Posaconazole versus fluconazole or itraconazole for prevention of invasive fungal infections in patients undergoing intensive cytotoxic therapy for acute myeloid leukemia or myelodysplasia: 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
This study investigated the cost-effectiveness of posaconazole compared with fluconazole or itraconazole, for the prevention of invasive fungal infections, in adults with acute myeloid leukaemia or myelodysplasia who were receiving cytotoxic chemotherapy. The authors concluded that posaconazole was cost-effective and cost-saving, in cancer patients with prolonged neutropenia, in Canada. The methods and analyses were not entirely clear, and it is not clear that the authors’ conclusions are appropriate given the limitations that they acknowledged.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
The aim was to examine the costs and health benefits of posaconazole for the prevention of invasive fungal infections in a hypothetical cohort of adults with acute myeloid leukaemia or myelodysplasia, who were undergoing intensive chemotherapy.

Interventions
Mould-active posaconazole, 200mg three times daily, was compared with fluconazole, 400mg daily, or itraconazole, 200mg twice daily. Patients were assumed to receive any of the three treatments orally for the first 100 days. If they were intolerant to posaconazole then fluconazole was given and if they were intolerant to fluconazole or itraconazole then micafungin 50mg was given.

Location/setting
Canada/community care.

Methods
Analytical approach:
A decision model was used to synthesise the evidence from published studies, epidemiological data, and one key clinical trial (Cornely, et al. 2007, see ‘Other Publications of Related Interest’ below for bibliographic details). The time horizon was 100 days from the start of posaconazole treatment. The authors stated that they took a Canadian health system perspective.

Effectiveness data:
The key clinical outcomes were the rates of developing invasive fungal infections while on posaconazole, treatment discontinuation due to adverse events, and deaths. Literature reviews were undertaken to search for relevant evidence in PubMed and on the Internet, using Google Scholar. Randomised controlled trials from 2000 to 2010 were selected. The key trial (Cornely, et al. 2007) was a randomised head-to-head comparison of posaconazole versus fluconazole or itraconazole, in 602 patients.

Monetary benefit and utility valuations:
Not relevant.

Measure of benefit:
The measure of benefit used was life-years saved.

Cost data:
The direct medical costs included pharmaceuticals, baseline electrocardiogram for posaconazole and systemic therapy for invasive fungal infections. Costs were valued using hospital prices, and Canadian and International economic literature. Fungal infection costs were weighted by the incidence of invasive aspergillus and candidiasis. The costs were presented in Canadian dollars (CAD), where CAD 1 was equal to one US $. Where necessary, they were adjusted to 2010 prices using the consumer price index for health care.

Analysis of uncertainty:
One-way analyses were performed, using 95% confidence intervals, for three parameters; drug discontinuations, the incidence of invasive fungal infections, and the costs of treating infections. Treatment duration was varied and tested according to results from the key clinical trial. The sensitivity analysis results were reported in a table.

Results
Over the first 100 days, for adults receiving chemotherapy for acute myeloid leukaemia or myelodysplasia, the average costs were CAD 6,913 for posaconazole, CAD 11,172 for fluconazole, and CAD 10,957 for itraconazole. The life-years saved were 0.28 for posaconazole, 0.27 for fluconazole, and 0.27 for itraconazole.

Posaconazole dominated the other two treatments, as it produced more life-years at a lower cost. The cost savings were CAD 4,259 for posaconazole versus fluconazole and CAD 4,044 for posaconazole versus itraconazole.

The one-way sensitivity analyses, relative to fluconazole, showed that the findings were most sensitive to changes in the duration of posaconazole and its effectiveness against aspergillosis infection. A reduction from 29 to 22 days of posaconazole increased the cost savings to CAD 4,505, and no effectiveness against aspergillosis reduced the savings to CAD 1,765. The findings were stable to variations in other inputs.

Authors’ conclusions
The authors concluded that posaconazole was cost-effective and cost-saving, compared with fluconazole or itraconazole, in cancer patients with prolonged neutropenia, in Canada.

CRD commentary
Interventions:
The therapeutic agents were well described. The trial report should be consulted to assess the details of treatment and the baseline characteristics of the two groups, to determine their applicability to other settings.

Effectiveness/benefits:
The clinical effectiveness was based on a head-to-head randomised controlled trial, which is likely to have provided valid outcomes, but the original trial report should be consulted to assess the extent of any bias, the quality of randomisation and measurement of outcomes, and the acceptability of adverse events. It was not clear if this was the only clinical trial identified by the literature review for the main clinical outcomes. The authors stated that there wasn’t much information on the shape of the hazard function and so survival beyond the end of the trial was not modelled. The statistical results for this were not reported. The incidence of invasive candidiasis and aspergillosis infections was not reported and this was a key outcome for the model. The authors acknowledged that it would have been preferable to include quality of life in the health outcomes.

Costs:
The resource quantities and unit costs were summarised in the report; it was unclear whether these were comprehensive and reasonable without reading their original sources. The costs of the side-effects of treatment were omitted and it is unknown what impact this had on the results. The authors acknowledged that they did not include invasive fungal infection morbidity costs. Some cost estimates from the USA were used and might not have been appropriate for Canada.

Analysis and results:
The sensitivity analyses did not vary the incidence of invasive aspergillosis infections, which would have affected the
costs and the outcomes. The authors found in another cost-effectiveness study that this had a large effect. They made some comparisons with other cost-effectiveness analyses.

Concluding remarks:
The analyses and results were appropriate and clearly reported, but the methods and quality of the clinical data and modelling were not entirely clear. It is unclear whether the authors’ conclusions were a reasonable assessment of the study findings.

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