Explaining survival differences between two consecutive studies with allogeneic stem cell transplantation in patients with chronic myeloid leukemia.


Abstract

PURPOSE:
In the two consecutive German studies III and IIIA on chronic myeloid leukemia, between 1995 and 2004, 781 patients were randomized to receive either allogeneic hematopoietic stem cell transplantation with a related donor or continued drug treatment. Despite comparable transplantation protocols and most centers participating in both studies, the post-transplant survival probabilities for patients transplanted in first chronic phase were significantly higher in study IIIA (144 patients) than in study III (113 patients). Prior to the decision on a combined analysis of both studies, reasons for this discrepancy had to be investigated.

METHODS:
The Cox proportional hazard cure model was used to identify prognostic factors for post-transplant survival.

RESULTS:
Donor-recipient matching for human leukocyte antigen, patient age, time between diagnosis and transplantation, and calendar time showed a significant influence on survival and/or the incidence of cure. Added as a further factor, affiliation to study IIIA had no significant impact any longer.

CONCLUSIONS:
Discrepancies in influential prognostic factors explained the different post-transplant survival probabilities between the studies. The significance of calendar time suggests a lack of consistency of transplantation practice over time. Accordingly, the prerequisite for a common assessment of overall survival in the two randomized transplantation arms was not met. Moreover, our analyses provide an independent validation of established prognostic factors and their cutoffs. The statistical approach in investigating and modeling potential prognostic factors for survival sets an example for the examination of studies with unexpected outcome differences in concurrent treatment arms.