Galore International Journal of Health Sciences and Research
Vol.5; Issue: 2; April-June 2020
Website: www.gijhsr.com
Original Research Article *P-ISSN: 2456-9321*

Hematological and Molecular Response Assessment of CP-CML Patients Treated with Imatinib: An Experience from a Tertiary Care Hospital in India

Namrata Bhutani[1], Deepika Arora[2], Neha Bhutani[3]

[1]Department of Biochemistry, Vardhaman Mahavir Medical College & Safdarjung Hospital, New Delhi, India
[2]Department of Anaesthesia, Royal London Hospital, NHS Barts Health, London, United Kingdom
[3]ESIC Dental College, Rohini, New Delhi, India.

Corresponding Author: Neha Bhutani

ABSTRACT

Background: Imatinib is a common drug for the treatment of CML. This study describes our experience with response to imatinib in patients of CML in a tertiary care hospital in India.
Materials and methods: After initiation of imatinib therapy, hematological response was monitored at regular intervals & molecular response assessed, in 30 newly diagnosed CML patients.
Results: Time to achieve CHR (THR) ranged from 1- 4.5 months. 26(86.66%) patients achieved CHR by the end of 3 months (n=17) had Optimal response (table 4),23.33% (n=7) warning and 20% (n=6) had failure to therapy. 2 patients were lost to follow-up and therefore excluded from the analysis, 1 patient had progression to BC and death, 1 patient had loss of CHR and 1 had progression to BC & death.
Conclusion: Imatinib mesylate is highly effective in the treatment of chronic phase CML and should be considered as the drug of first choice in CML. Molecular response evaluation after six months can predict the subsequent molecular response and can also be used as a surrogate monitor of marrow cytogenetic response.

Keywords: chronic myeloid leukemia, imatinib, drug resistance.

INTRODUCTION

Chronic myeloid leukemia (CML) is the most common form of adult leukemia in India[1]. BCR-ABL tyrosine kinase is a well-validated therapeutic target in Chronic Myeloid Leukemia (CML)[2]. Imatinib, a tyrosine kinase inhibitor is highly drug used in CML. This study describes our experience with response to imatinib in patients of CML in a tertiary care hospital in India.

METHODOLOGY

30 newly diagnosed BCR-ABL positive CML patients in chronic phase&30 healthy control subjects, all ethnic Indians, were recruited in the study. Patients underwent detailed clinical examination &hematological tests. After initiation of imatinib therapy, hematological response was monitored at regular intervals & molecular response (BCR-ABL1/ABL1 ratio) assessed either at 6 or 12 months using RT-qPCR for BCR-ABL.

RESULTS AND DISCUSSION

Age of cases ranged from 18-80 years (mean 39.70 ± 18.04 years)*;* including 22 males (73.34%)& 8 females (26.67%). Mean TLC(*10^9/L) at baseline was 203±176.73, at 6 months was 6.82±1.63 and at 12 months was 6.47± 2.21.Mean Duration of follow up was 8.93 ± 2.36 months. Time to achieve CHR (THR) ranged from 1- 4.5 months. (Mean THR 2.3 ±0.93 months). 26(86.66%) patients achieved CHR by the end of 3 months; all 30 cases had it by the end of 6 months.(table 1&2)

TABLE 1 : Achievement of complete hematological response (CHR)

	3 months	6 months	12 months
No. of patients, n=	30	30	27
CHR achieved, n(%)	26 (86.66 %)	30 (100%)	26 (96.29 %)
CHR not achieved,n(%)	4 (13.34 %)	0	1 (3.70 %)*

* Loss of CHR was seen in one patient at 11 months.

TABLE 2: Achievement of CHR at3 months

CHR at 3 months	Yes	No
No. of patients (%)	26 (86.66 %)	4 (13.34 %)

Molecular Response (BCR-ABL1/ABL1 %) was assessed once, either at 6 months (n=20) or at 12 months (n=10) after beginning of imatinib therapy. At 6 months 25% patients (n=5), achieved MMR,; 5% (n=1) had 4-log reduction; 5% (n=1) had 4.5 log reduction; 20%(n=5) had molecularly undetectable leukemia. At 12 months, 60%(n=6) had achieved MMR, 10%(n=1) had 4-log reduction; 10% (n=1) had 4.5 log reduction;10%(n=1) had molecularly undetectable leukemia.56.66% (table 3). Moreover, (n=17) had Optimal response (table 4),23.33% (n=7) warning and 20% (n=6) had failure to therapy.(ELN 2013 guidelines).1 patient progressed to blast crisis (CML-BC)&died at 9 months from start of imatinib therapy;1 had loss of CHR at 11 months;2 were lost to follow up at 6 months and 7 months respectively. (table 5)

TABLE 3: Categorization of patients on the basis of molecular response

	OPTIMAL	WARNING	FAILURE
No.of patients, n (%)	17 (56.66)	7 (23.33)	6 (20)

TABLE 4 : Achievement of molecular response

	6 months	12 months
No. of patients, n=	20	10
MMR, n(%)	5 (25%)	6 (60%)
$MR_{4.0}$ (4-log reduction), n(%)	1(5%)	1(10%)
$MR_{4.5}$(4.5-log reduction), n(%)	1(5%)	1(10%)
Molecularly Undetectable Leukemia ,n(%)	4(20%)	1(10%)
None,n (%)	9(45%)	1(10%)

TABLE 5: Survival analysis at follow up

	3 months	6 months	12 months
No. of patients, n=	28*	28	27
PFS(progression free survival) , n=	28*	28	27**
OS(overall survival) ,n=	28	28	27
EFS(Event-free survival)	28	28	26***

*2 patients were lost to follow-up and therefore excluded from the analysis, ** 1 patient had progression to BC and death, ***1 patient had loss of CHR and 1 had progression to BC & death.

