AML FAB M0-7, excluding Fanconi anemia, Down syndrome, secondary AML, and granulocytic sarcoma, in contrast to 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. 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. 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. And although several other pediatric studies reported superior results of allogeneic BMT, 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 M4eo or 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), 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. 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.

References

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
To the editor:

**Treatment of children with acute myeloid leukemia**

In a recent article, Woods et al report that postremission bone marrow transplantation (BMT) produced better overall survival than chemotherapy in children with acute myeloid leukemia (AML). They also indicate that intensive timing induction improved postremission survival. Their study is impressive in its design, conduct, and magnitude, but their article raises several questions.

First, in comparing initial characteristics of patients in the allogeneic BMT (allo-BMT) and chemotherapy groups, no mention is made of ethnicity or socioeconomic and insurance status. Because these appear to be important variables in accessibility to allo-BMT and may also influence prognosis, should they not be taken into consideration? Is it possible that access to allo-BMT itself is a selective factor for better prognosis?

Second, the article compares overall survival after remission rather than from diagnosis. As described elsewhere, the remission induction mortality due to drug toxicity was 12% for the intensive timing group and 5% for the standard group. Is it possible that this higher treatment-related mortality during induction removed from the intensive-timing group patients with less favorable prognosis, for example, patients more vulnerable to chemotherapy toxicity and interruption during postremission chemotherapy? In other words, were the postremission intensive-timing patients selected for better prognosis by the mortality of the intensive-timing induction?

Third, as the article points out, survival curves for AML do not plateau until 6 or more years. Because the plateau is the closest measure of cure or near-cure, the plateaus must be compared to determine curability. Comparison of the 6- and 7-year survival of the allo-BMT and chemotherapy groups in Woods et al’s Figure 2 reveals no apparent significant difference. This is reflected in the configuration of the 2 survival curves, which indicate that the wide gap at 3 years progressively narrows in subsequent years. In children, should entire survival curves or plateaus be used to compare success? To revive an argument from the 1960s, is the prime goal of treatment to prolong survival or to cure leukemia?

Finally, the article justifiably celebrates progress in curing children of AML. But for the sake of perspective, should not event-free survival and overall survival from diagnosis be indicated, and should not the treatment-related mortality and morbidity, late and early, be summarized? From my reading of this article and similar reports cited by Woods et al, I fail to reach their conclusion that allogeneic BMT is the treatment of choice for children with AML in first remission who have a matched related donor.

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**References**


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