REFERENCES

1. Karray S, Merle-Béral H, Vazquez A, Gérard JP, Debré P, Galanaud P: Functional heterogeneity of B-CLL lymphocytes: Dissociated responsiveness to growth factors and distinct requirements for a first activation signal. Blood 70:1105, 1987
2. Perri RT: Impaired expression of cell surface receptors for B cell growth factor by chronic lymphocytic leukemia B cells. Blood 67:943, 1986
3. Perri RT, Kay NE: Malignant chronic lymphocytic leukemia B cells express interleukin 2 receptors but fail to respond to interleukin 2's proliferative signal. Leukemia 1:127, 1987
4. Freedman AS, Boyd AW, Bieber FR, Daley J, Rosen K, Horowitz JC, Levy DN, Nadler LM: Normal cellular counterparts of B cell chronic lymphocytic leukemia. Blood 70:418, 1987
5. Benjamin D, Bazar LS, Wallace B, Jacobson R: Heterogeneity of B-cell growth factor receptor reactivity in healthy donors and in patients with chronic lymphatic leukemia: Relationship to B-cell derived lymphokines. Cell Immunol 103:394, 1986
6. Kluin-Nelemans JC, Hakvoort HWJ, Falkenburg JHF, Herion JC, Willemze R: pseudo-proliferation of hairy cell leukemia (HCL) in vitro. Blood 70:262, 1987 (abstr)

RESPONSE

To the Editor:

As pointed out by H.G. Drexler, the term *proliferation* is indeed misused in our discussion.[1] We used DNA synthesis (which may not necessarily be followed by cell growth) to assess the effect of B-cell growth factor and interleukin-2 (IL-2). We obtained positive results with cells from some (but not all) B-chronic lymphocytic leukemia (B-CLL) patients, which fits with results from other studies[2-4] not quoted in H.G. Drexler's letter. The real growth of (normal as well as monoclonal) B cells under the influence of these factors is still a matter of controversy.

As suggested by H.G. Drexler, we performed double staining on our cell preparations and found 93% of the cells positive for both CD5 and CD19 markers. Thus, our preparations contain essentially B-CLL cells. Moreover, a role for residual normal B cells in our results seems improbable on the following arguments: (*a*) By using identical experimental conditions, we could obtain terminal B-cell differentiation in B-CLL cultures; and only IgM was produced in contrast to normal B-cell cultures, which produce both IgM and IgG.[5] (*b*) In our hands, B-CLL cells display patterns of responsiveness to interferon-γ[6] and to IL-4[7] that are clearly different from that of normal B or T cells.

S. KARRAY
P. GALANAUD
INSERM U. 131
Clamart, France

REFERENCES

1. Karray S, Merle-Bérral H, Vazquez A, Gérard JP, Debré P, Galanaud P: Functional heterogeneity of B-CLL lymphocytes: Dissociated responsiveness to growth factors and distinct requirements for a first activation signal. Blood 70:1105, 1987
2. Lantz O, Grillot-Courvalin C, Schmitt C, Fermand JP, Brouet JC: Interleukin 2–induced proliferation of leukemic human B cells. J Exp Med 161:1225, 1985
3. Kabelitz D, Pfeffer K, Steldern DV, Bartmann P, Brudler O, Nerl C, Wagner H: In vitro maturation of B cells in chronic lymphocytic leukemia. I. Synergistic action of phorbol ester and interleukin 2 in the induction of Tac antigen expression and interleukin 2 responsiveness in leukemic B cells. J Immunol 135:2876, 1985
4. Touw I, Dorssers L, Löwenberg B: The proliferative response of B cell chronic lymphocytic leukemia to interleukin 2: Functional characterization of the interleukin 2 membrane receptors. Blood 69:1667, 1987
5. Emilie D, Karray S, Crevon MC, Vazquez A, Galanaud P: B cell differentiation and interleukin 2 (IL2) corticosteroids interact with monocytes to enhance the effect of IL2. Eur J Immunol 17:791, 1987
6. Karray S, Vazquez A, Merle-Béral H, Olive D, Debré P, Galanaud P: Synergistic effect of recombinant IL2 and interferon gamma on the proliferation of human monoclonal lymphocytes. J Immunol 138:3824, 1987
7. Karray S, Defrance T, Berol HM, Bancherau J, Debré P, Galanoud P: Interleukin 4 counteracts the interleukin 2 induced proliferation of monoclonal B cells. J Exp Med (in press)

INTERFERON GAMMA IN CHRONIC MYELOID LEUKEMIA: DOSE AND SIDE EFFECTS

To the Editor:

We have attempted to treat 14 patients with Ph positive chronic myeloid leukemia (CML) by recombinant human gamma interferon (IFN-γ) (kindly supplied by Boehringer Ingelheim) administered intramuscularly (IM) at a schedule similar to that described by Kurzrock et al[1]: 0.10 mg/m^2 daily during the first week, 0.25 mg/m^2 daily during the second week, and 0.50 mg/m^2 daily from the third week onward. Fever, night sweats, chills, myalgias, and headaches were observed as in Kurzrock's experience (ie, in 100% to 64% of cases). However, in spite of a constant use of paracetamole (1 to 2 g daily), the intensity of the side effects did not decrease after the first weeks of treatment, and this led to a progressive deterioration of the performance status of our patients, with a Karnofsky's index $\leq$60 in 21% of cases and $\leq$70 in 57% of cases. From the fourth to the twentieth week of treatment, the median maximum tolerated dose was 0.25 mg/m^2/d, but only two of 14 patients were able to tolerate 0.50 mg/m^2/d. Therefore, we agree with Kurzrock et al[1] that side effects of IFN-γ are qualitatively similar to those experienced with IFN-α, but we do not agree that tachyphylaxis often occurs after the first week of treatment as it usually does with IFN-α. Kurzrock et al[1] reported that most patients were able to tolerate 0.25 to 0.50 mg/m^2/d of IM IFN-γ, but they did not specify how many of them did actually tolerate 0.25 or 0.50 mg, and how many patients received <0.25 mg.

In our experience, the maximum tolerated dose was always <0.25 mg in two cases, equal and sometimes <0.25 in eight cases, 0.35 mg in two cases, and 0.50 mg in two cases only. Also at these doses the Karnofsky's index remained $\leq$80 in 78% of the cases throughout the study.