Brief report

Complete molecular responses are achieved after reduced intensity stem cell transplantation and donor lymphocyte infusion in chronic myeloid leukemia

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Patients with newly diagnosed chronic phase chronic myeloid leukemia were treated with imatinib mesylate (IM) for 6 to 12 months to establish disease control, before reduced intensity stem cell transplantation (RISCT). Escalating doses of donor lymphocyte infusions were given from 6 months after transplantation to eradicate residual disease. A total of 18 patients entered the study and 15 received RISCT (median follow-up, 31 months). RISCT was well tolerated with rapid engraftment, short inpatient stays, and few readmissions. Viral reactivation was common, although extensive graft-versus-host disease occurred infrequently. Donor lymphocyte infusions were given as part of the RISCT protocol in 13 of 15 patients. BCR-ABL transcripts continued to decrease after RISCT, and 8 (53%) patients achieved sustained undetectable levels. All patients are currently off IM. Although IM is now established as first-line therapy for chronic phase chronic myeloid leukemia, this protocol is a safe, well-tolerated, and effective strategy in these patients. This study is registered at http://www.controlled-trials.com as ISRCTN86187144. (Blood. 2008;111: 5252-5255)

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Introduction

The recommended first-line therapy for patients with chronic phase (CP) chronic myeloid leukemia (CML) is imatinib mesylate (IM; Novartis, Basel, Switzerland).1 IM is effective in inducing durable responses in the majority of patients.2 The use of allogeneic stem cell transplantation (SCT) for CML is declining yet remains a curative option for those with available donors.3 Transplant regimens with reduced intensity conditioning (RISCT) are less toxic, appropriate for a broader patient group, and have particular efficacy in CML.4-5 The requirement for IM in the context of RISCT is not established, in particular whether IM is necessary after transplantation where the safety and efficacy of escalating doses of donor lymphocyte infusions (DLIs) have been shown.6-8 We established a protocol for newly diagnosed patients using IM to establish disease control (complete cytogenetic response [CCyR]) before RISCT. IM was discontinued before RISCT and escalating doses of DLI were given after transplantation to those with residual disease (BCR-ABL ≥ 0.02%). Because residual disease after IM therapy may relate to stem cell persistence, RISCT followed by prophylactic DLI delivered when disease burden is low should induce graft-versus-leukemia effect within the stem cell population, leading to disease eradication.

Methods

Approval was obtained from the Multicentre Research Ethics Committee of London for these studies. Informed consent was obtained in accordance with the Declaration of Helsinki.


*N.B.H. and M.C. contributed equally to this work.
Unsatisfactory answer.
for those intolerant or resistant to other therapies will result in patients who receive transplants having higher EBMT risk scores as a result of the longer time to transplantation, increased age, and the risk of disease progression.

It is probable that the majority of patients in this study would have maintained a CCyR if maintained on IM in lieu of RISCT. We think that the proportion achieving undetectable BCR-ABL after RISCT and DLI is comparable with the response that would be expected with IM alone (41% at 4 years) and is consistent with published data on undetectable BCR-ABL after SCT (71% at median 6.6 years of follow-up). The RISCT procedure was well tolerated, and all patients are currently off any CML therapy. Regular monitoring is necessary because follow-up is relatively short and the risk of late relapse must be significant. However, if this occurs, it should be DLI responsive and is to be compared with the published annual rates of IM resistance and of disease progression on IM. We note that, in our series, one of 15 patients died and transplantation-related mortality of 23% at 2 years after RISCT for CML has been reported (although this value includes all phases of CML). We agree with the use of IM first-line in CML in CP and have discontinued RISCT at diagnosis in our institution. However, our approach highlights the safety and efficacy of RISCT as a potential therapeutic option that might be used when there are financial constraints or local access issues with TKIs, when the patient has a strong preference for transplantation and against continuous drug therapy, and for cases with severe TKI intolerance or early evidence of TKI resistance in CP.

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Authorship

Contribution: N.B.H., M.C., and K.S. collected and analyzed the data; M.C., J.G., A.N.P., I.G.M., G.M.S., C.C., P.S., and T.L.H. designed the research; N.B.H., M.C., and T.L.H. wrote the paper.

Conflict-of-interest disclosure: The authors declare no competing financial interests.

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