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Acquired immunodeficiency syndrome-related lymphoma [letter; comment]

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ACQUIRED IMMUNODEFICIENCY SYNDROME-RELATED LYMPHOMA

To the Editor:

In the review of non-Hodgkin's lymphoma (NHL) occurring in the setting of human immunodeficiency viral (HIV) infection,¹ the investigator suggests "certain progress has been made" and clinicians should adopt a treatment strategy that includes: (1) "very low-dose chemotherapy," and (2) "mandatory CNS prophylaxis." The evidence cited for these recommendations is the investigator's own study² of a phase II treatment program that produced a 46% complete remission rate and a participants' median survival of 5.6 months. This result is similar to those seen with other experimental therapies^{3,4} (Table 1A). Standard staging and treatment of HIV-NHL with established NHL therapy such as CHOP chemotherapy⁵ have produced results that are at least equivalent and possibly superior in response rate (59% v 50%, $P < .05$) and survival (11 months v 6 months, $P < .0001$) (Table 1).^{3,4,6,7}

One must conclude that no progress has been made in the treatment of HIV-NHL. As for other curable malignancies, major

Table 1. Results of Therapy for HIV-NHL

Study	Evaluable Patients (n)	Treatment	CR (%)	Median Survival (mo)
A. Experimental therapy for HIV-NHL				
Kaplan et al ⁴	38	COMET-A	58	5.8 ± 0.7
Levine et al ²	35	Low-dose m-BACOD	46	6.5 ± 2.0
Gill et al ³	9	"Novel"	33	6.0 ± 2.0*
Total	82		50 ± 29	6.07 ± 1.40
B. Standard therapy for HIV-NHL				
Kaplan et al ⁴	26	"Standard"	46	11.3 ± 3.5
Kaplan et al ⁶	24	CHOP ± GM-CSF	67	10.0 ± 0.4
Gill et al ³	13	m-BACOD	54	11.0 ± 2.0*
Newcom et al ⁷	10	CHOP	80	13.0 ± 1.3
Total	73		59 ± 19.6	11.05 ± 1.91

*Standard deviation was estimated. CR rate and survival were significantly higher for standard therapy ($t = 2.23$, $P < .05$); ($t = 23.62$, $P < .0001$).

alterations in therapy for HIV-NHL should be based on the results of well-designed phase III trials that show a significant improvement in survival.

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RESPONSE

The author writes to take exception to my statement that "certain progress has been made" in the therapy of acquired immunodeficiency syndrome (AIDS)-related lymphoma, and believes that it would be more appropriate to believe that "no progress has been made" in this area. While I do not believe that this particular debate is one of grave importance, I do think that Dr Newcom's view serves to obscure the subtleties that are important in this area, as it relates to patient care. His first point is that "standard" therapy using a regimen such as CHOP is as good as low-dose chemotherapy. Basically, this is the whole point. At the onset of the epidemic, it was common practice to use very dose-intensive regimens because of the widespread, high-grade nature of disease. Further, such regimens were commonly being used in other settings as well. As recently demonstrated by Fisher et al, in what was considered a high-priority, national trial, the newer, more dose intensive regimens (m-BACOD, MACOPB, ProMACE-CytaBOM) were found no better than CHOP, although toxicity was significantly increased.¹ Therefore, should one conclude that no progress has been made in the therapy of lymphoma over the past decade? I think not: a hypothesis was made, was tested, and was found to be incorrect. We will now proceed with alternative hypotheses, in the manner of all scientific investigation. As it relates to the patient with AIDS-related lymphoma, my point was that low-dose chemotherapy² may be associated with equivalent (or superior) survival times, with decreased toxicity, when compared with more dose-intensive regimens,^{3,4} especially if one considers the data in terms²⁻⁴ of underlying poor-prognostic factors. Results from these recent trials would indicate that patients with AIDS-related lymphoma, especially those with poor-prognostic factors, do not "require" dose-intensive multi-agent therapy,

which is associated with increased toxicity. The precise issue of dose intensity in the setting of human immunodeficiency virus (HIV)-related lymphoma is currently being explored prospectively in a randomized national trial conducted by the AIDS Clinical Trials Group (ACTG).

As it relates to the need for central nervous system (CNS) prophylaxis, CNS involvement has been shown in 17% to 42% of patients with HIV-related lymphoma.⁵ Further, in a series of patients with systemic AIDS-lymphoma followed from diagnosis to autopsy at the University of Southern California, a total of 66% were found to have CNS involvement at some time during the course of disease.⁶ In the "Novel" regimen of Gill et al, which did not use CNS prophylaxis, six of nine subjects experienced CNS relapse.³ The low-dose m-BACOD regimen, which required prophylactic intrathecal cytosine arabinoside, was associated with no case of isolated CNS relapse,² similar to the series of Kaplan et al that used the same regimen of CNS prophylaxis.⁷ These data would indicate to me that routine CNS prophylaxis is warranted in patients with systemic AIDS-related lymphoma.

While not a major point, then, I believe that we have learned something over the past decade, and that some progress has been made, allowing a better understanding of how to manage the patient with AIDS-related lymphoma. Obviously, additional hypotheses and further progress will be required in the years ahead.

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