To the Editor:

We read with interest the recent report by Berman et al., describing the response rate and response duration of patients with hairy cell leukemia, treated with recombinant interferon alfa-2a. The authors describe the clinical outcome of a series of 35 patients who were either previously untreated (10) or treated (25) for their leukemia. Patients received interferon daily for 6 months; then three times a week for an additional 18 months or until disease progression or intolerable toxicity. Response was evaluated on all 35 patients and was appropriately presented by prior treatment (none, splenectomy, and/or chemotherapy). The response rates achieved in this series appear similar to other reports.

Durability of response was based on the 23 patients who completed the 2 years of treatment. At the time of analysis, 11 of the 23 patients had disease progression, which occurred between 0.5 and 25
months from completion of therapy. The median value for these 11 progression times was 10 months. At the time of analysis, 12 patients continued in unmaintained remissions at 12+ to 32+ months. The Kaplan-Meier estimate of median response duration based on all 23 patients was 25 months.

The authors contrast their results with those of three other published series. In comparing time to disease progression among the trials, we noted that the authors chose to cite their median time to disease progression as 10 months, which had been based solely on the 11 failures known at the time of the analysis. This point estimate does not involve the continued response times of the 12 censored patients and is entirely dependent on the time at which the analysis is performed. Perhaps the choice of this estimate reflects the authors’ belief that patients who have reached some posttreatment landmark are subsequently unlikely to fail. A Kaplan-Meier estimate is preferable as it makes proper use of remission times from those patients in continuous response.

The median cited from our study was 25.4 months, nearly identical to that reported by Berman et al. A footnote was appended to the results of our study, indicating that we do not make a similar assumption regarding subsequent failure. A more recent analysis of our data showed a median failure-free survival of 28.7 months, with relapses noted up to 5 years after treatment.

We disagree with the summary statement that “half of the patients who relapse will do so within 1 year of completion of therapy.” We believe this to be an incorrect statement that is neither consistent with the results from our study nor from those of the authors.

Ms Mick and Drs Ratain and Golomb raise questions concerning the statistical assessment of our group of hairy cell leukemia patients treated for 2 years with recombinant interferon alfa-2a (rIFN-α2a; Roferon, Hoffman-LaRoche, Inc, Nutley, NJ). Specifically, they disagree with the conclusion that half of the patients who relapse after therapy will do so within 1 year of completion of treatment and contend that neither our results nor the results of the three other previously published series included for comparison are consistent with this observation.

In our study, we estimated both the unconditional median duration of remission (using the Kaplan-Meier estimate) and the median duration of remission conditional on the subset of patients who relapsed. We acknowledge the error of including Ratain’s study in the conditional estimates, as that particular report provided only the unconditional median duration of remission. As outlined in Table 5 in our article, Quesada et al reported that the median time to disease progression in his group of relapsed patients was 6 months (range, 3 to 10); moreover, Golomb et al reported a median time to disease progression of 6.5 months (range, 2 to 19) in a group of patients who relapsed in a multi-institutional study. Therefore, based on three or four reports published in the literature concerning length of remission after completion of therapy, we can still conclude that among the patients who relapse, half will do so within 1 year of completion of therapy.

In addition, we would also like to comment on the statement made by Ms Mick that Kaplan-Meier estimates make proper use of remission time. In leukemia, where there are multiple causes of treatment failure (infectious death, disease progression, organ failure due to drug toxicity, etc), it is preferable to estimate the median duration of remission in the presence of other causes of failure by the cause-specific estimate of relapse. In our data, since the only type of failure observed was relapse, the Kaplan-Meier curve we presented was equivalent to the cause-specific curve for relapse. However, as data continue to accrue, these curves will almost surely be distinct. In hindsight, we should have used the cause-specific label to avoid confusion.

REFERENCEs


Duration of response after interferon treatment of hairy cell leukemia
[letter; comment]

R Mick, MJ Ratain and HM Golomb