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### Introduction

Pediatric chronic myeloid leukaemia (CML) is relatively uncommon. Lacking strong clinical study evidence, therapy of CML in children is not standardised and frequently adheres to recommendations made for adults. The clinical presentation of adolescents and young adults is typically more aggressive than that of older individuals, and prognostic ratings for adult CML do not apply to children [1]. Although it has been assumed that the biology of CML in children and adults is the similar, recent studies show that there are some genetic differences between the two. Children with CML may experience morbidities that are different from those in adults because they may get tyrosine kinase inhibitor (TKI) therapy for many years and are exposed to TKIs during a time of active growth.

Children may benefit more from aggressive approaches such the temporary elimination of CML stem cells and rigorous chemotherapy and TKI regimens because they won't be exposed to TKIs and their side effects for the rest of their lives. The acute and long-term toxicities of blood and marrow transplantation in children with CML should be carefully weighed against the problems brought on by using TKIs for the rest of one's life. This strategy is currently only suggested for recurrent progressive illness [2].

In Western registries, the median age of diagnosis for chronic myeloid leukaemia (CML) is 60 to 65 years, and CML in children and adolescents is uncommon. CML makes up 9% of all leukemias in teenagers between the ages of 15 and 19 and 2% of all leukemias in children under the age of 15. Practice guidelines for the management of juvenile CML patients are less established than those for adult patients due to the low frequency of CML and the dearth of reliable clinical trial data in children and adolescents.

The biology of CML varies between children and adults. Both juvenile and adult CML patients contain the fusion gene BCR-ABL1, with breakpoints distributed over a large intronic distance (encompassing 200 kb) in the ABL1 gene and in the same main breakpoint cluster regions (M-BCR) in the BCR gene on chromosome 22 [4]. According to Krumbholz et al., juvenile CML exhibits a distinct breakpoint distribution in BCR from adult CML. Given the varying rates of CML in patients who are children and adolescents compared to those who are adults, it is possible that distinct mechanisms account for initiation of chromosomal translocation in each cohort. In comparison to adults with CML-CP, children with the disease show a distinct

breakpoint distribution pattern in the BCR gene and a larger percentage of breakpoints within Alu repeat regions. In contrast to juvenile CML, which has a second cluster in the telomeres that mostly overlaps with an extended Alu repeat area, adult CML has a considerable enrichment of DNA fusion sites inside the BCR major breakpoint cluster region in the centromere [5, 6]. The latter distribution resembles the pattern seen in adult Philadelphia-positive M-BCR rearrangement-positive acute lymphoblastic leukaemia (Ph1 ALL). These variations in the genetic environment may be a factor in the more aggressive clinical traits of paediatric CML in comparison to adult CML [7].

Children with CML have more aggressive clinical characteristics, and current research has started to show that adults and children with CML have different biology, which may explain the clinical disparities in CML presentation, progression, and therapy response. Clinicians must be aware of the host factors that contribute to the many morbidities brought on by TKI treatment in children. The possibility of decades-long TKI treatment prompts the question of whether or not to offer BMT to children in the initial CML-CP, but this should be left to the results of more research. Children should be given preference in clinical trials that examine the viability of discontinuing TKI therapy or switching to intermittent TKI therapy as well as novel medicines that target CML stem cells. International cooperation, funding, and construction of larger studies for pediatric CML are urgently needed to address unanswered questions and issues [8].

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