Linezolid for the Treatment of Nosocomial Pneumonia Due to Methicillin-Resistant Staphylococcus aureus

To the Editor—We read with interest the article by Wunderink et al [1] that showed better efficacy of linezolid compared with vancomycin for the treatment of nosocomial pneumonia due to methicillin-resistant Staphylococcus aureus (MRSA). The authors should be congratulated for the high quality of this study. In the discussion, it is stated that linezolid superiority was obtained despite vancomycin dose optimization. That statement could be challenged if the vancomycin trough levels are considered. Serum vancomycin levels were not available for 21% of the patients, and day-3 trough levels for the remaining 138 patients were <12.3 µg/mL for 72 (52%). These concentrations are below the 15–20 µg/mL vancomycin serum levels recently recommended by the Infectious Disease Society of America to treat severe MRSA infections such as pneumonia [2]. In a recent study including 320 patients with MRSA bacteremia, initial trough levels <15 mg/L were independently associated with an increased risk of therapeutic failure [3]. As in most previous clinical trials, patients received vancomycin (15 mg/kg every 12 hours) without a loading dose. This standard dosing approach is unlikely to achieve optimal pharmacodynamic targets (ie, a 0–24-hour vancomycin area under the concentration-time curve to minimum inhibitory concentration ratio >400 [4]). In addition, appropriate dosing is crucial during the early stage of the infection, when the bacterial load is the highest. Through a modeling approach, Roberts et al recently showed that higher-than-recommended vancomycin loading (35 mg/kg) and daily (35 mg/kg continuously infused) doses seem to be necessary to rapidly achieve therapeutic serum concentrations in critically ill patients with normal renal function [5]. In the present trial, clinical success rates were strictly identical in the 2 arms in the subgroup of patients with glomerular filtration rates <50 mL/min. A possible explanation could be the higher serum vancomycin levels obtained in those patients with impaired renal function. Vancomycin will probably remain the comparator in future trials on serious gram-positive infections. In our opinion, the design of these trials should take into account all data recently accumulated on pharmacodynamic parameters predictive of vancomycin efficacy.

Note

Potential conflicts of interest. Both authors: No reported conflicts.
All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

Michel Wolff and Bruno Mourvillier
Université Paris Diderot, Sorbonne Paris Cité, Assistance Publique–Hôpitaux de Paris, Hôpital Bichat–Claude-Bernard, Service de Réanimation Médicale et des Maladies Infectieuses, France
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Correspondence: Michel Wolff, MD, Université Paris Diderot, Sorbonne Paris Cité, Assistance Publique–Hôpitaux de Paris, Hôpital Bichat–Claude-Bernard, Service de Réanimation Médicale et des Maladies Infectieuses, 46 rue Henri-Huchard, 75877 Paris Cedex 18, France (michel.wolff@bch.aphp.fr).

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