins to vary, by reducing the cost of a particular statin by 25% and keeping the price of the other statins constant.

**Estimated benefits used in the economic analysis**
The mean reduction in LDL-C levels was:

- for rosuvastatin, 45.8% (95% CI: 43.8 - 47.8) with 10 mg, 52.4% (95% CI: 50.4 - 54.4) with 20 mg, and 55% (95% CI: 53 - 57) with 40 mg;
- for atorvastatin, 36.8% (95% CI: 34.8 - 38.7) with 10 mg, 42.6% (95% CI: 40.6 - 44.7) with 20 mg, 47.9% (95% CI: 45.9 - 49.8) with 40 mg, and 51.1% (95% CI: 49.3 - 53.0) with 80 mg;
- for pravastatin, 20.1% (95% CI: 18.2 - 22.1) with 10 mg, 54.4% (95% CI: 22.4 - 26.3), and 29.7% (95% CI: 27.7 - 31.7) with 40 mg;
- for branded simvastatin, 28.3% (95% CI: 26.3 - 30.2) with 10 mg, 35.0% (95% CI: 33.1 - 37.0) with 20 mg, 38.8% (95% CI: 36.9 - 40.8) with 40 mg, and 45.8% (95% CI: 43.8 - 47.7) with 80 mg; and
- for generic simvastatin, 28.3% (95% CI: 26.3 - 30.2) with 10 mg, 35.0% (95% CI: 33.1 - 37.0) with 20 mg, 38.8% (95% CI: 36.9 - 40.8) with 40 mg, and 45.8% (95% CI: 43.8 - 47.7) with 80 mg.

The proportion of patients reaching LDL-C European goals was:

- for rosuvastatin, 68.6% (95% CI: 60.9 - 75.4) with 10 mg, 86.3% (95% CI: 80.1 - 90.7) with 20 mg, and 82.8% (95% CI: 76.1 - 87.9) with 80 mg;
- for atorvastatin, 43.7% (95% CI: 36.2 - 51.5) with 10 mg, 58.4% (95% CI: 50.5 - 65.9) with 20 mg, 71.8% (95% CI: 64.3 - 78.3) with 40 mg, and 74.5% (95% CI: 67.4 - 80.6) with 80 mg;
- for pravastatin, 2.5% (95% CI: 1.0 - 6.3) with 10 mg, 12.2% (95% CI: 8.0 - 18.1) with 20 mg, and 21.7 (95% CI: 16.1 - 28.7) with 40 mg;
- for branded simvastatin, 20.0% (95% CI: 14.6 - 26.8) with 10 mg, 36.4% (95% CI: 29.4 - 44.1) with 20 mg, 47.5% (95% CI: 39.8 - 55.2) with 40 mg, and 66.3% (95% CI: 58.7 - 73.1) with 80 mg; and
- for generic simvastatin, 20.0% (95% CI: 14.6 - 26.8) with 10 mg, 36.4% (95% CI: 29.4 - 44.1) with 20 mg, 47.5% (95% CI: 39.8 - 55.2) with 40 mg, and 66.3% (95% CI: 58.7 - 73.1) with 80 mg.

**Cost results**
The mean annual cost per patient was:
with rosuvastatin, 235, 387 and 387 for 10-, 20- and 40-mg doses, respectively;

with atorvastatin, 235, 387, 387 and 387 for 10-, 20-, 40- and 80-mg doses, respectively;

with pravastatin, 211, 387 and 387 for 10-, 20- and 40-mg doses, respectively;

with branded simvastatin, 235, 387, 387 and 387 for 10-, 20-, 40- and 80-mg doses, respectively; and

with generic simvastatin, 156, 209, 274 and 375 for 10-, 20-, 40- and 80-mg doses, respectively.

**Synthesis of costs and benefits**
The costs and benefits were combined using an incremental cost-effectiveness ratio (i.e. the additional cost per 1% reduction in LDL-C levels, or the additional cost per patient reaching European goals). The authors ranked all interventions by effectiveness and ruled out all those interventions that were either dominated (i.e. more expensive and less effective) or extended dominated (i.e. for a lower incremental cost-effectiveness ratio the comparator is more effective).

