Reply to Robinson

To the Editor—We thank Robinson [1] for the comments about our report [2] and for the opportunity to clarify our findings. As we stated in our research protocol (clinical trials registration NCT00500578) in the Materials and Methods section in our report, as well as in our response to Fätkenheuer et al [3], the prespecified significance threshold for declaring one arm superior to the other was 0.95. We did not reach that level; however, our posterior probability that the intermittent schedule of ribavirin (ISR) is superior to the continuous schedule (CSR) was 0.88. It is true that the $P$ value (calculated by the Fisher exact test) for comparing the success rates of the 2 treatment arms was .230. This nonsignificant value is to be expected. As discussed by Greenland and Poole [4], under a uniform prior distribution, the $P$ value/2 is equal to the posterior probability that CSR is superior to ISR (i.e., the opposite calculation from that in our article, which would yield a posterior probability that CSR is superior to ISR of 0.12).

We agree with Robinson that during the first few months after transplantation, the risk for progression to pneumonia is high; however, there are multiple other risk factors that may classify patients at risk for progression, even many months after transplantation, including lymphocytopenia, graft-versus-host disease, and steroid use at the time of diagnosis. After further analysis, we found no significant difference between the 2 treatment arms with respect to the time from transplantation ($P = .72$). Furthermore, the 2 treatment arms were almost identical with respect to their baseline characteristics thus minimizing any potential bias due to these risk factors.

Finally, in view of the available evidence regarding the benefit of ribavirin for preventing respiratory syncytial virus–associated pneumonia in high-risk stem cell transplant recipients, although on the basis of retrospective studies, with all of their inherent biases, as pointed out by Robinson and expanded on in our systematic review on this subject [5], we believe that the use of a placebo arm would be unethical. Hence, we compared the efficacy of 2 dosing schedules of aerosolized ribavirin in our adaptive randomized clinical trial. On the basis of the outcome of the trial and practical considerations, we recommend
the intermittent dosing schedule of aerosolized ribavirin as a better alternative than a continuous dosing schedule for preventing respiratory syncytial virus–associated pneumonia in at-risk patients with cancer.

Notes

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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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