epidemiological studies in our country and there are few in the world. After comparing our results with those of other European studies, we found only minimal differences between our incidence rates, distribution by FAB subtypes, sex and age groups and those reported in other reference studies.

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Key words: myelodysplastic syndromes, epidemiology, incidence, elderly.

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Safety and efficacy of stem cell mobilization under imatinib therapy

In order to investigate the safety and efficacy of stem cell mobilization in chronic myeloid leukemia patients under imatinib therapy we treated 10 such patients with granulocyte colony-stimulating factor. We observed that none of the patients developed progressive disease under this treatment. Instead, sufficient CD34+ apheresis could be performed in 7 patients and, as assessed by nested reverse transcriptase polymerase chain reaction (RT-PCR), bcr/abl-negative stem cell products could be generated in 3 patients. Interestingly, in 3 other patients with bcr/abl-positivity in 1st round RT-PCR of peripheral leukocytes, bcr/abl transcripts in stem cell products could only be detected by nested RT-PCR.

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Despite encouraging results from clinical trials using imatinib mesylate in patients with chronic myeloid leukemia (CML), some of these patients do not achieve complete cytogenetic remission and/or develop relapsing disease after an initial response. Thus, the emerging problem is how CML patients should be counselled concerning stem cell transplantation (SCT) in the imatinib era.[1] In this context the question frequently raised is whether autologous SCT is a favorable option in this population and whether pre-treatment with imatinib may influence its outcome. This topic is currently widely discussed and it is speculated that autografting in combination with imatinib therapy may provide substantial progress in CML treatment.[2] We support the suggestion of re-evaluating the place of autologous SCT, especially in patients who are not candidates for allografts, and of investigating the efficacy of *in vitro* or *in vivo* purging with imatinib. Such an approach may not only be an important therapeutic alternative in individuals who become refractory to imatinib but could also be of relevance in patients with persisting/resting CML clones despite cytogenetic remission.[3]

To assess the safety and efficacy of stem cell mobilization (SCM) under imatinib therapy we stimulated 10 patients with 10 μg/kg body weight (b.w.) granulocyte colony-stimulating factor (G-CSF) and continued imatinib medication. Written informed consent was obtained from all patients. Three patients were in accelerated phase and received 600 mg imatinib while seven were in chronic phase and received 400 mg imatinib daily. The median duration of CML was 33 months (range: 8–91) and the median duration of imatinib therapy was 15.5 months (range: 6–22). All patients were previously pretreated with interferon-α and developed subsequent intolerance or resistance to this drug. In all patients complete cytogenetic remission was confirmed at least twice by cytogenetic or fluorescent *in situ* hybridization (FISH) analysis before SCM. None of our patients progressed with CML after stimulation with G-CSF (median observation time 18 months). Three patients had sufficient numbers of circulating $CD34^+$ cells (>5/μL) but apheresis did not generate appropriate harvests. Leukapheresis yielding at least a total of 2.0×10^6/kg b.w. $CD34^+$ cells was successful in 7 patients. In 6 of these patients repeated separations[2-4] were needed. In patients with successful SCM the median concentration of $CD34^+$ cells was 3.05×10^6/kg b.w. (range: $2.0\text{-}4.6\times10^6$/kg b.w.). Subsequently, bcr/abl transcripts were detected by nested RT-PCR[4] both in the stem cell preparations (SCP) as well as in peripheral blood leukocytes which were collected within the 2 days before stem cell apheresis.

In two out of three patients who were bcr/abl-negative in peripheral blood samples bcr/abl-negative SCP could be

Table 1. RT-PCR bcr/abl results in CML patients during simultaneous imatinib therapy and stem cell mobilization. Peripheral blood leukocytes were taken within the 2 days before stem cell apheresis. Symbols in brackets indicate weak positivity.

	peripheral blood leucocytes		*stem cell preparations*	
	1st round PCR	*nested PCR*	*1st round PCR*	*nested PCR*
Pat. 1	–	–	–	–
Pat. 2	–	–	–	–
Pat. 3	–	–	–	+
Pat. 4	–	+	(+)	+
Pat. 5	+	+	–	(+)
Pat. 6 1st mobilization	+	+	–	(+)
Pat. 6 2nd mobilization	+	+	–	(+)
Pat. 7	+	+	–	–

obtained while the SCP of the remaining patient tested bcr/abl-positive by nested RT-PCR. In two patients with bcr/abl-positive first round RT-PCR in peripheral blood samples we obtained SCP that were bcr/abl-negative in first round RT-PCR but positive in nested RT-PCR in at least one SCP. In one patient who tested bcr/abl-positive in the peripheral blood by nested RT-PCR the SCP remained bcr/abl-positive. Interestingly, one patient with bcr/abl positivity in the peripheral blood achieved nested RT-PCR negative SCP (Table 1).

Recently, another group published a similar report in which one of 18 patients exhibited a negative SCP as assessed by quantitative real-time RT-PCR.[5] Here we provide additional information that bcr/abl transcripts could not be detected in one of our patients even by the most sensitive nested RT-PCR. However, a limitation of both studies is that no statements can be made concerning growth and engraftment potential of the collected harvests. We conclude that G-CSF stimulation of imatinib treated CML patients is feasible and safe. Further, separation of $CD34^+$ stem cells in complete cytogenetic responders was successful in 7 out of 10 patients (70%). It is of note that in two patients who were bcr/abl-positive by first round RT-PCR in peripheral leukocytes, SCP were only weakly positive by nested RT-PCR indicating a reduction of bcr/abl-positive cells during simultaneous imatinib treatment and SCM. Finally, as a bcr/abl-negative SCP could be generated in one bcr/abl-positive patient, *in vivo* purging under imatinib therapy may be successfully achieved. Further studies should aim to confirm these observations in larger study populations and to investigate the feasibility of autografting using imatinib-purged SCP in CML patients.

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