Response Assessment in Invasive Aspergillosis

TO THE EDITOR—In a recent article published in Clinical Infectious Diseases, Noué 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 Noué 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 Noué 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 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.
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