

Response:

Incidence of cytomegalovirus infection and disease after autologous CD34-selected peripheral blood stem cell transplants

We found the observations of Emilio P. Alessandrino et al to be very interesting. Our groups, however, defined cytomegalovirus (CMV) infection and disease differently. As is outlined in our paper,¹ we defined CMV infection as either evidence of any quantitative pp65 antigenemia or a positive blood or marrow culture. We defined CMV disease as a positive shell viral or conventional culture of bronchoalveolar lavage fluid, lung biopsy, or gastric/duodenal biopsy in association with symptoms. Unlike Alessandrino et al's group, our group of patients was transplanted for a number of different hematologic and nonhematologic malignancies and autoimmune diseases.

As is outlined in our paper, we found that 6 of 19 (31.6%) and 34 of 172 (19.8%) developed a CMV infection, and 7 of 31 (22.6%) and 10 of 237 (4.2%) developed CMV disease in the CD34-selected and -unselected groups, respectively. Two of 3 CD34-selected patients and 3 of 5 unselected patients had no evidence of CMV antigenemia prior to developing CMV disease.

By univariate logistic regression analysis, steroid use and CD34 selection were associated with a highly significant chance for developing CMV infection, ie, OR of 3.0 ($P = .003$) and OR of 2.69 ($P = .04$), respectively. Only CD34 selection was highly significant for the development of CMV disease: OR of 6.62 ($P = <.001$).

We agree with Alessandrino et al that close monitoring for CMV should be done in autologous transplant patients at high risk for developing CMV disease and infection.

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Reference

1. Holmberg LA, Boeckh M, Hooper H, et al. Increased incidence of cytomegalovirus disease after autologous CD34-selected peripheral blood stem cell transplantation. *Blood*. 1999;94:4029-4035.

To the editor:

PCR-detectable transcripts in long-term remission of P190^{BCR/ABL}-positive acute lymphoblastic leukemia

During the past decade, we monitored longitudinally by reverse transcriptase polymerase chain reaction (RT-PCR) 22 adult patients with Ph1-positive and BCR/ABL-positive acute lymphoblastic leukemia (ALL) who were not eligible for allogeneic bone marrow transplantation (BMT). Although like other investigators¹ we found that PCR-positivity during remission was associated with poor outcome in the whole population (data not shown), we observed prolonged persistence of PCR-detectable minimal residual disease (MRD) in 2 P190^{BCR/ABL}-positive patients who remained in long-term hematologic complete remission (HCR). The main presenting features, type of treatment, and clinical and molecular outcome of these 2 patients are reported in Table 1. Patients received induction chemotherapy (CHT) according to the GIMEMA ALL-0288 and ALL-0394 protocols,^{2,3} respectively. As postremission therapy, patient 1 (diagnosed in 1989) was treated with CHT alone, including intensive consolidation and 2-year conventional maintenance.² In addition, due to hepatitis C virus (HCV) infection diagnosed in 1997 while off therapy for 6 years, he received 1 year's treatment with interferon alpha (IFN- α). He remains presently in continuous PCR-positive HCR after more than 114 months

from HCR achievement. Patient 2 underwent, after CHT consolidation, early autologous stem cell transplantation (ASCT), followed by 1 year's maintenance with IFN- α according to the European Intergroup trial for Ph1-positive adult ALL.⁴ She remained in HCR and persistently PCR-positive for 52 months, at which point hematologic relapse was documented. The patient died of disease progression 3 months later. Persistence of P190 BCR/ABL transcripts was detected in all sequential marrow specimens collected at 3-to-6-month intervals from the 2 patients. The sensitivity of the employed RT-PCR assay ranged between 10^{-4} and 10^{-5} , as reported elsewhere.⁵ The following precautions were undertaken to avoid contamination: (i) RNA extraction and RT-PCR analyses were always performed in separate rooms; (ii) plugged aerosol-resistant pipettes were used at all stages; and (iii) a negative control (all reagents plus water with no template) was included in each experiment. Finally, 2 bone marrow samples were processed for RNA extraction and analysed by RT-PCR in an another laboratory using the same assay, and positivity was confirmed in both cases. Diagnostic and some of the follow-up RNA samples still available were reanalysed recently by the real-time quantitative PCR (Q-PCR)

Table 1. Clinical and biological features of P190^{BCR/ABL} patients with prolonged PCR-positive hematologic remission

Patient	Age (y)	WBC $\times 10^9/L$	Phenotype	Treatment	Maintenance	HCR duration (mo)	Outcome
1	29	54.2	Pre-B	CHT	CHT*	114+	First HCR
2	22	13.1	Hybrid†	CHT + ASCT	IFN- α	52	Relapsed, died

WBC, white blood cell count; HCR, hematologic complete remission; CHT, chemotherapy; ASCT, autologous stem cell transplantation.

*Patient received, in addition to chemotherapy maintenance, IFN- α for 1 year, due to HCV infection.

†ALL blasts coexpressed myeloid antigens.