Response Assessment in Invasive Aspergillosis

TO THE EDITOR—In a recent article published in Clinical Infectious Diseases, Nouér and colleagues recommend that the Aspergillus galactomannan index (GMI)–based response criteria be used as a primary endpoint in clinical trials of invasive aspergillosis (IA) rather than the European Organisation for Research and Treatment of Cancer/Mycoses Study Group (EORTC/MSG) outcome definitions [1] based on the results of their retrospective study [2]. We believe that this proposal should be revised based on several points.

First, the study population of patients used was not representative of those usually included in clinical trials [3, 4]. Almost all of the patients in the study conducted by Nouér et al had multiple myeloma and <5% of cases involved allogeneic hematopoietic stem cell transplantation or acute leukemia, whereas myeloma patients were a minority group in previous therapeutic studies. Patients with myeloma have some particularities in both the clinical and mycological presentation of IA [5, 6]. Second, only patients with a positive GMI were included, but a significant proportion of patients with IA have a negative GMI [7]. Third, and most important, the authors did not prospectively and sequentially compare the GMI response (defined as survival and repeated negative serum GMI for ≥2 weeks after the first negative GMI) and EORTC/MSG response criteria. Indeed, although the GMI-based response was assessed at weeks 3, 4, 5, and 6 and after week 6, the EORTC/MSG response was only assessed at week 6 and after week 6. In their study, among the 71 of 115 patients who did not meet the criteria of GMI-based success at week 3, 32 patients met the criteria at week 6, and 7 more patients met the criteria after week 6. We recently evaluated the performance of clinical and biological markers to predict the outcome of IA in a representative population of hematological patients in a prospective study [8]. In this study, we showed that clinical and radiological response criteria assessed at day 14 were highly predictive of the week 6 outcome. Conversely, we could not find any association between early changes in serum GMI values and outcome, although we confirmed that the kinetics of the serum GMI within the first 6 weeks were associated with outcome. Notably, in our series, 3 of the 30 patients with a positive GMI at diagnosis met the GMI-based response criteria according to Nouér et al but had a subsequent positive GMI. These 3 patients were assessed as nonresponders according to the clinical and radiological response criteria at day 14 and had a poor outcome at week 6. We thus believe that clinical and radiological evaluation remains the most reliable method to assess the response to anti-Aspergillus treatment, although a complementary analysis of GMI may be discriminatory in some situations. For instance, in our study, when we considered the subgroup of patients with a positive GMI at diagnosis of IA (53% of the population), all 8 of the patients who had both a negative GMI and a nonfailure response (ie, complete, partial, or stable) at day 14 were responders at week 6, whereas only 12 of 17 patients with a nonfailure response at day 14 (without considering GMI) were responders at week 6. It is likely that a composite score including both GMI and radiological criteria would allow for the better assessment of the early treatment response. The current evaluation of low-dose lung computed tomography scans will certainly make this strategy safer [9].

Note

Potential conflicts of interest. All 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.

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Clinical Infectious Diseases 2012;55(3):475–6
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DOI: 10.1093/cid/cis415