Improvements in the survival of children and adolescents with acute lymphoblastic leukemia

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Over the past 50 years, the treatment of young patients with acute lymphoblastic leukemia (ALL) has significantly improved, and is one of the success stories of cancer treatment. This success is measured by the improved survival of childhood ALL patients from less than 10% in the 1960s to more than 80% in more recent reports. Based on a study by Stephen Hunger and colleagues,[1] these numbers are continuing to improve with 5-year overall survival rates now above 90% for the first time (83.7% in the period 1990-1994; 90.4% in the most recent period 2000-2005). This study is based on information on 21,626 ALL patients between 0 and 22 years who were enrolled onto the Children's Oncology Group (COG) ALL clinical trials from 1990 to 2005.[1]

What lessons can we learn from the available data? First of all, it is clear that survival improved in all subgroups of ALL, except for infants under the age of one year, and 5-year overall survival also remains significantly lower (81.6%) for children over the age of ten years.[1] The general increase in survival was mainly due to a 44% decrease in the risk of death following relapse or disease progression. Based on this and other studies, the major benefit from the new treatment strategies comes from the prevention of relapse, and relapse itself remains a highly adverse event.[2,3] Second, patients with T-ALL had a significantly lower 5-year survival than children with B-ALL. This study confirms that T-cell ALL remains a more aggressive disease than B-cell ALL and that additional treatment options need to be explored for T-ALL.[1,4] Recent studies have identified new targets for therapy in T-ALL,[5] although trials to investigate the importance of new targeted drugs will be difficult due to the relatively low number of T-ALL patients (about 10% of ALL cases).[1] Similarly, patients in the NCI (National Cancer Institute) high-risk group had only 82.9% 5-year overall survival, while patients from the standard risk group had 95% 5-year overall survival. Nevertheless, 36% of deaths still occurred among children with standard risk, highlighting that also for this subgroup further improvements are needed.[1]

This study brings hope to the children with ALL by pointing out that refinements in therapy are continuously improving their chances of cure, but also identifies specific difficulties and areas where there is a need for further research. Infant ALL is one of the subgroups with a poor outcome, where no progress has been made as reductions in deaths due to relapse have been counteracted by inreases in deaths related to toxicity. In addition, T-cell ALL remains a risk factor; this was also shown in a recent study published by Martin Schrappe and colleagues who studied outcomes after induction failure in childhood ALL.[2] Also in this study, T-ALL (among other factors such as high leukocyte count, older age, presence of BCR-ABL1 or MLL fusions) was found to be more prevalent in children who failed induction therapy, and T-ALL conferred a worse prognosis. On a positive note, the study suggests that the use of allogeneic stem cell transplantation may be associated with improved outcomes in patients with T-ALL who did not achieve a complete remission with induction therapy. This benefit was specific for T-ALL and not observed for B-ALL.[2]

References

1. Hunger SP, Lu X, Devidas M, Camitta BM, Gaynon PS, Winick NJ, et al. Improved survival for children and adolescents with acute lymphoblastic leukemia between 1990 and 2005: a report from the children's oncology group. J Clin Oncol. 2012 Mar 12. [Epub ahead of print].
2. Schrappe M, Hunger SP, Pui CH, Saha V, Gaynon PS, Baruchel A, et al. Outcomes after induction failure in childhood acute lymphoblastic leukemia. N Engl J Med. 2012;366 (15):1371-81.
3. Zeidler L, Zimmermann M, Möricke A, Meissner B, Bartels D, Tschan C, et al. Low platelet counts after induction therapy for childhood acute lymphoblastic leukemia are strongly associated with poor early response to treatment as measured by minimal residual disease and are prognostic for treatment outcome. Haematologica. 2012;97(3):402-9.
4. Lauten M, Möricke A, Beier R, Zimmermann M, Stanulla M, Meissner B, et al. Prediction of outcome by early bone marrow response in childhood acute lymphoblastic leukemia treated in the trial ALL-BFM 95. Differential effects in precursor B-cell and T-cell leukemia. Haematologica. 2012 Jan 22. [Epub ahead of print].
5. Cools J. Genetic and epigenetic studies offer new therapeutic options for the treatment of T-cell acute lymphoblastic leukemia. Haematologica. 2012;97(3):323.