Poster PS1588

✉ Andreas Hochhaus | Andreas.Hochhaus@med.uni-jena.de

Improved Patient-Reported Outcomes With Asciminib vs Investigator-Selected Tyrosine Kinase Inhibitors in Newly Diagnosed Chronic Myeloid Leukemia: ASC4FIRST Week 48 Analysis

Andreas Hochhaus,[1] Timothy P. Hughes,[2] Ghayas C. Issa,[3] Richard A. Larson,[4] Felice Bombaci,[5] Jianxiang Wang,[6] Dong-Wook Kim,[7] Dennis Dong Hwan Kim,[8] Jiri Mayer,[9] Yeow-Tee Goh,[10] Philipp le Coutre,[11] Inho Kim,[12] Gabriel Etienne,[13] Shruti Kapoor,[14] Tracey McCulloch,[15] Kamel Malek,[15] Denise D'Alessio,[14] Lillian Yau,[15] Naoto Takahashi,[16] Jorge E. Cortes[17]

[1]Hematology and Medical Oncology, Universitätsklinikum Jena, Jena, Germany; [2]South Australian Health and Medical Research Institute and University of Adelaide, Adelaide, SA, Australia; [3]University of Texas MD Anderson Cancer Center, Houston, USA; [4]University of Chicago, Chicago, IL, USA; [5]CML Patients Group, CML Advocates Network, Turin, Italy; [6]State Key Laboratory of Experimental Hematology, National Clinical Research Center for Blood Diseases, Institute of Hematology and Blood Diseases Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Tianjin, China; [7]Uijeongbu Eulji Medical Center, Geumo-dong, Uijeongbu-si, South Korea; [8]Princess Margaret Cancer Centre, University Health Network, University of Toronto, Toronto, QC, Canada; [9]Hematology and Oncology, University Hospital Brno, Brno, Czech Republic; [10]Singapore General Hospital, Singapore; [11]Charité-Universitätsmedizin Berlin, Berlin, Germany; [12]Seoul National University Hospital, Biomedical Research Institute, Cancer Research Institute, Seoul National University College of Medicine, Seoul, South Korea; [13]Institut Bergonié, Bordeaux, France; [14]Novartis Pharmaceuticals Corporation, East Hanover, NJ, USA; [15]Novartis Pharma AG, Basel, Switzerland; [16]Akita University, Akita City, Japan; [17]Georgia Cancer Center at Augusta University, Augusta, GA, USA.

CONCLUSIONS

- In the week 48 ASC4FIRST PRO analysis, asciminib was associated with improved HRQOL and reduced symptom burden compared with IS-TKIs, suggesting better tolerability with asciminib
  - Per the EORCTC QLQ-C30 and EORTC QLQ-CML24 questionnaires, more patients in the ASC^{IMA} arm compared with IS-TKI^{IMA} had improvements from baseline in functional scales, most symptoms, and overall HRQOL, and similar proportions of patients in the ASC^{2G} and IS-TKI^{2G} arms had improvements across aspects of QOL
  - The exploratory sensitivity analyses to evaluate the impact of missing baseline data and adjustment of the global health status/QOL domain in EORTC QLQ-C30, resulting in an additional response option, indicated no substantial impact on conclusions (data not shown)
  - Based on PRO-CTCAE, patients in the ASC^{IMA} and IS-TKI^{IMA} arms had fewer symptoms overall; symptoms were relatively less severe and had less interference with daily activities
  - More patients in the asciminib arm were not bothered by treatment side effects per FACT-GP5
  - A similar proportion of patients in the ASC^{IMA} and ASC^{2G} arms, compared with IS-TKI^{IMA} and IS-TKI^{2G}, reported no problems with anxiety/depression, mobility, pain/discomfort, self-care, and usual activities per EQ-5D-5L
- These results align with the overall trend in PROs observed with asciminib in the ASCEMBL clinical trial[11]
- Findings from the PROs week 48 analysis, along with the superior efficacy and remarkable safety and tolerability profile of asciminib in the ASC4FIRST primary and key secondary analyses, continue to support asciminib as a treatment of choice for newly diagnosed CML-CP

