

## Letter to the Editor

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

Linga VG\*

Department of Pediatrics, TTUHSC, Amarillo, USA

\*Corresponding author: Vijay G Linga, Department of Pediatrics, TTUHSC, Amarillo, USA

Received: June 27, 2016; Accepted: June 28, 2016;

Published: June 30, 2016

## Letter 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 naïve 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.

## References

- Andolina JR, Neudorf SM, Corey SJ. How I treat childhood CML. *Blood*. 2012; 119: 1821-1830.
- Giona F, Moleti ML, De Benedittis D, Santopietro M, Nanni M, Testi AM. Can chronic myeloid leukaemia in children and adolescents be successfully treated without haematopoietic stem cell transplant? A single centre experience. *Br J Haematol*. 2016; 173: 749-753.
- Linga VG, Ganta RR, Kalpathi KI, Gundeti S, Rajappa SJ, Digumarti R. Response to imatinib mesylate in childhood chronic myeloid leukemia in chronic phase. *South Asian J Cancer*. 2014; 3: 203-205.
- Millot F, Frédéric, Baruchel A, Guihot J, Petit A, Leblanc T, et al. “Imatinib is effective in children with previously untreated chronic myelogenous leukemia in early chronic phase: results of the French national phase IV trial.” 2011: 2827-2832
- Narayanan KR, Bansal D, Walia R, Sachdeva N, Bhansali A, Varma N. Growth failure in children with chronic myeloid leukemia receiving imatinib is due to disruption of GH/IGF-1 axis. *Pediatr Blood Cancer*. 2013; 60: 1148-1153.
- Kavalerchik E, Goff D, Jamieson CH. Chronic myeloid leukemia stem cells. *J Clin Oncol*. 2008; 26: 2911-2915.
- Jiang X, Zhao Y, Smith C, Gasparetto M, Turhan A, Eaves A. Chronic myeloid leukemia stem cells possess multiple unique features of resistance to BCR-ABL targeted therapies. *Leukemia*. 2007; 21: 926-935.
- Mustjoki S, Ekblom M, Arstila TP, Dybedal I, Epling-Burnette PK, Guilhot F. Clonal expansion of T/NK-cells during tyrosine kinase inhibitor dasatinib therapy. *Leukemia*. 2009; 23: 1398-1405.
- Rousselot, Philippe, Rea D, Legros L, Cayuela JM, Maarek O, et al. “Imatinib mesylate discontinuation in patients with chronic myelogenous leukemia in complete molecular remission for more than 2 years.” *Blood*. 2007; 109: 58-60.
- Mahon François-Xavier, Rea D, Guilhot F, Huquet F, Nicolini F, Legros L, et al. “Discontinuation of imatinib in patients with chronic myeloid leukaemia who have maintained complete molecular remission for at least 2 years: the prospective, multicentre Stop Imatinib (STIM) trial.” *The lancet oncology*. 2010; 11: 1029-1035.
- Mahon, Francois-Xavier, et al. “Discontinuation of imatinib therapy after achieving a molecular response in chronic myeloid leukemia patients.” *Blood*. 2009; 144: 859-859.
- Ross DM, Branford S, Seymour JF, Schwazer AP, Arthur C, Yeung DT. Safety and efficacy of imatinib cessation for CML patients with stable undetectable minimal residual disease: results from the TWISTER study. *Blood*. 2013; 122: 515-522.
- Millot F, Claviez A, Leverger G, Corbaciglu S, Groll AH, Suttrop M. Imatinib cessation in children and adolescents with chronic myeloid leukemia in chronic phase. *Pediatr Blood Cancer*. 2014; 61: 355-357.