Asciminib Management In Chronic Myeloid Leukemia (CML) Patients With T315I Mutation

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INTRODUCTION

Asciminib is an allosteric tyrosine kinase inhibitor (TKI) that showed efficacy and a good safety profile in resistant CML patients, including those with T315I mutations.[1,2]

AIM

To present the updated results of asciminib use in T315I-positive CML patients in 3 Russian centers within the Managed Access Program.

METHOD

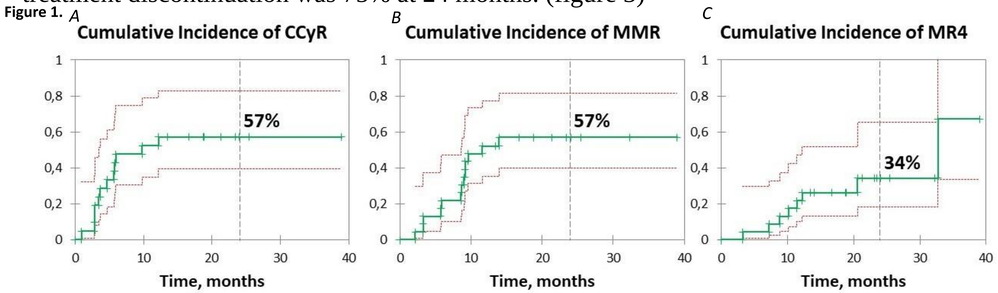
Data from 24 T315I-positive CML patients in a 200 mg BID dose group were analyzed. Complete cytogenetic response (CCyR), major molecular response (MMR), and deep molecular response (MR4) were assessed by cumulative incident function (CIF) with Gray's test for comparison responses in subgroups. Survival analysis was performed by the Kaplan-Meier method.

RESULTS

All patients were adults with Ph-positive CML in CP with/without a history of AP/BC. The median age was 49 (range 32-71), and 63% were female. Median CML duration before asciminib was 6.9 years (range 1-34). In patients who received ≥ 2 prior TKIs, 45% had ≥ 4 TKIs. The median follow-up was 21 months (range 6-39), and 5 (21%) patients discontinued asciminib (4 due to resistance, 1 due to bone marrow transplantation), no one progressed to AP/BC.

CIF of CCyR, MMR, and MR4 at 24 months was 57%, 57%, and 34%, respectively. (figure 1) Thirteen (54%) patients were ponatinib-pretreated. CIF of MMR in ponatinib-naive patients was higher compared to ponatinib-pretreated ones (90% vs. 25% [p=0.001]). (figure 2) Four patients lost CCyR or MMR. Two-year overall survival at 24 months was 100%. The survival rate without treatment discontinuation was 75% at 24 months. (figure 3)

Figure 1.



Thirteen (54%) patients experience AEs of any grade (mostly thrombocytopenia, neutropenia, skin rash, pleural effusion), and 4 (17%) had AEs of grade 3 (neutropenia, hypercholesterinemia). No patients discontinued treatment due to toxicity.

Figure 2.

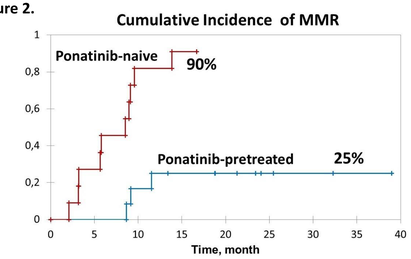
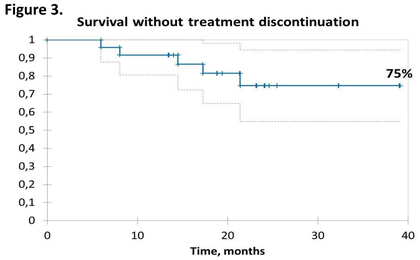


Figure 3.



Six (25%) of 24 patients had additional chromosomal abnormalities before asciminib, and 4 achieved MMR. Seven patients had a history of non-T315I BCR::ABL1 mutations, and 5 achieved MMR/MR4. (table 1)

Table 1. Characteristics of the patients with additional genetic events.

Pts №	ACAs	History of BCR::ABL1 mutations**	Response to asciminib	Loss of response	Additional therapy
1	-7, del 7p, del 16q;	T315I	CCyR	loss of CCyR	-
2*	der9, der17, der22	T315I, F317L	MMR	loss of CCyR	Bosutinib*
3*	der22	F359V, T315I	CCyR	loss of CCyR	Dasatinib*
4	trisomy 8	T315I, F317L	MMR	-	-
5	der22	T315I	MMR	loss of MMR	-
6	trisomy 8	S348L, T315I	MMR	-	-
7	-	G250E, T315I	MR4	-	-
8	-	E255K, T315I	MR4	-	-
9	-	H396R, F317V, T315I	CHR	-	-

**Two pts achieved CCyR/MMR on the asciminib monotherapy, then lost the responses. MR4 was achieved on combined therapy asciminib + bosutinib/dasatinib in these patients.*
*** Mutations, detected at asciminib start, are marked in blue.*
ACAs – additional chromosomal abnormalities, CCyR – complete cytogenetic response, MMR – major molecular response, MR4 – molecular response of 4 log reduction, CHR- complete hematological response.

CONCLUSIONS

Asciminib is effective in highly pre-treated CML-CP patients with T315I mutation and other genetic events, though some situations are still challenging for clinicians. The results were significantly better in patients without prior resistance to ponatinib. A 200 mg BID dose safety profile was favorable, with no evidence of severe toxicity. Overcoming the resistance by adding other therapy should be investigated.

REFERENCES

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2. Hughes, T.1,; Cortes, J. E.2; Réa, et al. X.19. P704: ASCIMINIB PROVIDES DURABLE MOLECULAR RESPONSES IN PATIENTS (PTS) WITH CHRONIC MYELOID LEUKEMIA IN CHRONIC PHASE (CML-CP) WITH THE T315I MUTATION: UPDATED EFFICACY AND SAFETY DATA FROM A PHASE I TRIAL. HemaSphere 6():p 599-600, June 2022.

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