1241 Safety and Efficacy Profile of Asciminib As Treatment in Chronic Myeloid Leukemia Patients after Several Tyrosine-Kinase Inhibitors Failure

Program: Oral and Poster Abstracts

Session: 632. Chronic Myeloid Leukemia: Therapy: Poster I

Hematology Disease Topics & Pathways:

Biological, CML, Diseases, Therapies, Adverse Events, Clinically relevant, Myeloid Malignancies, TKI

Saturday, December 5, 2020, 7:00 AM-3:30 PM

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Introduction: Asciminib is a new BCR-ABL1 inhibitor that differs from previous tyrosine kinase inhibitors (TKIs) in that it does not bind to the ATP-binding site of the kinase. Data from different clinical trials has shown an adequate safety and efficacy profile in chronic myeloid leukemia (CML) patients failing previous TKIs. However, no findings have been communicated in real life experience.
The aim of our study is to present first results of asciminib in CML patients failing previous TKIs under the current compassionate use program.

Methods: We retrospectively collected data from 31 patients treated with asciminib in 25 centers under compassionate use program. Data collecting was performed between October 2018 and June 2020. Patients baseline characteristics are shown in table 1. Most patients were heavily pretreated with 28 patients receiving 3 or more TKIs previous to asciminib. Eleven patients (35.5%) had been treated with ponatinib at some point throughout the disease. Twelve patients showed BCR-ABL1 mutations (only 1 case with T315I mutation). Switch to asciminib was due to intolerance in 22 patients and due to resistance in the remaining 9. Median dose of asciminib was 80mg per day (40mg every 12 hours). Treatment responses were evaluated according to European Leukemia Net recommendations. Data compilation and analysis were performed with REDCap Software and IBM SPSS (Version 25.0).

Results: Median time on asciminib for the entire cohort was 35 weeks. Regarding toxicities, 13 patients (42%) experienced mild extra-hematological side effects (grade 1-2) being the most frequent fatigue (19%), joint pain (16%) and nausea (9%). Four patients (12,9%) showed severe (grade 3-4) extra-hematological events: fatigue, hepatotoxicity, hypertension and pericardial effusion (1 patient each). Three patients (9,7%) suffered from grade 4 thrombocytopenia, 2 of them associating grade 4 neutropenia. All toxicities according to previous TKIs adverse effects as well as cross-intolerance data is shown in table 2. Dose reduction had to be carried out in 9 patients (29%), 7 of those with temporary treatment interruptions; most owing to hematological adverse effects. In terms of efficacy (Graph 1), probability of reaching or at least maintaining previous response was 100%, 61.3% and 35.5% for complete hematological response (CHR), complete cytogenetic response (CCyR) and major molecular response (MMR), respectively. Regarding probabilities to improve previous responses, rates of CCyR and MMR were, respectively, 22,2% (2/9) and 22,2% (2/9) for resistant patients and 44% (4/9) and 62,5%. (10/16) for intolerant group. Amid the 11 patients previously treated with ponatinib, 3 patients (27,3%) showed improvement of

response achieving at least MMR, 2 of them from the TKI-intolerant group and 1 from the TKI-resistant group. The median follow-up time was 40 weeks, after which 27 patients (87.1%) continued with asciminib. Treatment cessation happened in 2 patients due to progression to blastic phase and in 2 patients due to lack of efficacy. No patients discontinued due to side effects.

Conclusion: The data presented, similar to that known from clinical trials, supports the use of asciminib in routine clinical practice in CML patients failing to previous TKIs.

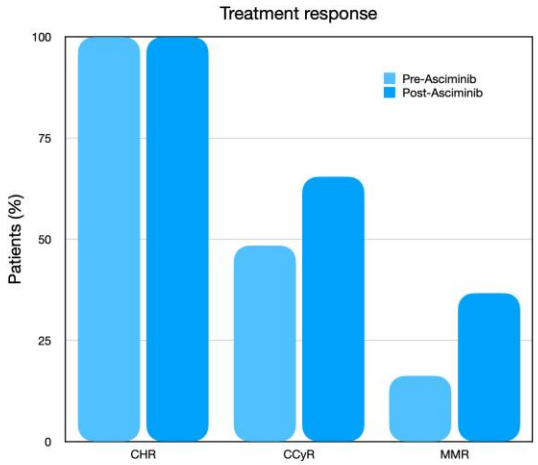
Table 1. Patients characteristics (n=31)

Age at data collection (years, median)	69
Age at diagnosis (years, median)	55
Female sex	64.5%
Time on asciminib (weeks, median)	35
Disease Stage	
Chronic Phase	96.8%
Accelerated Phase	3.2%
Blast Phase	0%
Sokal Risk	
Low	32.1%
Intermediate	35.7%
High	32.1%
TKI at diagnosis	
Imatinib	74.2%
Dasatinib	9.7%
Nilotinib	12.9%
Bosutinib	3.2%
Ponatinib	0 %
Prior use of ponatinib	35.5%
Mutations found	38.7%
E255K	9.67%
Exon 7	6.4%
T315I	3.2%
Status at data collection	
Asciminib continuation	83.9%
Suspension due to loss of efficacy	9.7%
Progression to blast phase	6.4%

Table 2. AEs pattern and Asciminib cross-intolerance in patients with CML Ph+.

AEs	Patients with any AE		Grade 1 or 2		Grade 3 or 4		Termination due to AE		Cross-intolerance
	Previous TKIs	Asciminib	Previous TKIs	Asciminib	Previous TKIs	Asciminib	Previous TKIs	Asciminib	
Fatigue	8	4	4	3	4	1	0	0	2
Joint pain	6	3	6	3	0	0	0	0	3
Diarrhea	13	0	9	0	4	0	2	0	0
Nausea	10	3	10	3	0	0	0	0	2
Appetite loss	4	1	4	1	0	0	0	0	1
Rash	5	1	2	1	3	0	1	0	0
Mucositis	1	0	0	0	1	0	0	0	0
Edema	11	0	8	0	3	0	1	0	0
Hypertension	1	1	1	0	0	1	0	0	0
Ischemic event	10	0	2	0	8	0	8	0	0
Pleural/pericardial effusion	8	2	0	1	8	1	6	0	1
Pneumonitis	1	0	0	0	1	0	1	0	0
Pulmonary hypertension	2	0	2	0	1	0	1	0	0
Elevated ALT/AST	3	0	1	0	2	0	0	0	0
Elevated cholestatic liver enzymes	0	1	0	0	0	1	0	0	0
Pancreatitis	4	0	1	0	3	0	0	0	0
Anemia	11	4	8	4	3	0	0	0	1
Thrombocytopenia	11	10	6	8	5	3	1	0	3
Neutropenia	8	3	3	2	5	2	0	0	1

AE: Adverse Effect. ALT: Alanine Aminotranferase. AST: Aspartate Transaminase.



Graph 1. Monitoring of response before and after switch to asciminib. CHR: Complete Haematological Response. CCyR: Complete Cytogenetic Response. MMR: Major Molecular Response.

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