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POSTER ABSTRACTS

632.CHRONIC MYELOID LEUKEMIA: CLINICAL AND EPIDEMIOLOGICAL

The Updated Results of Asciminib Managed-Access Program (MAP) in Patients with Chronic Myeloid Leukemia in Russia

Elena Kuzmina[1], Ekaterina Chelysheva, MD PhD[2], Elza Lomaia, MD PhD[3], Elena V Morozova[4], Oleg Shukhov, MD PhD[2], Anna Petrova, MD[5], Tamara Chitanava[6], Julia Vlasova[4], Evgenia Sbitiakova[6], Natalia Lazorko[6], Irina Nemchenko[2], Anastasiya Vitalievna Bykova, MD[2], Margarita Gurianova, MD[2], Alina Kokhno[2], Anna Turkina, MD[7]

[1] National Medical Research Center for Hematology, Moscow, Russian Federation (Russia), Moscow, Russia
[2] National Medical Research Center for Hematology, Moscow, Russian Federation (Russia), Moscow, Russian Federation
[3] Almazov National Medical Research Centre, St. Petersburg, Russian Federation
[4] Pavlov First Saint Petersburg State Medical University, Saint-Petersburg, Russian Federation
[5] National Medical Research Center for Hematology, Moscow, Russian Federation (Russia), Moscow, RUS
[6] Almazov National Medical Research Centre, Saint-Petersburg, Russian Federation
[7] National Medical Research Center for Hematology, Moscow, Russian Federation

Background: Therapy choice in chronic myeloid leukemia (CML) patients (pts) with ≥2 lines of tyrosine kinase inhibitors (TKIs) failure or in pts with T315I mutationis a relevant problem. Efficacy and good tolerability of a first-in-class BCR::ABL1 allosteric inhibitor Asciminib (ASC) in chronic phase (CP) CML pts were confirmed in clinical trials. The out-study world data of ASC use in Managed Access Program (MAP) is of particular interest.
Aim: to report the updated results of the ASC use within MAP in 3 clinical centers of Russia.
Methods : Adult (≥18 years) CML pts with the lack of efficacy or intolerance to ≥2 lines of TKIs or T315I-positive pts after ≥1 prior TKI were included into a MAP. Inclusion criteria for our analysis were: CML-CP, ASC therapy for >3 months (mo). Two dosing regimen were used: 40 mg BID in BCR::ABL1 ^{T315I}-negative pts (40BID group) and 200 mg BID in BCR::ABL1 ^{T315I}-positive pts (200BID group). Complete cytogenetic response (CCyR, equivalent of MR2 or *BCR::ABL1*≤1%), major molecular response (MMR) and deep molecular response (MR4) achievement was assessed by cumulative incidence function (CIF) with Gray's test for comparison. Survival analysis was performed by Kaplan-Meier method according to "intention-to-treat" principle.
Results: A total 82 pts received ASC in the MAP, 68 of them met the criteria for analysis (baseline characteristics are in table 1), while 14 were excluded. The median follow-up was 26 mo (range 4-49).
The 2-year overall survival was 93% and 83%, the progression free survival was 90% and 70% in 40BID and 200BID groups, respectively. In 40BID group 17/43 pts discontinued ASC: 2 progressed to AP/BP, 2 - for bone marrow transplantation (BMT), 13 - failure (3 pts died due to CML after ASC discontinuation). In 200BID group 12/25 pts discontinued ASC: 2 developed AP, 3 -BMT, 7 - failure (one pt died).
CIF of CCyR/MMR/MR4 by 24 mo was 58%/68%/19% in 40BID group and 65%/56%/32% in 200BID group. The achieved CCyR was preserved in 93% (14/15) and 77% (10/13) pts in 40BID and 200BID group, respectively. CIF of MMR in ponatinib-naïve pts was higher in both groups than in ponatinib-pretreated pts (picture).
Dose escalation to 80-100 mg BID in 8/43 pts of 40BID group (due to lack of efficacy) resulted in achieving MMR for 2/8 pts with no MMR before escalation. Dose reduction in two groups was done both for adverse events (AEs) grade 3-4 (n=8) and stable MR4,5. In 4 pts (200BID) with no AEs and having a stable MR4,5 for >1 year, no MR4,5 loss was observed after ASC dose reduction to 100 mg BID.
Subclone with emerging a new mutation was detected in 3 pts of 40BID group (A337T, G250A, T315I) while no new mutations were found in 200 mg BID group.
AEs associated with ASC have been identified in 27/43 pts and 13/25 pts in 40BID and 200BID group, respectively, with no significant difference in AE spectrum and frequency. Most common (≥5%) AEs in two groups were: thrombocytopenia (29%), neutropenia (18%), cholesterol high (13%), anemia (6%), skin rash (5%). AEs grade 3-4 were detected in 13 (30%) and 4 (16%) pts in 40BID and 200BID group, respectively, and mostly presented by hematologic/cytopenic AEs (24%). No pt discontinued ASC due to toxicity, no arterial occlusive AEs were observed.

