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Treatment of invasive aspergillosis with posaconazole in patients who are refractory to or intolerant of conventional therapy: an externally controlled trial.

Walsh TJ, **Raad I**, **Patterson TF**, **Chandrasekar P**, **Donowitz GR**, **Graybill R**, **Greene RE**, **Hachem R**, **Hadley S**, **Herbrecht R**, **Langston A**, **Louie A**, **Ribaud P**, **Segal BH**, **Stevens DA**, **van Burik JA**, **White CS**, **Corcoran G**, **Gogate J**, **Krishna G**, **Pedicone L**, **Hardalo C**, **Perfect JR**.

Immunocompromised Host Section, National Cancer Institute, Bethesda, MD 20892, USA. walsht@mail.nih.gov

BACKGROUND: Invasive aspergillosis is an important cause of morbidity and mortality in immunocompromised patients. Current treatments provide limited benefit. Posaconazole is an extended-spectrum triazole with in vitro and in vivo activity against Aspergillus species. METHODS: We investigated the efficacy and safety of posaconazole oral suspension (800 mg/day in divided doses) as monotherapy in an open-label, multicenter study in patients with invasive aspergillosis and other mycoses who were refractory to or intolerant of conventional antifungal therapy. Data from external control cases were collected retrospectively to provide a comparative reference group. RESULTS: Cases of aspergillosis deemed evaluable by a blinded data review committee included 107 posaconazole recipients and 86 control subjects (modified intent-to-treat population). The populations were similar and balanced with regard to prespecified demographic and disease variables. The overall success rate (i.e., the data review committee-assessed global response at the end of treatment) was 42% for posaconazole recipients and 26% for control subjects (odds ratio, 4.06; 95% confidence interval, 1.50-11.04; P=.006). The differences in response between the modified intent-to-treat treatment groups were preserved across additional, prespecified subsets, including infection site (pulmonary or disseminated), hematological malignancy, hematopoietic stem cell transplantation, baseline neutropenia, and reason for enrollment (patient was refractory to or intolerant of previous antifungal therapy). An exposure-response relationship was suggested by pharmacokinetic analyses. CONCLUSIONS: Although the study predates extensive use of echinocandins and voriconazole, these findings demonstrate that posaconazole is an alternative to salvage therapy for patients with invasive aspergillosis who are refractory to or intolerant of previous antifungal therapy.

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