Cerivastatin versus branded pravastatin in the treatment of primary hypercholesterolaemia in primary care practice in Canada: a one-year, open-label, randomized, comparative study of efficacy, safety, and cost-effectiveness

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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
Cerivastatin (third-generation statin) and branded pravastatin (first-generation statin) were evaluated for the treatment of primary hypercholesterolaemia:

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised adult patients with documented primary hypercholesterolaemia that did not respond adequately to dietary interventions. The patients were aged between 18 and 75 years. The patient's eligibility for the study was determined on the grounds of two lipid profiles at baseline. The patients were required to have the following:

- two fasting low-density lipoprotein cholesterol (LDL-C) measurements with a mean LDL-C level of at least 160 mg/dL,
- and
- at least 1 fasting triglyceride measurement of less than or equal to 400 mg/dL.

The exclusion criteria included, for example, uncontrolled hypertension, chronic liver disease, and drug or alcohol abuse.

Setting
The setting was a primary care practice. The economic study was carried out in Canada.

Dates to which data relate
The dates during which the effectiveness and resource use data were gathered were not reported. The price year was not indicated.

Source of effectiveness data
The effectiveness evidence was derived from a single study.

Link between effectiveness and cost data
The costing was undertaken prospectively on the same patient sample as that used in the effectiveness analysis.
Study sample
Power calculations were not performed to determine the sample size. A total of 654 patients were enrolled, of which 417 patients were randomised (209 to cerivastatin and 208 to branded pravastatin). Twenty-five patients in the cerivastatin group withdrew, as did 14 in the pravastatin group. Overall, 378 patients completed the study (184 in the cerivastatin group and 194 in the pravastatin group), although outcomes were available for larger numbers of patients. For example, for lipid change, data were available for 200 patients in the cerivastatin group and 206 in the pravastatin group.

Study design
The study was a randomised, open, parallel-group controlled trial carried out in 48 sites (General Practitioners and Community Specialists) in 9 Canadian provinces. The treating physician initially recorded a lipid target for each patient, after which the patients were randomised to the two drugs in a 1:1 ratio. The patients were then supplied the initial recommended dose, although the physicians could use any dose they deemed appropriate for a given patient. The patients were followed for 12 months, and visits were conducted at baseline and at 3, 6, 9 and 12 months.

Analysis of effectiveness
The effectiveness was analysed on an intention to treat basis. The primary health outcome used in the analysis was the success rate. This was measured as the percentage change from the baseline to the end point in plasma lipid parameters (proportion of patients whose LDL-C level was reduced by less than or equal to 20%). The incidence of adverse events (safety analysis) was also reported. The groups were stated to have been similar in terms of their mean age, body weight, racial mix, clinical characteristics (smokers, history of coronary artery disease, hypertension), and their baseline lipid variables, the data being given.

Effectiveness results
The LDL-C level at the end point was reduced by at least 20%, relative to the baseline, in 74.2% of the cerivastatin patients and in 74% of the pravastatin patients. The difference was stated to be not significant.

The mean LDL-C reductions were 29.8% for cerivastatin and 27.5% for branded pravastatin, (p=0.35).

Approximately one half of all patients achieved the lipid targets by the end of the trial: 47.8% in the cerivastatin group and 46.2% in the pravastatin group. The difference was not statistically significant.

The safety analysis indicated that the incidence of treatment-related adverse events was similar between the groups: 73.6% in the cerivastatin group and 74.9 in the pravastatin group. The difference was stated to be not significant.

Clinical conclusions
The analysis of effectiveness indicated that cerivastatin and pravastatin were similarly effective, both in terms of the success rate and the incidence of adverse effects, and there was no statistically significant difference between them.

Measure of benefits used in the economic analysis
There was no summary measure of benefit, indicating that a cost-consequences analysis was carried out. However, the authors reported the study to have been a cost-minimisation analysis.

