recognized that these results may not be extrapolated to all transplantation situations and that a different outcome may be achieved if higher doses of CY are used or if CY is used in other diseases. Such differences may explain apparent divergences between observations in this report and other reports. Two of these other prospective studies included only patients with CML. 2-4 First, CML patients are exposed to no or only to low-dose chemotherapy prior to transplantation. This may explain why BU may be less toxic in CML patients than in patients with AML. Second, BU is known to be an active drug in CML even at much lower doses. Its activity on AML cells may be different. Third, CML is probably the disease for which the graft-versus-leukemia (GVL) effect is the most potent. It can thus be hypothesized that the GVL effect in CML may be strong enough to overcome limitations of the antileukemic effect from the preparative regimen. Indeed, a recent encouraging report of nonmyeloablative preparative regimens in CML supports this hypothesis. 5 The third trial reporting a different conclusion from ours may not be comparable, as only 51 such patients with AML in CR1 were randomized. 3 A retrospective registry analysis from European Blood and Marrow Transplant Group (EBMT) also failed to find a difference between BUCY and CYTBI. 4 But this analysis includes many variables and markedly various doses of CY, and this may be critical. Indeed, a report in a pediatric population with AML in CR1 found a higher relapse rate in the BUCY group than in the CYTBI group, but this difference disappeared when the CY dose was increased up to 200 mg/kg. 7 The long-term follow-up of our study also indicates that secondary neoplasia represent the major cause of late failures, and this may even increase with longer-term follow-up. The occurrence of secondary neoplasia emphasizes that close attention should be given to patients who may be considered cured from the initial disease. An evaluation of the quality of survival of long-term survivors is also important and is presently being addressed in a joint study of the 4 prospective trials that have been discussed. 8 Finally, nonmyeloablative conditioning regimens have recently been developed with promising preliminary results indicating lower initial toxicity. But long-term results from this approach should be compared with the results achieved after a standard CYTBI preparation for patients with AML in CR1.

To the editor:

Intensive chemotherapy versus bone marrow transplantation in pediatric acute myeloid leukemia: a matter of controversies

Woods et al 1 emphasized allogeneic bone marrow transplantation (BMT) as treatment of choice for children with acute myeloid leukemia (AML) in first remission. They supported this recommendation with the results of the randomized Children’s Cancer Group (CCG) 2891 study comparing 3 aggressive treatment regimen in children with AML in remission. A superior survival after achieving remission was achieved with matched related allogeneic BMT (60% ± 9%), compared with chemotherapy alone (53% ± 8%) or autologous BMT (48% ± 8%). Results were even better in patients receiving intensive-timing induction treatment.

We disagree with the general recommendation of allogeneic BMT for all AML patients. From a methodological point of view, this statement should not be generalized, but it may be right for specific therapy regimens. Furthermore, in children with favorable cytogenetics [t(15;17), inv(16), or t(8;21)] the indication for allogeneic BMT in first complete remission (CR) cannot be seen. Thirty (38%) of the 79 children receiving transplants in the CCG study belonged to this group, 1 whereas in the chemotherapy group only 18 (23%) of 77 patients had favorable cytogenetics (P = 0.048). But outcome did not differ, compared with the non-BMT group. 1 Regarding children with AML FAB M3 and t(15;17) who probably will be cured by less intensive chemotherapy (especially, when treated in combination with differentiating agents like all-trans-retinoic acid), there is generally no indication for BMT. 3,4

We do agree that intensification of induction treatment has improved outcome in children with AML. 5 Analysis of patient groups in the Berlin-Frankfurt-Münster study (AML-BFM 93) (n = 471) comparable with those of the CCG trial (children with
AML FAB M0-7, excluding Fanconi anemia, Down syndrome, secondary AML, and granulocytic sarcoma, in contrast in AML-BFM 93 only patients younger than 18 years) showed that the overall 5-year survival rate of all children, not only those in remission, was 59% ± 2%. This was considerably higher than of the total patient group of the CCG 2891 trial (CCG estimated 40%; intensive timing 49% ± 5%; standard timing 34% ± 6%). Events 5 years after diagnosis were extremely rare in the BFM studies, and therefore, estimates are comparable. It is surprising that the survival curve from the BMT group in the CCG study shows no plateau after more than 5 years.11(FIG 2) This is in contrast to the chemotherapy groups in the CCG and in the BFM study.

Regarding children in remission only, as reported in the CCG paper, the 5-year overall survival in the AML-BFM 93 study (n = 386) was 71% ± 3% (matched related-BMT 70% ± 8%, n = 30; chemotherapy alone 71% ± 3%; n = 356). Considering all children with AML in remission of studies AML-BFM 87 and 93 (between 1987 and June 1998, n = 616), the 5-year overall survival was 67% ± 2%. In contrast to the CCG study, outcome was predominantly achieved by intensive chemotherapy alone (chemotherapy, n = 546; MR-BMT in first remission, n = 44 [7%]; other, n = 26 [ie, 4%]; autologous BMT, n = 11; alternative donor BMT, n = 15).

Most recently, our data were supported by the results of the Medical Research Council (MRC) 10 and 12 trials, failing to show a benefit for allogeneic BMT.6,7 Intensive chemotherapy regimens such as AML-BFM 93 or MRC 10/12 including intensive induction, consolidation, and high-dose postremission treatment and sufficient supportive care seem to achieve therapy results similar to allogeneic BMT, with less severe late effects.8-10 And although several other pediatric studies reported superior results of allogeneic BMT,11-14 results for the total groups were inferior. Therefore, a benefit of allogeneic BMT may be achieved for patients treated with less intensive induction and consolidation treatment.

As a consequence, one could argue that allogeneic BMT should always be considered in context with the applied protocol. Due to the favorable outcome (survival rate higher than 70%) in children with standard risk AML (standard risk group: AML M1/M2 with Auer rods or t(8;21), AML M4eoro inv(16), and less than 5% blasts at day 15; AML FAB M3 with t(15;17) regardless of their blast count on day 15),15 these patients were excluded from matched related-BMT in first CR in study AML-BFM 93. This had the advantage that the potential morbidity of the transplantation procedures can be avoided in the majority of these patients. Patients with standard-risk AML will either not suffer from relapse at all or suffer predominantly from late relapse. According to our data, the probability to achieve a second remission is high in late relapses allowing BMT in second CR.16 Whether there is a benefit by BMT in first CR for high-risk patients treated with BFM protocols is the subject of our current study.

**To the editor:**

**Intensive chemotherapy and bone marrow transplantation for children with acute myeloid leukemia**

In a recent article, Woods et al detail the findings of a well-designed Children’s Cancer Group study comparing matched sibling allogeneic bone marrow transplantation (BMT), autologous bone marrow transplantation, and intensive chemotherapy for children with acute myeloid leukemia (AML) in first complete remission (CR). The authors drew 2 conclusions that are subject to debate. First, referring to beneficial effect of intensively timed induction therapy, they state that “for the first time in North America we have

**References**


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