To the Editor:

Although the investigators state that "paired specimens" of bone marrow (BM) and peripheral blood stem cell (PBSC) were obtained from each patient, it is not clear whether they were obtained at the same time. If the BM was analyzed at diagnosis and the PBSC were obtained after induction therapy, the observed difference in tumor cell contamination may be a result of therapy and not reflect a biologically significant difference in the incidence of tumor cell contamination between BM and PBSC. Similarly, if the samples were obtained after chemotherapy, how did the type of chemotherapy and number of cycles affect the incidence of tumor cell contamination in BM and PBSC?

In addition, it is not clear whether the presence of tumor cells determined the type of BM rescue used, ie, PBSC or BM. If this was not the case, it would be important to know whether there is any available information regarding outcome and pattern of relapse. Recent studies show that hematopoietic recovery is rapid and complete with mobilized PBSC infusion alone. Therefore, if tumor cell contamination proves to be predictive of relapse and PBSC is less likely to be contaminated with tumor cells than BM, the current practice of infusing both BM and PBSC after high-dose chemotherapy should probably be discontinued.

Emile Salloum
Michael Reiss
Dennis Cooper
Yale University School of Medicine
Yale New Haven Cancer Center
New Haven, CT

REFERENCES


RESPONSE

We would like to address the comments made by Dr Salloum et al regarding our study recently published in Blood. 1

The bone marrow (BM) specimens analyzed were collected at time of, or immediately preceding, peripheral blood stem cell (PBSC) leukapheresis. In no case was a BM specimen obtained longer than 2 weeks preceding leukapheresis. We apologize if use of the term "paired specimens" was unclear. Further, all marrow and PBSC specimens were obtained after induction therapy but before intensification therapy. Thus, we believe that is appropriate to compare tumor cell concentrations between marrow and PBSC in this series of patients.

In this study we have no data that address the issue of tumor cell reduction by chemotherapy. However, in a separate study of the effects of tumor contamination of marrow and PBSC following five successive cycles of combination therapy with cyclophosphamide, doxorubicin, and 5-fluorouracil in stage III-IV breast cancer patients we were able to document reduction of tumor contamination in marrow and PBSC during the course of therapy. 2 Similar results of tumor reduction by chemotherapy have been reported in patients with neuroblastoma by Moss et al. 3

We are currently monitoring breast cancer patients on a variety of stem cell mobilization protocols to see if mobilization procedures may influence the presence of tumor cells in the circulation. However, we would like to cite the recent study by Brugger et al 4 which showed that an increased number of tumor cells were detectable by immunocytochemical analysis in the peripheral blood of patients with breast cancer, small cell lung cancer, and non-small cell lung cancer after chemotherapy/cytokine stem cell mobilization procedures. It is possible that mobilization procedures may also mobilize tumor cells into the circulation, and that successive cycles of chemotherapy may provide an "in vivo tumor-purging" effect. Additional studies are certainly warranted to address these issues.

In closing, we state that patients in our study were treated at many different institutions using a variety of transplantation protocols. Some were transplanted with marrow, some with PBSC infusion, some with a combination of the two. We are in the process of analyzing the available data on these patients to determine if tumor cell contamination of marrow, PBSC, or both is associated with posttransplant clinical outcome. However, we are in provisional agreement with Dr Salloum that the practice of infusing marrow and
PBSC after high-dose chemotherapy should be re-examined if tumor contamination of autologous hematopoietic stem cell grafts is predictive of treatment failure.

Amy A. Ross
Biologic & Immunologic Science Laboratories
Reseda, CA

REFERENCES
Detection and viability of tumor cells in peripheral blood stem cell and bone marrow collections from breast cancer patients [letter; comment]

E Salloum, M Reiss and D Cooper