CORRESPONDENCE

Therapy of Myeloma

To the Editor:

I would like to comment on Dr. Cohen’s article1 in the Journal, employing the combination of BCNU, cyclophosphamide, and prednisone in multiple myeloma and his interpretation of the M-2 results.2 There are important differences in the Southeastern Cancer Study Group program that may have affected the results and demonstrated the report benefits of the M-2. A response3 to an article by Dr. Bergsagel using melphalan and prednisone4 has also been submitted for publication.

The important distinctions between these studies are the drugs, doses, and timing of therapy. Melphalan, effective even as a single drug, was not included in Dr. Cohen’s paper. Vincristine has been shown to add 9 mo to the remissions attained with multiple alkylating agent programs2 and enhances tumor cell kill once the initial labeling index has increased.6 Higher doses and more aggressive timing may have compromised the data in the present paper. Four drug deaths were seen, and four patients had therapy discontinued because of toxicity. Moderate to severe nausea and vomiting as well as central nervous system and cardiac problems are described. These side effects and complications were not encountered with the M-2 program with moderate doses and spaced therapy.

The early mortality with the M-2 program is only 5% in the first 15 mo. This success relates to the moderate doses and timing of therapy. The M-2 program has made a significant contribution to the care and therapy of patients with multiple myeloma.

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REFERENCES


To the Editor:

We appreciate Dr. Case’s comments on our study of BCNU, cyclophosphamide, and prednisone in multiple myeloma1 and the relationship to the M-2 results.2 We agree that there may be many differences between the two studies including those related to the various drug doses and scheduling, as well as those related to potential patient selection differences. The results with the M-2 protocol are very intriguing indeed and should be pursued. However, in order to establish the relationship of the response rate and survival for the M-2 regimen to that of other regimens a concurrent controlled trial will be required. Certainly, uncontrolled trials and small individual studies will not accomplish this.

The danger of making assumptions from historically controlled studies is pointed out by Dr. Case’s statement concerning vincristine. In the study cited,3 based on historical controls, the Southwest Oncology Group (SWOG) suggested that vincristine might augment survival when used in combination. However, in a more recent SWOG study using concurrent controls, the addition of vincristine to an alkylating agent combination does not appear to result in a significant survival advantage.4 Moreover, since those myeloma patients who achieve a durable remission are those who continue to have a low labeling index,5 it is not clear whether even the theoretic basis for the use of vincristine in this situation is valid.

In any event we feel that only a study that compares alternative regimens concomitantly under controlled circumstances and in comparable patient groups will conclusively establish a response or survival advantage. We certainly look forward to such studies in the future.

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Therapy of myeloma [letter]

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