DISCUSSION

Imatinib in the treatment of chronic myeloid leukemia (CML) is a significantly cost effective drug, but there are issues related to efficacy, safety, and quality associated with it.[3,4] This study assessed the outcome of CML patients after administration of imatinib after one year of therapy and reflects experience of treating patients with CML in a developing country. Similar studies have been done previously, including IRIS III (International Randomized Study of Interferon and STI571) and Gupta et al.[5,6] It was concluded that , Imatinib is effective in treating patients with CML in chronic phase and proves to have a durable outcome. Monitoring molecular responses in CML may be a good parameter, especially in developing country like India[7,8], as it avoids bone marrow examination procedure, which is a painful invasive test for which almost all of patients feel reluctant to undergo periodically[9]. However, cytogenetic testing could be reserved for special circumstances like increasing BCR-ABL transcripts, which may indicate loss of response and help in detecting clonal evolution.[10,11] Thus, Imatinib can be considered as a potential first-line treatment option for CML-CP.

CONCLUSIONS

Imatinib mesylate is highly effective in the treatment of chronic phase CML and should be considered as the drug of first choice in CML. Molecular response

evaluation after six months can predict the subsequent molecular response and can also be used as a surrogate monitor of marrow cytogenetic response.

REFERENCES

1. Deninger M.W., O'Brien S.G., Ford J.M. Practical management of patients with chronic myeloid leukemia receiving imatinib. J Clin Oncol. 2003;21:1637–1647.
2. Hughes P., Kaeda J., Branford S. Frequency of major molecular responses to imatinib or interferon alfa + cytarabine in newly diagnosed patients with chronic myeloid leukemia. N Engl J Med. 2003;349:1423–1432.
3. Gupta A., Prasad K. Hematological and molecular response evaluation of CML patients on imatinib. J Assoc Physicians India. 2007;55:109–113.
4. Bhutani M., Kochupillai V. Hematological malignancies in India. In: Kumar L., editor. Progressing Hematologic Oncology. The Advanced Research Foundation New York; New York: 2003. p. 10.
5. Druker B.J., Lee S.J. Chronic leukaemias. In: DeVita V.T., Lawrence T.S., Rosenberg S.A., editors. Cancer: Principles and Practice of Oncology. 8th ed. Lippincott Williams & Wilkins; Philadelphia, Pa: 2008. pp. 2267–2278.
6. Jiang Q, Zhao D, Jin J, Wu D, Meng F, Hu J, et al. A prospective, multi-centre clinical trial to evaluate the early clinical efficacy and safety of a generic imatinib in treating patients with chronic phase of chronic myelogenous leukemia. Zhonghua Xue Ye Xue Za Zhi. 2015 Aug;36(8):651–5.
7. Hughes T., Deininger M., Hochhaus A. Monitoring of CML patients responding to treatment with tyrosine kinase inhibitors; review and recommendations for harmonising current methodology for detecting BCR ABL transcripts and kinase domain mutations and for expressing results. Blood. 2006;102:28–37.
8. Sawyers Charles. Imatinib induces hematological and cytogenetic responses in CML patients. Blood. 2002;99:3530–3539.
9. Druker BJ, Guilhot F, O'Brien SG, Gathmann I, et al. IRIS Investigators: Five-year follow-up of patients receiving imatinib for chronic myeloid leukemia. N Engl J Med. 2006;355(23):2408–2417.
10. Koffi KG, Nanho DC, N'dathz E, Kouehion P, Dissieka R, Attia A, et al. The Effect of Imatinib Mesylate for Newly Diagnosed Philadelphia Chromosome-Positive, Chronic-Phase Myeloid Leukemia in Sub-Saharan African Patients: The Experience of Côte d'Ivoire. Advances in Hematology. 2010:6. Article ID 268921.
11. Kayastha Gyan K, Gurung Padma, Acharya Paras K, et al. Patan hospital experience in treating Philadelphia chromosome/BCR-ABL1 positive chronic myeloid leukemia patients with gleevec (imatinib mesylate); the first generation specific tyrosine kinase inhibitor. BMC Blood Disorders. 2010; 10:8.

How to cite this article: Bhutani N, Arora D, Bhutani N. Hematological and molecular response assessment of CP-CML patients treated with imatinib: an experience from a tertiary care hospital in India. Gal Int J Health Sci Res. 2020; 5(2): 53-55.

******