The treatment of acute lymphoblastic leukemia has come a long way but the best is yet to come

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The success of acute lymphoblastic leukemia therapy is a consequence of numerous studies that have being conducted since 1950. At first, treatment was introduced in a trial and error method, but afterwards it was based on scientific knowledge drained from observational and laboratory research. If, on one hand, a group of drugs was established as the main therapeutic option since impressive results were observed after their use, on the other, patient and leukemic cell features were also detected as important for treatment outcome[1]. In fact, conventional risk criteria presented at diagnosis, such as age, elevated white blood cell count, adverse immunophenotypic pattern and cytogenetic or molecular aberrations provide the basis for upfront risk stratification. However, patient performance status, concomitant diseases, treatment compliance, host pharmacodynamics and pharmacogenetics are also relevant. In addition, proprieties of the leukemia cell, such as proliferative capacity, susceptibility to drugs or escape mechanism as well as intensity of drugs to eradicate the disease compose the group of features in which treatment outcomes depend. Notwithstanding this, relapses were still a problem and the main cause of reduction of survival. Indeed, the criteria used to define remission after induction chemotherapy (less than 5% of blasts in the marrow with hematological recovery) did not mean that leukemia cells were totally eradicated, but that their level was beyond the sensitivity limits of classic morphology methods. In most of these situations, malignant cells still remained representing minimal residual disease (MRD)[2]. The source of relapse was persistent MRD. In order to detect the level of MRD, diagnostic improvements were achieved by evaluations either by molecular genetic methods or by flow cytometry, which has been shown to be predictive for outcome in a number of studies on children and adults. Furthermore, MRD monitoring during the first year of intensive chemotherapy led to an MRD-based risk stratification. Thereafter, protocols have been designed considering MDR as an important aspect to allow a tailored treatment in order to achieve a longer survival and it is now established that the level of MDR represents a powerful prognostic factor as well. In addition, when MRD monitoring shows increasing levels one can anticipate impending relapse[3]. Consequently, a prerequisite for the application of MRD to tailor treatment is an adequate, sensitive and standardized method. Most of these methods are expensive, quite complex and require expertise. A low cost, reliable and easy to perform methodology is desired. This was precisely what Assumpção et al. are presenting in their paper published in this issue of *Revista Brasileira de Hematologia e hemoterapia*[4]. These authors tried to detect markers in MRD monitoring based on conventional polymerase chain reaction (PCR) for immunoglobulin (Ig) and T-cell receptor (TCR) rearrangements, and Sil-Tal1 deletion in patients with acute lymphoblastic leukemia (ALL) treated in three hospitals in Minas Gerais, Brazil. The methodology proposed has a low sensitivity to detect small amounts of residual cells nevertheless it allowed the discrimination of high-risk patients. Certainly, there is a long way to go before these methods may be considered a good option, and studies comparing them with gold-standard techniques are being performed. Therefore the feeling that the best is yet to come can be detected from ongoing research.

References

1. Pui CH, Evans WE. Treatment of acute lymphoblastic leukemia. N Engl J Med. 2006;354(2):166-78.
2. Campana D. Minimal residual disease in acute lymphoblastic leukemia. Hematology Am Soc Hematol Educ Program. 2010;2010:7-12.

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3. Brüggemann M, Raff T, Kneba M. Has MRD monitoring superseded other prognostic factors in adult ALL? Blood. 2012;120(23):4470-81.

4. Assumpção JG, Paula FD, Xavier SG, Murao M, Aguirre Neto JC, Dutra AP, et al. Gene rearrangement study for minimal residual disease monitoring in children with acute lymphocytic leukemia. Rev Bras Hematol Hemoter. 2013;35(5):337-42.

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