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Letter to the Editor

Is it Safe to Stop Tyrosine Kinase Inhibitor in Pediatric Chronic Myeloid Leukemia

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Latter to the Editor

Pediatric CML (Chronic Myeloid Leukemia) constitute less than 3% of pediatric leukemia [1]. There is a paradigm shift in the first line treatment of pediatric CML from allogeneic bone marrow transplant to use of Tyrosine Kinase Inhibitors (TKI) [2]. In children the Complete Cytogenetic Response (CCyR) to Imatinib Mesylate (IM) in a naïve CML patient ranges from 56-89.5% in different studies [3]. A phase IV study enrolled naive pediatric CML patients, at the end of one year CCyR and Major Molecular Response (MMR) were 61% and 31% respectively taking IM [4]. IM in children causes peculiar problem with bone growth, resulting in long term short stature and bone diseases [5]. In adults there is a particular group who are defined as "cure" in whom IM could be safely stopped; this editorial is to look for any scope of similar intervention in children.

There is growing evidence of Chronic Myeloid Leukemia Stem Cells (CMLSC) and its role in treatment response and resistance [6]. The response to treatment depends on mainly two factors: firstly the efficacy of pharmacological agent targeting the CMLSC and secondly the functional capacity of T/NK cells against the CMLSC. In an *in-vitro* experiment the CML stem cells were partially resistant to Imatinib Mesylate (IM) [7]. Other group of investigators has identified patients with CML and Acute Lymphoblastic Leukemia (ALL) on TKI having clonal expansion of T/NK cells had better disease control and there were distinct adverse effect profile [8].

In a pilot study adult CML patients on IM who were in continuous complete molecular response for more than 2 years, IM was stopped; in nearly 50% of patient the disease was in remission for more than 18 months of follow up [9]. In a large multicenter non-randomized trial nearly 40% were in Complete Molecular Response (CMR) after stopping IM [10]. The factors which predicted the long term remission after stopping IM are male patient, higher peripheral blood NK cells prior to stopping IM, longer duration of Interferon, quicker response to IM [11,12]. Most of relapses were within 6 months of stopping IM, and they responded after re-exposure to IM. Monitoring after stopping IM is crucial, monthly once RQ-PCR for one yr and there on bimonthly for next one year. In small observation study in children who have stopped IM on their own shown that all the patient had molecular relapse [13].

IM and other TKI have long-term toxicities in children, in patients who attains CMR for desired length of time is worth considering for stopping IM, if close molecular monitoring is feasible, under strict clinical studies.

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