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Conclusion: ASC shows effectiveness and good safety profile in pts after prior failure to TKIs and those with T315I mutation. The CIF of any response was higher in ponatinib-naive pts at any dose. Different mutational subclones evolution was observed, including emergence of myristoyl-site mutation in 1 pt. ASC half dose reduction was safe in pts with previous MR4,5 stable response.

Disclosures Chelysheva: *Novartis:* Consultancy, Speakers Bureau; *Pfizer:* Speakers Bureau. **Lomaia:** *Fusion Pharma:* Speakers Bureau; *Pfizer:* Other: Travel, accommodation, and expenses, Speakers Bureau; *Novartis:* Other: Travel, accommodation, and expenses, Speakers Bureau. **Morozova:** *Novartis:* Consultancy, Speakers Bureau; *Pfizer:* Speakers Bureau; *AMGen:* Speakers Bureau. **Shukhov:** *Novartis:* Consultancy, Speakers Bureau; *Pfizer:* Speakers Bureau; *Johnson & Johnson:* Speakers Bureau; *Sanofi:* Speakers Bureau. **Petrova:** *Novartis:* Speakers Bureau. **Vlasova:** *Novartis:* Speakers Bureau; *Pfizer:* Speakers Bureau. **Sbitiakova:** *AstraZeneca:* Speakers Bureau; *Novartis:* Speakers Bureau. **Kokhno:** *Novartis:* Speakers Bureau; *Bristol-Myers Squibb:* Speakers Bureau. **Turkina:** *Pfizer:* Other: Travel, accommodation expenses, Speakers Bureau; *Fusion Pharma:* Speakers Bureau; *Novartis:* Other: Travel, accommodation expenses, Speakers Bureau.

OffLabel Disclosure: Dose reduction of asciminib from 200 mg BID to 200 mg QOD in patients with stable deep molecular response

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		40 mg BID (n=43)	200 mg BID (n=25)
Age, Me (min-max)		53 (27-85)	49 (28-71)
Gender, female, n (%)		25 (58)	14 (56)
CML duration before asciminib, Me (min-max), years		8,2 (0,9-27,4)	5,8 (0,8-34,7)
No ACAs/hidden/variant, n (%)		37 (86)	18 (72)
ACAs*, n (%)		6 (14)	7 (28)
Number of TKIs before asciminib, n (%)	≤2	5 (12)	7 (28)
	3	10 (23)	8 (32)
	≥4	28 (65)	10 (40)
Mutations of *BCR::ABL1*, n (%)	T315I	1 (2)	24 (96)
	Other than T315I	8 (19)	1 (4)
Ponatinib-pretreated, n (%)		13 (30)	13 (52)
BCR::ABL1 level at asciminib start, n (%)	<1 %	8 (19)	4 (16)
	≥1 -<10%	7 (16)	6 (24)
	≥10 %	28 (65)	15 (60)
Best anytime *BCR::ABL1* level before asciminib, n (%)	<1 %	22 (51)	12 (48)
	≥1 -<10%	14 (33)	7 (28)
	≥10 %	7 (16)	6 (24)