Drugs 2005; 65 (11): 1568-1569
0012-6667/05/0011-1568/$39.95/0

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Posaconazole

A Viewpoint by John R. Perfect

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Posaconazole is a new extended-spectrum triazole and is one of a new generation of azoles that have excellent activity against both yeast and mould infections. Its development platform has been supported by extensive *in vitro* and animal model assessments. These studies support the claim that the agent represents the broadest-spectrum azole to reach phase III development. The initial open clinical studies in refractory or intolerant invasive fungal infections support the excellent clinical activity of this triazole in a very difficult patient population. For instance, its success in refractory aspergillosis is reported at approximately 40–45%. This is exactly the range of success reported with liposomal amphotericin B, caspofungin and voriconazole. Although concurrent historical control studies are never optimal for assessment, it is reasonable to conclude that this drug is an improvement over amphotericin B deoxycholate.

It is also clear by combining the results of *in vitro* studies, animal models and open clinical experience that this agent will have a therapeutic place in the management of a wide range of fungal infections including candidiasis, cryptococcosis, aspergillosis, endemic mycoses, fusariosis, scedosporiosis, black mould infections and zygomycosis. It is the first azole drug which has accumulated enough clinical experience to consider its use in the rising numbers of zygomycosis cases presently observed in certain immunocompromised patients. It is also encouraging that posaconazole treatment may be effective in some yeast and mould infections which are resistant to azoles. Present results support the fact that there is not complete cross resistance with other azoles and broadens the potential use of posaconazole. Finally, with substantial clinical experience, posaconazole presently appears to have a very reasonable safety profile and its tolerability is acceptable to most patients.

The concerns about posaconazole are several. First, it has only been studied as an oral preparation. It will be helpful to understand the consistency of bioavailability in all patient populations and its impact. At least some clinicians will have hesitation about using it during the critically ill phase of infection without certainty of serum drug concentrations. Hopefully, an intravenous preparation will be available in the near future. Second, it would be helpful to see its performance in the primary therapy of invasive mycoses. It is anticipated that posaconazole would do very well in this group, but the majority of experience is in refractory/intolerant patients, who are a very selected group. Third, although posaconazole is associated with fewer drug interactions than other extended-spectrum azoles, there is still some need for monitoring when used with certain other drugs.

Fortunately, this drug continues to be carefully studied and its broad-spectrum antifungal activity and relatively safe features make it an attractive agent for use in prophylactic/empiric strategies. Prophylactic studies with posaconazole in high-risk patients like those with acute leukaemias and allogeneic bone marrow transplant recipients with grafts versus host disease have been completed and it will be interesting to see the results.

From this clinician's perspective, it is clear that recent antifungal development to extend the spectrum of azole drugs with a particular emphasis on dreaded mould infections has been successful and they have or will become an important part of the 'therapeutic tool box' for clinicians managing seriously immunosuppressed patients. Like voriconazole, posaconazole represents an advance in antifungal therapeutics and it is hoped that it will soon be available to the ill patients who can benefit from its administration. ▲