

Editorial

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Treatment Development of Chronic Myeloid Leukemia

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Chronic Myeloid Leukemia (CML) is a hematologic stem cell disorder leading to myeloproliferation and its attendant consequences [1]. CML typically evolves in 3 distinct clinical phases; An indolent or chronic phase (CP) course easily controlled with therapy that can last for 3 to 5 years and accelerated phase (AP) that lasts for less than 12 months and blast phase (BP), characterized by rapid expansion of a population of myeloid or lymphoid blasts of at least 30% in the peripheral blood or bone marrow resulting in the patient's death within 4 to 6 months [2]. Busulfan is the oral anti-CML alkylating agent in the 1950s and was convenient to administer and inexpensive but associated with severe and prolong myelosuppression. Busulfan was largely replaced by hydroxyurea in 1970s. Hydroxyurea was the available and effective anti-CML agents in the 1980s. These were able to control the clinical manifestations of the disease, but were rarely, if ever, capable of eliminating the malignant clone. In 1990s the interferon alpha has constituted first-line therapy for patients with CML resulted in major cytogenetic responses of 25% [3]. The combination of interferon alpha with hydroxyurea or with Ara-C was effective in clinical practice and induces cytogenetic remissions in some patients [4].

Treatment of chronic myeloid leukemia improved dramatically with the development of tyrosine kinase inhibitors (TKIs), especially the introduction of imatinib (Gleevec) in May 2001 into the clinical practice. Imatinib is the golden standard tyrosine kinase inhibitor target therapy in CML and considered the first-line drug of choice in the chronic phase of CML [5]. However, up to 33% of patients will not achieve optimal response. This led researchers to develop new second and third generation tyrosine kinase inhibitors.

In 2006 dasatinib (Sprycel) represents a promising treatment option for patients in all phases of chronic myeloid leukemia and also as a second line treatment for patients with CML if imatinib therapy fails and for Philadelphia chromosome-positive acute lymphoblastic leukemia (Ph+ALL) [6,7].

In 2007 FDA approved for use nilotinib (Tasigna) as a selective treatment for Philadelphia positive chronic myeloid leukemia. Until recently, it had been used mostly and quite successfully as a second-line agent, and it is now licensed for first-line use at a dose of 300 mg twice a day and can be replaced instead of imatinib without any complications [8].

In September 2012, FDA approved bosutinib (Bosulif) for the treatment of adult patients who have chronic, accelerated, or blast phase Philadelphia chromosome positive (Ph+) chronic myeloid leukemia. Bosutinib was found to inhibit the proliferation of CML progenitors about 200 times better than imatinib and demonstrated durability of clinical outcomes among patients with chronic phase who had previously treated with imatinib and dasatinib or nilotinib [9].

In December 2012 FDA approved ponatinib (Including) as pan-BCR-ABL tyrosine kinase inhibitor for treatment of chronic phase , accelerated phase, or blast phase chronic myeloid leukemia (CML) who are resistant to dasatinib or nilotinib or intolerant to dasatinib or nilotinib and in Philadelphia chromosome positive acute lymphoblastic leukemia resistant to imatinib, dasatinib, or nilotinib [10].

The monitoring of tyrosine kinase inhibitor target therapy can be performing according to laboratory recommendations for scoring molecular responses by using either molecular or cytogenetic tests, or both, depending on the available facilities. Molecular testing performed by RQ-PCR on buffy coat of 10 ml blood to measure BCR-ABL1 transcript level, which is expressed as BCR-ABL1% on the International Scale (IS). The monitoring should be performed every 3 months until a MMR is achieved, then every 6 months [11]. The standardization of monitoring techniques is expected to affect both the use of heath care resources and outcome (Table 1).

CCyR: complete cytogenetic responses, MMR: Major molecular response AP; Accelerated phase, BP; Blast phase

Kantarjian et al (2010) reported in Dasision study that, the response were more better with dasatinib than imatinib, including higher response at 12 months rate of complete cytogenetic response (CCyR in dasatinib 83% vs. 72% in Imatinib (P. 0.0001) and higher response at 24 months rate of major molecular response (MMR) 64% in Dasatinib vs. 46% in Imatinib (P 0.001) [12]. Saglio et al. report the response of nilotinib was better than imatinib and the higher cytogenetic response rate (CCyR) at 24 months was 87% in nilotinib vs. 77% in imatinib and MMR response rate at 24 months was 71% in nilotinib vs. 44% in imatinib [8]. Cortes et al. reported there were no significant difference between the imatinib and bosutinib in CCyR response rate at 12 months study, while the MMR rate at 12 months study was significantly higher with bosutinib better than imatinib (41% vs. 27%; P<0.001) [13].

