Chronic Myeloid Leukemia in Children

Clinical Findings, Management, and Unanswered Questions

Nobuko Hijiya, MD[a,b,*], Frederic Millot, MD[c], Meinolf Suttorp, MD[d]

KEYWORDS

- Chronic myeloid leukemia • Tyrosine kinase inhibitor
- Hematopoietic stem cell transplant • BCR-ABL1

KEY POINTS

- There are few data showing biological differences between adult and pediatric chronic myelogenous leukemia (CML), but the clinical presentations are distinct and the host factors are different in adults and growing children, which raises issues specific to the care of pediatric patients with CML.
- Children have longer life expectancies than adults; therefore, the goal of CML treatment in children should be cure rather than disease suppression.
- Because of the possibility of decades-long tyrosine kinase inhibitor (TKI) treatment, which also occurs during periods of active growth, morbidity related to TKI therapy for CML is different in children than in adults. Careful monitoring of bone growth and other possible long-term morbidity is crucial.
- The role of hematopoietic stem cell transplant in the first chronic phase should be defined for pediatric patients with CML.

INTRODUCTION

Chronic myelogenous leukemia (CML) is diagnosed in approximately 6000 patients every year in the United States according to the Surveillance Epidemiology and End Results (SEER) Program.[1–3] CML in children is usually considered to be rare, but it

[a] Division of Hematology, Oncology, and Stem Cell Transplantation, Ann & Robert H. Lurie Children's Hospital of Chicago, 225 East Chicago Avenue, Box #30, Chicago, IL 60611, USA; [b] Department of Pediatrics, Northwestern University Feinberg School of Medicine, Chicago, IL, USA; [c] Centre d'Investigation Clinique 1402, Institut National de la Santé et de la Recherche Médicale (INSERM), University Hospital of Poitiers, 2 rue de la Milétrie, 86000 Poitiers, France; [d] Department of Pediatrics, University Hospital "Carl Gustav Carus", Fetscherstrasse 74, D-01307 Dresden, Germany
* Corresponding author. Division of Hematology, Oncology, Stem Cell Transplantation, Ann & Robert H. Lurie Children's Hospital of Chicago, 225 East Chicago Avenue, Box #30, Chicago, IL 60611.
E-mail address: nhijiya@luriechildrens.org

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accounts for 10% to 15% of myeloid leukemia and is more common than acute promyelocytic leukemia, which accounts for 5% to 10% of cases. At one time, hematopoietic stem cell transplant (HSCT) was the only curative treatment of CML in children as well as in adults; however, the treatment landscape has changed drastically over the last 15 years since the introduction of the tyrosine kinase inhibitor (TKI) imatinib.[4–6] Continuing TKI treatment indefinitely has become standard practice for adult patients in chronic phase (CP), and the feasibility of discontinuing TKI therapy in patients in deep molecular remission has been studied.[7] However, because of a lack of data from large clinical studies, standardized treatment and interventions have not been established in the pediatric CML population. This article discusses some controversial issues and unanswered questions (**Table 1**), as well as current recommendations, in the management of pediatric CML (**Boxes 1** and **2**, **Fig. 1**).

Table 1
Unanswered questions and issues specific to pediatric CML

Issues and Questions	Notes
Children have longer life expectancy than adults	• No studies have proved the efficacy of TKIs to suppress disease beyond 15 y • There may be unexpected morbidities after decades of TKI treatment
Morbidities from TKIs in children are different from those in adults	• Children require multiple decades of TKI treatment • TKIs cause growth disturbances • There is no human study showing the effect of TKIs on the future fertility of young children • Immune dysfunction, thyroid, cardiac, vascular, and liver toxicities have been reported in adults, but there are no long-term data in children
Treatment should be designed for cure, rather than suppression, of the disease	• New agents that target leukemic stem cells or overcome TKI resistance may be particularly helpful in pediatric patients
HSCT may still play a role in children in first CP	• The outcome of HSCT is better in children in general • HSCT may provide sustained remission or cure by eradicating leukemic stem cells • Recent techniques such as reduced-intensity conditioning may be effective • There are very few large studies on long-term outcomes and morbidity of HSCT for CML • Very late relapse is possible
Efficacy of newer TKIs has not been validated	• There are ongoing phase 2 studies of 2G TKIs
Pediatric-specific treatment guidelines are lacking	• Modification of ELN and NCCN guidelines may be needed • Recommendations from the I-BFM study group based on adult data have been published • International harmonization is needed
CML scoring system has not been validated in children	• Sokal, Hasford, and EUTOS scores are not reliable in children • Prognostic value of early response and kinetics of *BCR-ABL1* transcript ratio need to be validated in children

Abbreviations: 2G, second generation; ELN, European Leukemia Net; iBFM, international Berlin-Frankfurt-Münster study group; NCCN, National Comprehensive Cancer Network.