The cost implications of the use of telmisartan or ramipril in patients at high risk for vascular events: the ONTARGET study


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 aim was to compare the costs for the angiotensin-receptor blocker (ARB), telmisartan, and the angiotensin-converting enzyme (ACE) inhibitor, ramipril, in patients with vascular disease or high-risk diabetes. The authors concluded that ramipril was less costly than telmisartan. The cost data and the results were well reported. There were some issues with the methods so the results are unlikely to be applicable to specific study settings.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
The aim was to compare the costs for the angiotensin-receptor blocker (ARB), telmisartan, and the angiotensin-converting enzyme (ACE) inhibitor, ramipril, for patients with vascular disease or high-risk diabetes.

Interventions
Telmisartan 80mg daily was compared with ramipril 10mg daily. Either drug was provided in addition to standard care, which included aspirin, diuretics, anti-angina therapy, anti-hypertensive medications, and cholesterol-reducing agents.

Location/setting
Forty countries/in-patient and out-patient care.

Methods
Analytical approach:
A cost analysis was undertaken, based on the finding that telmisartan was not inferior to ramipril, from the Ongoing Telmisartan Alone and in Combination with Ramipril Global Endpoint Trial (ONTARGET; see Other Publications of Related Interest). The time horizon was the duration of the trial, which was 56 months. The authors stated that they took a health service perspective.

Effectiveness data:
The ONTARGET was a large, multicentre, multinational randomised controlled trial of 25,260 patients from 733 centres in 40 countries. It included a group receiving telmisartan plus ramipril, but this was excluded from the analysis, because there were more adverse events in this group. There were 8,542 patients randomised to telmisartan, and 8,576 patients randomised to ramipril. The average follow-up was 56 months. The trial found that telmisartan was not inferior to ramipril for the primary combined outcome (cardiovascular death, myocardial infarction, stroke, and hospitalisation for heart failure).

Monetary benefit and utility valuations:
Not relevant.

Measure of benefit:
No measure of benefit was compared.

Cost data:
The resource use and costs were from the ONTARGET. The resource categories included hospitalisations, procedures,
and study and non-study drugs. Community care and investigations performed outside the hospital were not recorded. Hospitalisations not related to cardiovascular disease, diabetes, or renal failure were recorded, but were excluded. Country-specific unit costs were collected in a variety of ways, depending on the country. Some were from diagnosis-related group (DRG) systems and others were from hospital accounts. These unit costs were assigned to all health care resource use, which was then converted to 2008 US $, using purchasing power parity rates. Costs were discounted at 3% annually. The ONTARGET countries were grouped by geographical location, health care system, and overall economic status. These groups were used to estimate any missing cost data.

Analysis of uncertainty:
The costs were analysed for statistically significant differences in all categories and in the total. One-way sensitivity analyses, varying parameters by ±25%, were conducted.

Results
There were no statistically significant differences, between the two drugs, in the costs for hospitalisation, procedures, and non-study drugs. The study drug costs for ramipril were $841 (95% CI 795 to 887) less than for telmisartan.

The total discounted cost for telmisartan was $11,722 compared with $11,019 for ramipril. The lower cost of ramipril was mainly driven by its lower estimated drug costs.

The sensitivity analysis did not significantly change the overall results.

Authors' conclusions
The authors concluded that ramipril was less costly than telmisartan.

CRD commentary
Interventions:
This study compared the costs for only two drugs plus standard care. These two drugs were briefly described; more details were available in the main trial publication. The inclusion of standard care plus the two drugs was useful for policy making, but there were many other ARBs and ACE inhibitors available; excluding relevant comparators can produce misleading results.

Effectiveness/benefits:
The effectiveness data were presented to show that a cost comparison was appropriate, as telmisartan was not inferior. It appears, from the presentation of the clinical data, that a cost-minimisation analysis was conducted. For such an analysis, demonstrating non-inferiority is not sufficient, equivalence is required. No tests for equivalence were reported, and so it is unclear if the two drugs were equivalent.

Costs:
It was indicated that ramipril was available in most countries as a generic drug in 2008. This means that the drug that is less expensive will vary by country, and local prices should be consulted for both drugs. If generic ramipril was available in all countries when the analysis was conducted, the cost differences would have been larger in favour of ramipril. Overall, the costs were clearly reported with a good variety of resource data. The study used country-specific costs, which were converted to US $ and aggregated. If the unit costs for each country had been individually presented, the variance between the 40 countries, with the availability of generic ramipril, could have been explored.

Analysis and results:
The analysis did not include all the relevant comparators, which could be misleading, and the sensitivity analyses were insufficient. The analysis was adequately described, and the results were clearly presented. Given the large amount of data and the small differences between the costs, a probabilistic sensitivity analysis would have been appropriate. This could have provided an estimate of the overall uncertainty in the results. The study assumed equivalent benefit, which may not have been appropriate, given that ONTARGET was a non-inferiority trial, not an equivalence trial.

Concluding remarks:
The cost data and the results were well reported. There were some issues with the methods so the results are unlikely to be applicable to specific study settings.
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