Correspondence

Mycograb for the Treatment of Invasive Candidiasis

To the Editor—Pachl et al. [1] report the results of a double-blind study comparing Mycograb (*Neu*Tec Pharma), a monoclonal antibody targeting heat shock protein 90, combined with a lipid-associated formulation of amphotericin B, with a placebo plus a lipid-associated formulation of amphotericin B, for the treatment of patients with invasive candidiasis. The main results are an improved overall response rate by day 10, a faster clearance of the fungal cultures and a reduced *Candida*-attributable mortality rate by day 33 among patients receiving the combination. Unfortunately, the methodology is questionable, and crucial data are lacking.

Seven (12.5%) of the 56 patients receiving combination therapy and 6 (9.8%) of the 61 patients receiving monotherapy were included in the study because they had symptomatic candiduria. Although symptomatic candiduria requires antifungal therapy, it is recognized that this disease is ill defined [2, 3]. Patients with candiduria are usually excluded from studies on culture-confirmed invasive candidiasis.

Three patients were excluded from the modified intent-to-treat population in the Mycograb group after treatment was started. One was withdrawn on the first day without indication regarding the reason for withdrawal, and 2 patients died on the first day of therapy. The reason for excluding these 2 patients who experienced a fatal outcome is not valid. They had the appropriate disease, received the study drug, and died. An early death is an assessable outcome in a patient with confirmed invasive candidiasis, and this outcome is considered to be a drug failure, even if another cause could also have contributed to it. By adding these 2 patients to the modified intent-to-treat population, the reduction in the attributable mortality rate by day 33 among the combination group is no longer significant (OR, 0.34; 95% CI, 0.10–1.12; $P = .097$).

The comparison of Kaplan-Meier plots of time to the last positive culture is impressive. However, we have to note that ∼35% of the patients in the Mycograb group had negative cultures before starting therapy, compared with ∼21% in the control arm with negative cultures. Although the difference might not be statistically significant at baseline, it may have a substantial impact on the comparison of Kaplan-Meier plots of time to the last positive culture, because the Mycograb group had an advantage of 14% at day 0.

In addition, there is no information on overall mortality at day 33 among the modified intent-to-treat population. We appreciate that the investigators tried to identify as precisely as possible the cause of death among these patients, and we know that this is very difficult, especially in the presence of another infection. Therefore, data on overall survival at day 33 is critical. Day 12 is too early to conclude that candidiasis has been fully controlled and has not left any visceral damage that might result in a delayed death. An overall survival curve through day 33 is mandatory for such a study.

The results of this study look promising. However, data provided in the article by Pachl et al. [1] are insufficiently convincing to warrant the use of Mycograb and a lipid-associated formulation of amphotericin B for the treatment of candidiasis.

Acknowledgments

Potential conflicts of interest. R.H. has been a member of the advisory boards for Pfizer, Schering-Plough, Gilead, and Merck Sharp and Dohme, and has served on the speakers' bureaus for Pfizer, Gilead, Zeneus, and Schering-Plough. C.F. and Y.A.: no conflicts.

Raoul Herbrecht, Cécile Fohrer, and Yasmine Nivoix

Department of Hematology and Oncology, Hôpital de Hautepierre, Strasbourg, France

References

1. Pachl J, Svoboda P, Jacobs F, et al. A randomized, blinded, multicenter trial of lipid-associated amphotericin B alone versus in combination with an antibody-based inhibitor of heat shock protein 90 in patients with invasive candidiasis. Clin Infect Dis **2006**; 42:1404–13.
2. Pappas PG, Rex JH, Sobel JD, et al. Guidelines for treatment of candidiasis. Clin Infect Dis **2004**; 38:161–89.
3. Sobel JD, Kauffman CA, McKinsey D, et al. Candiduria: a randomized, double-blind study of treatment with fluconazole and placebo. The National Institute of Allergy and Infectious Diseases (NIAID) Mycoses Study Group. Clin Infect Dis **2000**; 30:19–24.

Reprints or correspondence: Dr. Raoul Herbrecht, Dept. of Hematology and Oncology, Hôpital de Hautepierre, 67098 Strasbourg, France (raoul.herbrecht@chru-strasbourg.fr).

Clinical Infectious Diseases 2006; 43:1083
 1058-4838/2006/4308-0023$15.00

Reply to Herbrecht et al.

To the Editor—This is in response to the letter by Herbrecht et al. [1] regarding the double-blind trial comparing combination therapy with Mycograb (*Neu*Tec Pharma) plus lipid-associated amphotericin B with amphotericin B monotherapy [2]. The protocol was designed to assess the efficacy of Mycograb against all forms of culture-proven invasive candidiasis commonly seen in hospital practice. Although restricting study entry to patients with candidemia [3–5] provides a more homogeneous study population, this restriction does not allow for the assessment of efficacy of combination therapy against other forms of invasive candidiasis that are equally prevalent and that can be difficult to eradicate with monotherapy. Candidemia with deep-organ involvement may carry a worse prognosis than candidemia