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 (nPR)” 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 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 with the Southwest Oncology Group and Eastern Cooperative Oncology Group as participants. In this Intergroup study, patients are randomly assigned one of the following three therapeutic arms: (1) fludarabine alone, (2) chlorambucil alone, and (3) a combination of fludarabine and chlorambucil. It is anticipated that new patient accrual on this study will end within a year.

It would be very helpful if O'Brien et al also provided us with the details of how many of their CRs actually had nodular PRs and whether the duration of remission and overall survival of nodular PR-achieving patients were closer to those of PRs or CRs.

There are two typographical and editorial errors in the paper by O'Brien et al which ought to be corrected: In the abstract “64% and 46%” have been given at two places, it should be replaced by “36% and 19%” for previously treated Rai III-IV disease. At the top of page 1697, in platelets less than 100×10^12, “100 X” is missing.

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Dr Rai raises the question as to whether patients whose response is nPR should be included in the PR category (rather than the CR category) because their prognosis may be similar. The time to progression in patients achieving CR versus nPR versus PR is different depending on whether the patients were previously treated or untreated. In the previously untreated group, the patients achieving nPR actually behave more like CR patients than PR patients as regards time to progression. At 18 months, 8% of CR patients have relapsed, versus 10% of nPR patients and 40% of PR patients. Thus, there is less difference between nPR and CR in previously untreated patients.

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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