
Comparative cost-effectiveness of posaconazole versus fluconazole or itraconazole prophylaxis in patients with prolonged neutropenia

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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

The objective was to examine the cost-effectiveness of posaconazole in comparison with fluconazole or itraconazole for the treatment of patients with prolonged neutropenia. The authors concluded that posaconazole was the most cost-effective strategy over either fluconazole or itraconazole. The study was based on valid methodology, but some sources of data were not presented in detail. The authors' conclusions appear to be robust due to the appropriate investigation of uncertainty.

Type of economic evaluation

Cost-effectiveness analysis

Study objective

The objective was to examine the cost-effectiveness of posaconazole in comparison with fluconazole or itraconazole for the treatment of patients with prolonged neutropenia.

Interventions

The two strategies were posaconazole versus either fluconazole or itraconazole. Posaconazole was administered at a dose of 200mg three times daily, fluconazole at 400mg once daily, and itraconazole at 200mg twice daily.

Location/setting

USA/hospital.

Methods

Analytical approach:

This economic analysis was based on a decision analytic model. The time horizon was restricted to the duration of treatment (or 100 days in an additional analysis). The authors stated that the analysis was carried out from the perspective of the hospital.

Effectiveness data:

The clinical evidence came from a published randomised controlled trial (RCT), with 602 patients with myelodysplastic syndrome or acute leukaemia, who were undergoing induction or consolidation therapy. There were 304 patients in the posaconazole group, 240 in the fluconazole group, and 58 in the itraconazole group. The follow-up corresponded to the duration of treatment or 100 days after initiation of treatment. The key clinical endpoint was the rate of development of proven or probable invasive fungal infections that occurred during treatment.

Monetary benefit and utility valuations:

Not included.

Measure of benefit:

The benefit measure was the rate of development of proven or probable invasive fungal infections that occurred during treatment and this was derived from the RCT.

Cost data:

The economic analysis included the costs of medication and treatment of invasive fungal infections. The costs of drugs

were derived from average wholesale prices and the dosages were derived from the RCT. The costs associated with adverse events were not included. The cost of invasive fungal infections came from a published case-control study. All costs were in US dollars (\$) and the price year was 2006.

Analysis of uncertainty:

A univariate sensitivity analysis was undertaken on all inputs to the model. The ranges of values appear to have been determined by the authors. Alternative scenarios were also considered: for example, a 100-day outcome analysis was performed using data from the RCT. A Monte Carlo simulation of 1,000 hypothetical patients was undertaken to assess the simultaneous and global uncertainty in the model. The costs associated with the management of serious adverse events were included, in the sensitivity analysis, using an arbitrary cost range.

Results

The rate of development of proven or probable invasive fungal infections that occurred during treatment was 2% with posaconazole and 8% with fluconazole or itraconazole. At 100 days the rates were 5% with posaconazole and 11% with fluconazole or itraconazole.

The expected costs were \$3,051 with posaconazole and \$5,529 with fluconazole or itraconazole. Thus, under base-case assumptions, posaconazole was the dominant strategy because it was associated with greater benefits and lower costs in comparison with fluconazole or itraconazole.

The results of the one-way sensitivity analysis did not substantially alter these base-case findings. For example, posaconazole remained the dominant strategy as long as the rate of development of proven or probable invasive fungal infections for fluconazole or itraconazole was above 3.6%.

In the probabilistic analysis, posaconazole remained the dominant strategy in 78.8% of simulations.

Authors' conclusions

The authors concluded that posaconazole, as prophylaxis in patients with prolonged neutropenia, was the most cost-effective strategy compared with either fluconazole or itraconazole.

CRD commentary

Interventions:

The authors justified their selection of the strategies, which were appropriately chosen.

Effectiveness/benefits:

The bulk of the evidence came from a published study. The methods and characteristics of this study were not presented, except for the sample size, but its randomised design should have ensured a high internal validity. The benefit measure was derived from the RCT and was disease-specific, which means it cannot be directly compared with the benefits of other health care interventions.

Costs:

The analysis of costs was consistent with the perspective; only those costs borne by the hospital were included. The analysis did not consider the costs of medication preparation, distribution, and administration, which could have been relevant. Also, the costs of severe adverse events were excluded, but a threshold analysis showed that these would have to have been unrealistically high to alter the cost-effectiveness results. The sources of costs were reported, but no details were given of the case-control study that was used to derive the costs of invasive fungal infections, which might limit the transparency of the economic analysis. Appropriate alternative assumptions were made in the sensitivity analysis. The price year was reported, which will facilitate reflation exercises for other time periods.

Analysis and results:

The costs and benefits were analysed in an incremental analysis, which was appropriate to show the dominance of one treatment over the other. The issue of uncertainty was extensively investigated using valid approaches, which considered both individual inputs and the overall uncertainty in the model. The authors stated that a conservative approach was taken to bias the study against posaconazole, especially in the sensitivity analysis. They acknowledged a

number of limitations, including the fact that cost savings depended on the rates of invasive fungal infections, which might vary across institutions.

Concluding remarks:

This study was based on valid methodology, but some sources of data were not presented in detail. The authors' conclusions appear to be robust due to the appropriate investigation of uncertainty.

Funding

Not stated.

Bibliographic details

Collins CD, Ellis JJ, Kaul DR. Comparative cost-effectiveness of posaconazole versus fluconazole or itraconazole prophylaxis in patients with prolonged neutropenia. *American Journal of Health-System Pharmacy* 2008; 65(23): 2237-2243

PubMedID

19020192

DOI

10.2146/ajhp070588

Original Paper URL

<http://www.ajhp.org/cgi/content/abstract/65/23/2237>

Other publications of related interest

Cornely OA, Maertens J, Winston DJ, et al. Posaconazole vs fluconazole or itraconazole prophylaxis in patients with neutropenia. *New England Journal of Medicine* 2007; 356: 348-359.

Johnson MD, Kleinber M, Danziger L, et al. Pharmacoeconomics of antifungal pharmacotherapy: challenges and future directions. *Expert Opinion in Pharmacotherapy* 2005; 6: 2617-2632.

Indexing Status

Subject indexing assigned by NLM

MeSH

Antifungal Agents /economics /therapeutic use; Clinical Trials as Topic; Cost-Benefit Analysis; Drug Therapy, Combination; Fluconazole /economics /therapeutic use; Humans; Itraconazole /economics /therapeutic use; Monte Carlo Method; Multicenter Studies as Topic; Mycoses /prevention & control; Neutropenia /chemically induced /drug therapy /economics; Triazoles /economics /therapeutic use

AccessionNumber

22009100270

Date bibliographic record published

22/04/2009

Date abstract record published

09/12/2009