

results indicate that the absolute degradation rate is approximately 50% per day (ie an increase of the Ct value with one cycle) in PB MNC.

Although our data are based on a limited and heterogeneous set of samples, they clearly indicate that transcripts are rapidly degraded *ex vivo* and that the rate of degradation can differ between different types of transcripts, between PB and BM, and between patients. As such differential degradation will result in an over- or underestimation of MRD levels, samples should preferably be processed on the day of sampling; this processing should include at least the Ficoll density centrifugation-based separation of MNC and the cell lysis step of the RNA extraction. Even better, because changes in transcript levels can already occur within the initial 4 h,⁵ samples should be collected in tubes with immediate stabilization of intracellular RNA, thereby preventing any degradation of control gene and/or fusion gene transcripts. Such reagents for stabilization of RNA have recently successfully been applied in a multi-center study (Mueller *et al*, *Blood* 2003; **102**: 64a abstract).

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Imatinib mesylate associated with delayed hematopoietic recovery after concomitant chemotherapy

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TO THE EDITOR

We read with interest the paper by Ruchatz *et al*¹ on the effect of imatinib on hematopoietic recovery following idarubicin exposure in murine model. We describe an elderly patient with

chronic myeloid leukemia (CML) and transformed large B-cell lymphoma treated with imatinib mesylate and combination chemotherapy.

This is an 87-year-old male with a history of follicular lymphoma involving left cervical nodes in 1996, and he refused further therapy. He presented again in July 2000 with a markedly elevated WBC of 223 000/ μ l. A bone marrow examination confirmed the diagnosis of CML in chronic phase with cytogenetic study showing 45X,-Y,t(9; 22)(q34; q11)[25]. He was initially started on hydroxyurea and subsequently anagrelide was added because of thrombocytosis. In November 2001, the therapy was switched to imatinib mesylate when it was available commercially. At the same time, he started to experience nasal congestion and difficulty in swallowing. Both

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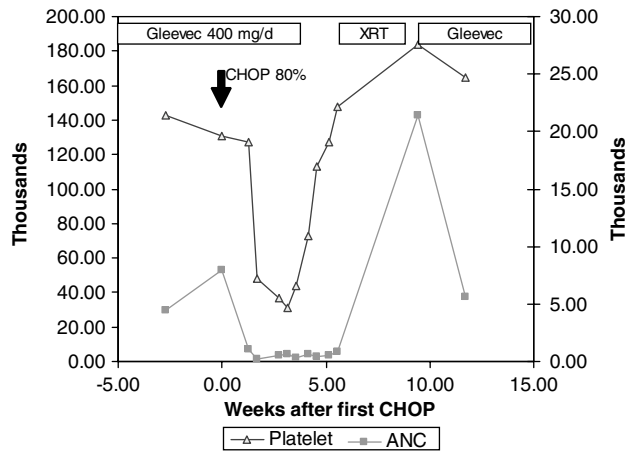


Figure 1 Delayed hematopoietic recovery after first course of CHOP chemotherapy.

ENT evaluation and CT imaging demonstrated a large nasopharyngeal mass with biopsy confirming the presence of CD20-positive, diffuse large B-cell lymphoma probably transformed from the preceding follicular lymphoma. He received a cycle of CHOP chemotherapy, consisting of cyclophosphamide, adriamycin, vincristine and prednisone at 80% of the normal dosage, on 9 January 2002 concomitant with imatinib, and it resulted in prolonged neutropenia (Figure 1). Imatinib was discontinued and eventually local radiation therapy was given instead. After completion of radiation, imatinib was restarted on 15 March 2002 with the daily dosage of imatinib adjusted to 300 mg per day based on the white blood counts. CT imaging in April 2002 revealed complete resolution of the nasopharyngeal mass. In January 2003, his peripheral blood was negative for BCR-ABL gene rearrangement by polymerase chain reaction. Unfortunately, his disease relapsed locally in February 2003. In view of the previous history of prolonged pancytopenia, the imatinib was discontinued and attenuated Rituxan-CHOP at 67% normal dosage was started. He tolerated the chemotherapy well with prompt marrow recovery and went on to receive second and third cycles of Rituxan-CHOP at 80 and 90% normal dosage, respectively, every 3 weeks. Subsequent CT scans in April 2003 again revealed complete resolution of the nasopharyngeal mass. Owing to the patient's advanced age and concomitant diagnosis

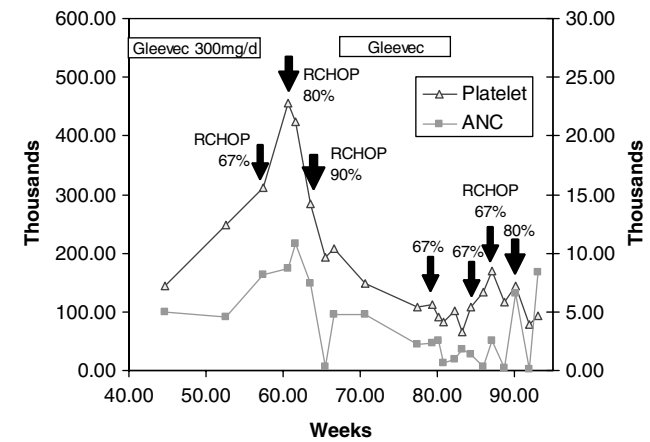


Figure 2 Improved hematopoietic recovery after discontinuation of imatinib.

of CML, the chemotherapy was discontinued as per the family's request. He was restarted on imatinib 300 mg/day in April 2003 when the peripheral blood turned positive for BCR-ABL. His nasopharyngeal disease again progressed in July 2003 and Rituxan-CHOP at 67% was restarted with him continuing on imatinib. However, the patient developed prolonged pancytopenia and the imatinib was promptly discontinued. His next course of chemotherapy was given in 5-week cycle instead of the usual 3-week cycle. Without concomitant imatinib, his subsequent courses of chemotherapy were successfully given every 3 weeks and with dose escalation (Figure 2) without the side effects.

Our case supports the finding of Ruchatz *et al* and suggests that caution be exercised when imatinib is to be used in combination with systemic chemotherapy.

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Response to Chand *et al*

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TO THE EDITOR

The report from Chand *et al.* offers clinical confirmation to our initial findings, although the data are, as for any unplanned

clinical observation on a single patient, far from definitive and require further verification.

In certain conditions of particular demand, such as the repopulation after cytotoxic treatment as described in our paper,¹ the stimulation with growth factors,² or the clinical situation presented by Chand, it is likely that the known inhibitory effect of imatinib on c-Kit, can cause clinically evident alterations.

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