month history of multiple cutaneous lesions, 1 ulcer on the left arm that was associated with nodular lymphangitis, and a nodule on the right elbow. Seven months earlier, he had been treated ineffectively in Mali with intramuscular injections of meglumine antimoniate. At admission, direct examination of a Giemsa-stained skin swab specimen revealed *Leishmania* species. The patient was assumed to be infected with *Leishmania major*, given the geographical location where he acquired LCL. A 6-week course of oral fluconazole (200 mg daily) failed to cure the patient clinically and parasitologically. Intramuscular PI (a 3-mg/kg dose given initially and then once again 2 days later) was administered during hospitalization. The treatment was well tolerated. Three months later, both the nodular and the ulcerative skin lesions had been cured, with hyperpigmented scar remaining, and the nodular lymphangitis had disappeared.

Patient 2 was a 50-year-old French woman who traveled to Egypt in January 2005 and who presented in September 2005 with a 6-month history of multiple skin lesions. Two months before her admission, she had received a diagnosis of LCL and had received a 6-week course of treatment with oral fluconazole (200 mg daily) without clinical success. Indeed, at admission, there were 3 papulonodular skin lesions on her face, 1 ulcer on her right elbow, and 2 maculopapular erythematous lesions each on her left knee and right forearm. Direct examination of a Giemsa-stained skin swab specimen confirmed the presence of *Leishmania* species. The patient was assumed to be infected with *L. major*, given the geographical location where she acquired LCL. Intramuscular PI (a 4-mg/kg dose given initially and then once again 2 days later) was administered during hospitalization. The treatment was well tolerated. Two months later, all of the cutaneous lesions had disappeared, some of which had left scars.

These 2 cases, in which first-line treatment with intramuscular antimonials or fluconazole failed, suggest that short-course treatment with intramuscular injections of PI may be as effective for Old World LCL as it is for some forms of New World LCL. Indeed, in Colombia, treatment with 4 injections of PI (3 mg/kg given every other day) yielded a 96% cure rate in an area where *L. panamensis* predominates [4]. Pentamidine is also considered to be the first-line treatment in French Guyana, where 2 injections of PI (4 mg/kg of pentamidine base every other day) yielded a 95% cure rate in 205 patients infected with *L. guyanensis* [6]. In an open-label study of 11 cases of imported LCL, three 4-mg/kg intramuscular injections of pentamidine base given every other day yielded a success rate of 73% with good tolerance [7].

According to our results, and because the use of pentamidine salts is limited by their toxicity (which is sometimes dose dependent), we recommend administering 2 intramuscular injections of 3 mg/kg PI on days 0 and 2 of treatment for LCL therapy. Additional investigations are needed to assess the effectiveness, safety, and modalities (e.g., daily dose and number of intramuscular injections) of PI for the treatment of Old World LCL.

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What Can We Learn from Studies Comparing Linezolid with Vancomycin in Neutropenic Patients When Vancomycin Dosages Are Not Optimized?

To the Editor—Jaksic et al. [1] compared the safety and efficacy of linezolid (600 mg every 12 h), and vancomycin (1 g every 12 h) in febrile neutropenic patients. Although the authors specified that co-investigators were allowed to monitor vancomycin levels in serum, in accordance with local practice, the article does not indicate whether adjustment of the vancomycin dosage could be performed throughout the study. The usual recommended intravenous dose of vancomycin is 30 mg/kg/day in adults; use of this dosage achieves serum concentrations of 25 mg/L (peak level) and 2 mg/L (trough level) in healthy volunteers [2], but pharmacokinetic studies of vancomycin therapy in neutropenic patients have shown a 3-fold increase of the initial volume of distribution and a shortened (3-fold) half-life, compared with values in healthy subjects [3, 4]. Although there have never been any definitive data correlating vancomycin efficacy and concentration, most experts will aim to achieve trough serum concentrations of ≥15 mg/L in patients with potentially severe infections [5], as...
recommended by the American Thoracic Society–Infectious Diseases Society of America guidelines for the treatment of methicillin-resistant *Staphylococcus aureus* pneumonia [6]. The pharmacodynamic parameters that best express vancomycin bactericidal activity are the time during which serum concentration is greater than the MIC for the organism [2] and the area under the curve divided by the MIC [7]. In neutropenic patients, pharmacodynamic principles suggest that an optimal regimen of a time-dependent killing agent with little postantibiotic effect, such as vancomycin, should achieve serum concentrations greater than the MIC 100% of the time. This may be easily obtained with therapeutic drug monitoring or when vancomycin dosages are adapted to the patient’s weight (i.e., 30 mg/kg/day) [8]. On the other hand, with the fixed dosages of vancomycin used in the study by Jaksic et al. [1] (1 g every 12 h), many patients may not achieve this pharmacodynamic parameter. Could the authors detail the range of vancomycin trough serum concentrations obtained in the health care centers where vancomycin serum levels were monitored?

In addition, given that the duration of neutropenia is an acknowledged risk factor for infectious complications [9], the delayed absolute neutrophil count recovery in patients receiving linezolid is of concern, despite the authors’ assumption that “it may be attributable to physiological processes during recovery from acute bacterial infection” [1, p. 605]. Indeed, these physiological processes would not explain why neutrophil count recovery was significantly delayed in patients receiving linezolid, compared with those receiving vancomycin. Reports of linezolid myelotoxicity could be a serious limitation to the use of this agent in neutropenic patients [10].

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**Reply to Tattevin and Camus**

To the Editor—In the letter by Tattevin and Camus [1], 2 interesting points were raised. The first concerns optimization of the vancomycin dosage. Although optimization of the vancomycin dosage may improve the efficacy of treatment, our study was not designed to address this question; rather, the study was designed to compare the 2 investigated medications in the usually recommended and prescribed doses for febrile, neutropenic patients with cancer, who can present with infections of varying sites and etiologies. For this reason, prespecified pharmacokinetic parameters were not defined, and systematic measurements of the vancomycin serum concentrations were not set by the protocol. The protocol directed sites to have 1 unblinded coinvestigator verify vancomycin serum concentrations and to adjust the dose, if necessary, in accordance with local practice guidelines. Because the study was not intended to look at dose optimization, sites were not required to send in concentration data. Therefore, we cannot address the pharmacokinetic/pharmacodynamic relationship with respect to vancomycin therapy, but we definitely can assess, in an unbiased way, the efficacy and tolerance of the drugs studied in their usually administered doses.

The second point concerns the delayed absolute neutrophil count recovery in certain subsets of patients who received linezolid. We were intrigued by the shorter time to defervescence and trends observed in prospectively defined hematologic events. Although the trends of hematologic events were not statistically significantly different in the overall patient population, we requested the post-hoc analysis that led to discovery that delayed neutrophil recovery was limited to the subset(s) of patients with good response to antimicrobial treatment, as shown by shorter time to defervescence. In contrast, there was no difference in time to defervescence in the fever of unknown origin (FUO) subset; the FUO subset also had no difference in time to neutrophil recovery (as shown in figure 2 of our study). This finding sheds a different light on the concern...