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Editorial

Chronic myeloid leukemia in children, do we have all the answers?

Chronic myeloid leukemia (CML) is the most common adult leukemia, however in children, the incidence is 2-3% of all childhood leukemias.[1] Since pediatric CML is not a very common disease, there is dearth of data on the various aspects of its presentation, history and the response to various treatment modalities.

To start with, in children approximately 10% of the newly diagnosed cases present with advanced phase, higher than reported in case of adults.[1] Pediatric oncologists always face lot of dilemma while treating this adult leukemia in children as there are no robust guidelines on dosage, choice of first line tyrosine kinase inhibitors (TKIs), time to offer allogeneic stem cell transplant and defined timelines to check the response to treatment. It is also important to remember that pediatric patient is not young adult.

In this present paper by Linga *et al*., it is interesting to note that 75% of the patients who progressed on Imatinib (IM), responded to dose hike, that also at 340 mg/m^2.[2] Since there is no data on mutation analysis, the reason to loss of response to Imatinib is not known. At the same time, such high percentage of patients responding to suboptimal dose hike raises the issue of noncompliance. In the literature, it is reported that IM doses of 400-500 mg/m^2 provide drug levels equivalent to 600 mg and 800 mg and are advised for accelerated phase and blast crisis respectively.

Noncompliance and development of resistance are major issues in the pediatric population. Indian patients do present in late chronic phase and have a high incidence of primary resistance due to various factors.[3] The mere extrapolation of adult data to pediatric group does not resolve many issues. Hence, the first step in providing the best treatment to pediatric patients is to have complete response monitoring. In India, this issue is always sidelined citing financial reasons. In my view, there is a lack of effort from the treating physician side as well may be due to time concerns or other reasons. I strongly feel that patients should be convinced to undergo response analysis as they get free Imatinib through various patient assistance programs and also we have very cheap and effective generics which cut the cost of treatment tremendously.

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Second, another important issue, median age of presentation in children with CML is 11 years which is a prepubertal age and it is important to remember that Imatinib is known to cause hypocalcemia, hypophosphatemia leading to dysregulated bone remodeling. There have been reports of stunted growth in patients on Imatinib. In the present study also they have reported 29% of growth retardation.[2] Similar kind of observations on the growth of prepubertal children was seen in French and German studies also.[4,5]

Finally, there is scarcity of trial in pediatric populations regarding usage of 2nd and 3rd generation TKIs and their long-term effects. In the present era, with so many choices available for the treatment of CML, there is a need for specific guidelines to offer the best treatment to pediatric patients in different cases scenarios. To answer these questions we need active enrollment of pediatric patients on CML trials and also we need to understand the importance of complete followup of response monitoring in these patients.

Shweta Bansal

Department of Oncology, Division of Pediatric Oncology, Sir. Harkishandas Nurrottamdas Reliance Foundation Hospital, Mumbai, Maharashtra, India
Correspondence to: Dr. Shweta Bansal,
E-mail: doc.shwetabansal@gmail.com

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