Direct costs
Discounting was irrelevant because the time horizon of the study was one year. The quantities and the unit costs were not reported separately. The resource/cost boundary adopted was that of the Canadian Provincial Ministries of Health. Four categories of costs were included in the economic analysis:
drug costs, including a dispensing fee and a 10% mark-up;

physician fees;

laboratory costs in relation to the treatment of hyperlipidaemia; and

hospital outpatient procedures, such as day surgery procedures performed for the treatment of adverse events.

Since a generic pravastatin (70% of the original price) became available, the analysis was based on both the branded and generic pravastatin acquisition costs. The costs were estimated using the actual data obtained from the Ontario Health Insurance Plan Schedule of Benefits. The costs were annualised. The price year was not reported.

Statistical analysis of costs
A statistical analysis of costs was reported.

Indirect Costs
The indirect costs were not included.

Currency
Canadian dollars (Can$).

Sensitivity analysis
A sensitivity analysis was conducted on the four cost categories, due to the fact that the patients were recruited from across Canada. However, the cost information only reflected the cost of the treatment in Ontario. The type of analysis conducted was not reported.

Estimated benefits used in the economic analysis
See the 'Effectiveness Results' section.

Cost results
The mean total treatment costs, plus or minus the standard deviation, were reported. These amounted to Can$1,224 (+/-239) in the cerivastatin group and Can$1,452 (+/-287) in the branded pravastatin group. The difference between the two groups, Can$228, was statistically significant. When the acquisition cost of generic pravastatin was considered, the difference in the overall treatment costs between the groups was no longer statistically significant. The cost of the medication changed from Can$831 (+/-192) to Can$589 (+/-135).

Synthesis of costs and benefits
Not applicable.

Authors' conclusions
The authors concluded that "cerivastatin was as effective as branded pravastatin in reducing LDL-C levels by greater than or equal to 20% in patients with hypercholesterolaemia, but at a significantly lower cost". They also attributed the lower cost to "not using the generic pravastatin".

CRD COMMENTARY - Selection of comparators
The reason for the selection of the comparators was clear. The authors stated that there was no evidence of comparison
of the two drugs in a non-protocol setting, which could simulate typical primary care and physician normal practice. You should consider whether both drugs are currently used in your own setting.

**Validity of estimate of measure of effectiveness**
The internal validity of the study was likely to have been high because the study design was a randomised multi-centre clinical trial. This design appears to have been appropriate for the study question. Further, the study sample was likely to have been representative of the study population given its size. In addition, the baseline characteristics of the participants were given, and the two groups of patients were shown to be comparable at analysis.

**Validity of estimate of measure of benefit**
No summary measure of benefit was used.

**Validity of estimate of costs**
All the categories of cost relevant to the perspective adopted appear to have been included in the analysis. The cost estimates used in the study were quite specific to the Canadian setting. Only a few details regarding the resources used were reported, and statistical analyses on the quantities were not conducted. The price year was not indicated. The unit costs and the quantities were not reported separately.

The authors reported their study as a cost-minimisation, based on the lack of a statistically significant difference in the effectiveness. However, this cannot be justified given the presence of uncertainty, in other words, the effectiveness was not equal for all of the patients. In fact, on average, the effectiveness was not equal. Even if it was assumed that the effectiveness generally showed little difference, the question would be at what cost does this small difference occur. Here again, the cost data are uncertain, so there might be an increase for some patients, no change for others or a decrease. On average, the cost difference is not unequivocally in one direction when accounting for the use of a generic pravastatin.

**Other issues**
The generalisability of the results to other settings was partially addressed by performing sensitivity analyses. However, the results appeared to be limited to the Canadian setting. The authors made some comparisons of their findings with those of other studies.

**Implications of the study**
The authors suggest that cerivastatin is preferred over branded pravastatin. However, they also indicated that from the perspective of the Canadian third party payer, generic pravastatin was as convenient as cerivastatin.

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