RESPONSE CRITERIA WITH FLUDARABINE THERAPY IN CHRONIC LYMPHOCYTIC LEUKEMIA

To the Editor:

I read with great interest a report by O'Brien et al. in a recent issue of Blood in which results on a large series of chronic lymphocytic leukemia (CLL) patients treated at the M.D. Anderson Cancer Center with a combination of fludarabine and prednisone have been presented. As stated in the report, although this combination "has significant activity in CLL, the response rates were no higher than seen with fludarabine used alone." However, the complete remission (CR) rate reported in this article is 63% among previously untreated patients.

I believe that, in this evaluation, the investigators have included among CRs patients achieving "nodular partial remissions (PRs)" as defined by Keating et al. Keating et al. in reporting their results on 33 previously untreated CLL patients showed 33% CRs, and this figure increased to 72% if an additional 39% nodular PRs were included among CRs. The clinical behavior of patients achieving nodular PR was later shown to be closer to that of PR- rather than CR-achieving patients. Even 33% is a major improvement in achieving CR in CLL and this, in itself, promises to result in an improvement in the natural history of this disease—which we have been unable to do during the past 3 decades.

The results with fludarabine in previously untreated CLL patients obtained at a single institution (M.D. Anderson Cancer Center) were considered to be so exciting (33% CRs) that 3 years ago, Cancer and Leukemia Group B (CALGB) initiated a major trial to test if these results can be reproduced in a multi-institutional setting. Other National Cancer Institute (NCI)-supported large groups have since joined this CALGB study, thus making it an Intergroup trial.

In the original publication by Keating et al using fludarabine in previously untreated patients with chronic lymphocytic leukemia, the complete remission (CR) rate was 33%. However, Keating et al defined a response category called nodular partial remission (nPR) that encompassed patients who otherwise met the criteria for CR by National Cancer Institute (NCI) Working Group, but had residual bone marrow biopsy nodules as the only evidence of disease. Thirty-nine percent of patients achieved this response (nPR).

In our recently published report using fludarabine in combination with prednisone, we note a CR rate of 63% in previously untreated patients who received fludarabine with prednisone. Response criteria were those defined by the NCI Working Group. Thus, we included patients with nPR in our CR group. The actual breakdown is as follows: Twenty-eight patients (30%) achieved a CR and 32 patients (34%) achieved a nodular remission. This is not different from the data reported by Keating et al with single-agent fludarabine.

In the abstract, the overall response (OR) and CR rates for previously treated Rai stage III-IV patients are 36% and 19%, not 64% and 46%. The other response rates noted by Dr Rai are correct as stated in the manuscript. I believe he is quoting the CR and PR rates whereas the rates quoted in the paper are for CR and overall response. This is also true for the rates referred to on pages 1696 and 1697.
REFERENCES


Response criteria with fludarabine therapy in chronic lymphocytic leukemia [letter; comment]

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