Economic evaluation of posaconazole vs. standard azole prophylaxis in high risk neutropenic patients in the Netherlands

Stam WB, O'Sullivan AK, Rijnders B, Lugtenburg E, Span LF, Janssen JJ, Jansen JP

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 objective was to assess the cost-effectiveness of posaconazole versus standard azoles for the prophylaxis of invasive fungal infection in neutropenic patients, with acute myeloid leukaemia or myelodysplastic syndrome, who were undergoing chemotherapy. The authors concluded that posaconazole was cost-effective compared with standard azoles. Despite some limitations, the analysis was based on valid methodology and the authors’ conclusions appear to be appropriate.

Type of economic evaluation
Cost-effectiveness analysis, cost-utility analysis

Study objective
The objective was to compare the cost-effectiveness of different oral pharmacological agents for the prophylactic treatment against invasive fungal infection (IFI) in neutropenic patients who were undergoing chemotherapy for acute myeloid leukaemia (AML) or myelodysplastic syndrome (MDS).

Interventions
The orally administered treatments were posaconazole at a dose of 600mg per day or standard azole treatment (either fluconazole or itraconazole at a dose of 400mg per day).

Location/setting
Netherlands/secondary care.

Methods
Analytical approach:
A decision analytic model, including a Markov model that captured the change in survival over time, was populated with data from the literature. The time horizon was the lifetime of the patients. The authors reported that the hospital perspective was adopted.

Effectiveness data:
The clinical data came from a randomised controlled trial (RCT) that explicitly compared the use of posaconazole with standard azoles for the prophylactic treatment of patients with neutropenia. Apart from the patients’ characteristics, little information on the methods and results of the RCT was given because this was published elsewhere. The primary clinical outcome was the probability of developing IFI. The long-term survival data were taken from a Dutch cancer registry. Adverse events were excluded due to a lack of statistical significance.

Monetary benefit and utility valuations:
The utilities were obtained from two published studies, the methods of which were not reported. Due to lack of available utility estimates for AML and MDS, the authors used the utilities for the accelerated state of chronic myeloid leukaemia.

Measure of benefit:
The authors used life-years gained (LYG) and quality-adjusted life-years (QALYs) as measures of benefit. These were discounted at an annual rate of 1.5%.
Cost data:
The economic analysis included the cost of IFI treatment and the cost of the prophylactic drug treatments. The IFI treatment cost was based on personal communication with an author of a relevant economic study and medical treatment costs were obtained from official national sources. The resource use and unit costs were only reported separately for the drug therapies. The costs were assumed to be incurred over a period of one year and were reported in Euros (EUR) for the price year 2006.

Analysis of uncertainty:
The parameter uncertainty was investigated using probabilistic sensitivity analysis and the probability distributions used were reported. A cost-effectiveness acceptability curve was generated. In addition, different scenarios were tested through one-way sensitivity analysis. All these scenarios were clearly reported.

Results
Posaconazole resulted in 3.70 LYG and 2.73 QALYs while standard azoles resulted in 3.60 LYG and 2.66 QALYs. The total treatment costs were EUR 4,412 for posaconazole and EUR 4,595 for standard azoles. Posaconazole was therefore more effective and less costly than standard azoles.

The cost-effectiveness acceptability curves demonstrated that, at a willingness-to-pay of EUR 20,000 per QALY, posaconazole had a 90% probability of being cost-effective compared with standard azoles.

These results were robust to the different assumptions investigated.

Authors' conclusions
The authors concluded that posaconazole was cost-effective for the prophylaxis of fungal infections in neutropenic patients, with ALM or MSD, who were undergoing chemotherapy.

CRD commentary
Interventions:
The interventions were clearly reported and justified. All the available orally administered treatments in the authors’ setting were included.

Effectiveness/benefits:
The clinical evidence came from a RCT, which was a high-quality source of data, given the strengths of its design. Only a few key features of the trial were presented, which makes it difficult to make an objective assessment of its internal and external validity. The authors acknowledged some limitations of the trial, such as its lack of statistical power, and they discussed the impact of these on the generalisability of the results. Little information was provided on the derivation of the utility valuations. QALYs are a validated benefit measure that allow cross-disease comparisons to be made. The authors justified excluding adverse events due to a lack of statistical significance, but the statistics were not reported.

Costs:
The costs appeared to reflect the perspective adopted. IFI treatment costs were given as one unit cost and a breakdown of the cost items was not reported. The price year was reported, which enhances the transparency of the economic analysis.

Analysis and results:
The approach used to synthesise the costs and benefits was appropriate. The uncertainty in the model was extensively addressed using a probabilistic as well as a deterministic approach. The results of the base case and sensitivity analyses were satisfactorily reported.

Concluding remarks:
Overall, in spite of some limitations, the analysis was based on valid methodology and the authors’ conclusions appear to be appropriate.
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