Compared with generic simvastatin 10 mg, the use of rosuvastatin 10 mg was associated with a cost of 4.48 per extra 1% reduction in LDL-C per patient, while the use of rosuvastatin 40 mg was associated with a cost of 8.64 per extra 1% reduction.

Compared with generic simvastatin 10 mg, the use of rosuvastatin 10 mg was associated with a cost of 162.04 per additional patient reaching LDL-C goals, while the use of rosuvastatin 20 mg was associated with a cost of 10.28 per additional patient.

The results of the sensitivity analysis showed that the cost-effectiveness results were robust to plausible variations in efficacy and substantial variation in price.

**Authors' conclusions**
In patients with hypercholesterolaemia, rosuvastatin was a cost-effective statin option for treating patients to low-density lipoprotein cholesterol (LDL-C) goals.

**CRD COMMENTARY - Selection of comparators**
The use of rosuvastatin as the comparator was justified on the grounds that trials had demonstrated it to have greater efficacy in lowering LDL-C levels than atorvastatin, pravastatin or simvastatin. You should decide if the comparator used represents current practice in your own setting.

**Validity of estimate of measure of effectiveness**
The analysis of effectiveness was based on an RCT. This was appropriate for the study question, as well-conducted RCTs are considered the 'gold' standard study design when comparing different health care interventions. However, the authors did not report the methods of the trial in detail, referring the reader instead to other publications for more information. The authors reported that all patient groups were shown to be comparable at baseline in terms of the target LDL-C levels to be achieved. Appropriate statistical analysis were undertaken to test for statistically significant differences between the groups. To fully assess the internal validity of the effectiveness measures the reader will need to consult the paper reporting the clinical study.

**Validity of estimate of measure of benefit**
The estimation of benefits was obtained directly from the effectiveness analysis, although the authors assumed that the efficacy of the different treatment options at 6 weeks was equivalent to that after one year. This assumption was not tested in sensitivity analysis. Ideally, the authors should have used a more generic health outcome (e.g. quality adjusted life-years or life-years gained) to make comparisons across different interventions in other disease areas.
Validity of estimate of costs
The authors' costing study was very limited and only included drug acquisition costs. Other relevant costs, such as physician and nurse visits, laboratory costs and the costs of treating diseases that could be prevented with statin use (e.g. cardiovascular diseases), were not included in the analysis. It was unclear if the inclusion of such costs would have altered the authors' conclusions. The authors reported the unit costs for a 28-tablet pack for each statin under investigation, making the results more generalisable to other settings. The unit costs were derived from the British National Formulary. Appropriate sensitivity analyses of the costs were undertaken. Discounting was not relevant, as all the costs were incurred in one year, and was therefore not performed.

Other issues
The authors compared their results with those from other studies evaluating the effectiveness and cost-effectiveness of rosuvastatin and which had also found rosuvastatin to be effective and highly cost-effective in the treatment of hypercholesterolaemia. The issue of generalisability to other settings was partially addressed in the sensitivity analysis. The authors do not appear to have presented their results selectively and their conclusions reflected the scope of the analysis. The authors did not report any other limitation to their study.

Implications of the study
The authors reported that rosuvastatin 10 mg was cost-effective in treating patients to goal and was likely to further reduce costs by avoiding the need for dose titration in most patients.

Source of funding
Supported by AstraZeneca, Pfizer, KOS and GlaxoSmithKline.

Bibliographic details

PubMedID
15703502

Other publications of related interest


Indexing Status
Subject indexing assigned by NLM

MeSH
Atorvastatin Calcium; Cardiovascular Diseases /economics /prevention & control; Cholesterol, LDL /drug effects; Cost-Benefit Analysis; Drug Costs /statistics & numerical data; Economics, Pharmaceutical; Fluorobenzenes /economics /therapeutic use; Heptanoic Acids /economics /therapeutic use; Humans; Hydroxymethylglutaryl-CoA Reductase Inhibitors /economics /therapeutic use; Hypercholesterolemia /drug therapy /economics; Pravastatin /economics
AccessionNumber
22005000487

Date bibliographic record published
28/02/2006

Date abstract record published
28/02/2006