International Journal of Hematology (2023) 117:153–154
https://doi.org/10.1007/s12185-023-03536-8

PROGRESS IN HEMATOLOGY

Recent progress in pediatric leukemia

Guest editorial: recent progress in pediatric leukemia

Toshihiko Imamura[1]

Received: 27 December 2022 / Revised: 6 January 2023 / Accepted: 6 January 2023 / Published online: 13 January 2023
© Japanese Society of Hematology 2023

Abstract
Recent progress in comprehensive genomic analysis and well-designed clinical trials has dramatically improved the treatment strategies for pediatric leukemia, resulting in better prognosis and reducing acute and late adverse events. This review series describes successes and challenges for the future in the management of pediatric leukemia.

Keywords Pediatric · Infant · Leukemia · Genomic analysis · Clinical trial

Recent advances in basic and clinical studies have delivered great progress in the treatment of pediatric leukemia. In terms of basic studies, comprehensive genomic analysis of pediatric leukemia has provided insights into leukemogenic mechanisms to enable the development of better therapeutic options, such as molecular targeting therapies [1]. It is also important to understand the role of genetic variations in the host, not only in leukemia susceptibility but also in optimal treatment interventions [2]. In terms of clinical studies, clinical trials conducted by international collaborative study groups have had great success in establishing better treatment strategies for pediatric leukemia. The Japan Children's Cancer Group (JCCG, http://jccg.jp) has conducted national multicenter clinical trials to answer clinical questions to establish better treatment for pediatric leukemia. Currently, JCCG collaborates with the Japan Adult Leukemia Study Group (JALSG, http://jalsg.jp) to conduct clinical trials for pediatric and adult acute lymphoblastic leukemia. This issue of ''Progress in Hematology'' includes four excellent review articles that summarize the recent progress in basic and clinical studies of pediatric leukemia. These reviews highlight the contribution of comprehensive genomic studies and well-designed clinical trials to progress made in the management of pediatric leukemia.

✉ Toshihiko Imamura
timamura@sa3.so-net.ne.jp

[1] Department of Pediatrics, Graduate School of Medical Science, Kyoto Prefectural University of Medicine, Kyoto, Japan

The review by Motohiro Kato discusses recent progress in pediatric acute lymphoblastic leukemia. He reviews the recent progress in molecular genomics of leukemic cells, molecular genomics in inherited germline variations, risk stratification based on minimal residual disease, and immunotherapy for B-ALL. The author's group demonstrated that *NUDT15* variants affect the tolerability of 6-mercaptopurine (6-MP) and the optimal duration of maintenance therapy for B-ALL [3, 4]. Based on their data, dose modification of 6-MP based on *NUDT15* genotype, randomization of maintenance therapy, and risk stratification based on PCR-MRD kinetics have been incorporated in the current clinical trial, ALL B-19.

Infant ALL with *KMT2A* rearrangement is a subtype of pediatric ALL with a dismal prognosis. To improve the prognosis of this subtype, clinical trials have been conducted by international collaborative study groups, such as the Interfant group, in recent decades. However, none of these clinical trials led to an improvement in prognosis [5]. A series of clinical trials for infant ALL has been also conducted in Japan [6]. Finally, the MLL-10 clinical trial achieved a great improvement in the prognosis of infant ALL with *KMT2A* rearrangement [7]. Daisuke Tomizawa, principal investigator of the MLL-10 clinical trial, reviews the history of the evolution and optimization of therapies for infant ALL.

JCCG established a banking system of clinical samples to perform basic studies. Comprehensive genomic analysis of pediatric acute myeloid leukemia (AML) revealed genetic alterations that were useful as prognostic markers or therapeutic targets [8]. Norio Shiba reviews the achievement of comprehensive genomic analysis of pediatric AML using

leukemic cells of the patients participating in clinical trials conducted by JCCG. He also describes how to combine these data with the current clinical trial of pediatric AML, AML20.

Finally, the review article from Haruko Shima et al. covers the management of pediatric chronic myeloid leukemia (CML). As in adult CML, tyrosine kinase inhibitors (TKIs) are first-line treatment for pediatric CML. However, as the authors' group demonstrated, it is essential to pay attention to the considerable adverse events related to TKIs, such as growth impairment, in pediatric patients [9]. Thus, the authors discuss proper management of TKI therapy for pediatric CML in this review.

In summary, this review series describes the recent progress in the management of pediatric leukemia based on the results of recent comprehensive genomic analysis and clinical trials conducted by international collaborative study groups and JCCG.

Each review discusses many clinical questions and hopefully will help physicians improve the management of pediatric, adolescent, and young adult leukemia.

Declarations

Conflict of interest The author has no conflict of interest to declare.

References

1. Iacobucci I, Mullighan CG. Genetic basis of acute lymphoblastic leukemia. J Clin Oncol. 2017;35(9):975–83.
2. Lee SHR, Yang JJ. Pharmacogenomics in acute lymphoblastic leukemia. Best Pract Res Clin Haematol. 2017;30(3):229–36.
3. Tanaka Y, Kato M, Hasegawa D, Urayama KY, Nakadate H, Kondoh K, et al. Susceptibility to 6-MP toxicity conferred by a NUDT15 variant in Japanese children with acute lymphoblastic leukaemia. Br J Haematol. 2015;171(1):109–15.
4. Kato M, Ishimaru S, Seki M, Yoshida K, Shiraishi Y, Chiba K, et al. Long-term outcome of 6-month maintenance chemotherapy for acute lymphoblastic leukemia in children. Leukemia. 2017;31(3):580–4.
5. Pieters R, De Lorenzo P, Ancliffe P, Aversa LA, Brethon B, Biondi A, et al. Outcome of infants younger than 1 year with acute lymphoblastic leukemia treated with the Interfant-06 protocol: Results from an international phase III randomized study. J Clin Oncol. 2019;37(25):2246–56.
6. Tomizawa D. Recent progress in the treatment of infant acute lymphoblastic leukemia. Pediatr Int. 2015;57(5):811–9.
7. Tomizawa D, Miyamura T, Imamura T, Watanabe T, Moriya Saito A, Ogawa A, et al. A risk-stratified therapy for infants with acute lymphoblastic leukemia: a report from the JPLSG MLL-10 trial. Blood. 2020;136(16):1813–23.
8. Fröhling S, Scholl C, Gilliland DG, Levine RL. Genetics of myeloid malignancies: pathogenetic and clinical implications. J Clin Oncol. 2005;23(26):6285–95.
9. Shima H, Tokuyama M, Tanizawa A, Tono C, Hamamoto K, Muramatsu H, et al. Distinct impact of imatinib on growth at prepubertal and pubertal ages of children with chronic myeloid leukemia. J Pediatr. 2011;159(4):676–81.

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.