The development of resistance toward TKI is the most common problem in the treatment of chronic myeloid leukemia. In Imatinib resistance, second generation TKIs and allogeneic stem cell transplantation are excellent treatment options. The second generation TKI is the best choice for all CML patients developed drug resistance [7]. Bone marrow transplantation considered the best option for CML patients developed resistance for second generation TKIs.

Results in months	DASISION, %		ENESTnd, %		BELA, %	
	Imatinib	Dasatinib	Imatinib	Nilotinib	Imatinib	Bosutinib
CCyR at 12 months	73	85	65	80	68	70
CCyR at 24 months	82	85	77	87	81	87
MMR at 12 months	28	46	27	55	27	41
MMR at 24 months	46	64	44	71	52	67
Progression to AP/BP	3.5	1.9	4	<1	4	2
PFS at 24 months	92	93	95	98		
OS at 24 months	95	95	96	97	95	97

Table 1: Comparison of the results of imatinib with other TKIs [8,12,13].

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References

- 1. Canellos GP (1999) chronic granulocytic leukemia. Med Clin North Am 340: 1330-1340.
- Kantarjian HM, Dixon D, Keating MJ, et al. (1988) Characteristics of accelerated disease in chronic myelogenous leukemia. Cancer 61: 1441-1446.
- Talpaz M, Kantarjian HM, McCredie KB, et al. (1987) Clinical investigation of human alpha interferon in chronic myelogenous leukemia. Blood 69: 1280-1288.
- Cannistra S, Tantravahi R, Robertson MJ, Griffin J, Canalos GP (2003) Low dose ctarabine arabinoside induces cytogenetic remissions in patients with stable phase chronic myeloid leukemia. Blood 76: 259a.
- Goldman JM, Melo JV (2001) Targeting the BCR-ABL tyrosine kinase in chronic myeloid leukemia. N Engl J Med 344: 1084-1086.
- Nam S, Kim D, Cheng JQ, Zhang S, Lee JH, et al. (2005) Action of the Src family kinase inhibitor, dasatinib (BMS-354825), on human prostate cancer cells. Cancer Res 65: 9185-9189.
- 7. Talpaz M, Shah NP, Kantarjian H, Donato N, Nicoll J, et al. (2006) Dasatinib in

imatinib-resistant Philadelphia chromosome-positive leukemia's. N Engl J Med 354: 2531-2541.

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- Saglio G, Dong-Wook K, Issaragrisill S, et al. (2010) Nilotinib versus imatinib for newly diagnosed Chronic Myeloid Leukemia. N Engl J Med 362: 2251-2259.
- Jean Khoury H, Jorge E. Cortes, Hagop M. Kantarjian, Carlo Gambacorti-Passerini, Michele Baccarani, et al. (2012) Bosutinib is active in chronic phase chronic myeloid leukemia after imatinib and dasatinib.Blood 119: 3403-3412.
- Verma D, Kantarjian HM, Jones D, Luthra R, Borthakur G, et al. (2009) Chronic myeloid leukemia (CML) with P190 BCR-ABL: analysis of characteristics, outcomes, and prognostic significance. Blood 114: 2232-2235.
- O'Brien S, Abboud CN, Akhtari M, et al. (2013) Clinical Practice Guidelines in Oncology. Chronic Myelogenous Leukemia, Version 1.2014, National Comprehensive Cancer Network (NCCN) 11: 1327-1340.
- Kantarjian H, Shah N, Hochhaus A, et al. (2010) Dasatinib versus imatinib in newly diagnosed chronic-phase chronic myeloid leukemia. N Engl J Med 362: 2260-2270.
- Cortes JE, Maru A, Souza CAAD, et al. (2011) Bosutinib versus imatinib in newly diagnosed chronic phase chronic myeloid leukemia: BELA trial 24-month follow-up [abstract]. Blood (ASH Annual Meeting Abstracts) 118: 455-458.