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This study is sponsored by Novartis Pharma AG. For more information, please refer to https://clinicaltrials.gov/study/NCT04971226
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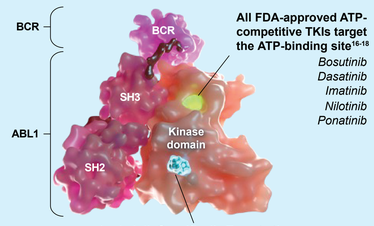
INTRODUCTION

- Up to 91% of patients with newly diagnosed CML-CP experience persistent low-grade AEs that can reduce HRQOL and treatment adherence, possibly resulting in treatment failure[1-8]
- CML treatment options that optimize efficacy without compromising safety and tolerability are needed
- ATP-competitive TKIs used in the treatment of CML-CP have broad specificity and can result in off-target effects; asciminib Specifically Targets the ABL Myristoyl Pocket (STAMP)[9] (**Figure 1**)
- In the primary (week 48) and secondary (week 96) analyses of ASC4FIRST (NCT04971226), a pivotal phase 3 trial of asciminib vs IS-TKIs in newly diagnosed CML-CP, asciminib demonstrated continued superior efficacy vs IS-TKIs and improved safety and tolerability[10,11]
- The superior efficacy of asciminib in the primary analysis resulted in the approval of asciminib for newly diagnosed CML-CP in the United States, China, Japan, Switzerland, and other countries worldwide[10,12]
- In the ASCEMBL study, patients with CML-CP resistant/intolerant to ≥2 TKIs experienced improvements in HRQOL and CML disease- and treatment-related symptoms relative to baseline when treated with asciminib compared with bosutinib[13]
- **Here we present the first report on PROs from the ASC4FIRST trial at the week 48 analysis cutoff (November 28, 2023) assessing the effect of asciminib vs IS-TKIs on patient-reported disease-related symptoms, functional scales of QOL, and HRQOL**

Figure 1. Asciminib: Designed to Improve Efficacy and Reduce Off-Target Effects vs Current ATP-Competitive TKIs[9,14,15]

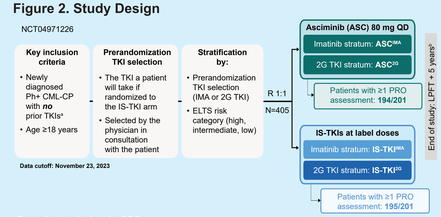


Adapted from Manley PW, et al. *Leuk Res*. 2020;98:106458. Copyright © 2020 Elsevier Ltd.[9]

METHODS

- ASC4FIRST is a phase III, randomized, multicenter, open-label trial of adults with newly diagnosed CML-CP wherein patients were randomly assigned 1:1 to receive asciminib 80 mg daily or an IS-TKI at approved doses for frontline therapy (imatinib 400 mg QD, nilotinib 300 mg BID, dasatinib 100 mg QD, or bosutinib 400 mg QD)[10] (**Figure 2**)
- PROs at week 48 were secondary and exploratory endpoints in ASC4FIRST
- The secondary PRO endpoints were changes in scores from baseline in the EORTC QLQ-C30 and EORTC QLQ-CML24 questionnaires[19,20]:
  - An increase in score (>5 points from baseline) for the functional scale represented improved level of functioning
  - An increase in score (>5 points from baseline) for the global health status/QOL represented improved quality of life
  - A decrease in score (>5 points from baseline) for a symptom scale/item represented improved symptom burden
- The exploratory endpoints were assessed longitudinally using PRO-CTCAE item scores, FACT-GP5, and the EQ-5D-5L instrument
- Patients completed PRO questionnaires on electronic devices (ePRO); the EORTC QLQ-C30 and EORTC QLQ-CML24 questionnaires were completed at baseline and within 2 days prior to scheduled study visits, and PRO-CTCAE and FACT-GP5 questionnaires were completed at baseline and weekly until week 24 or every 4 weeks until 12 weeks after end of treatment

Figure 2. Study Design



Secondary endpoints for PROs:
Change in scores from baseline in EORTC QLQ-C30 and EORTC QLQ-CML24

Exploratory endpoints for PROs:
PRO-CTCAE item scores,[c] FACT-GP5, and change in score from baseline per EQ-5D-5L

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[a]Either imatinib, bosutinib, dasatinib, or nilotinib is allowed for up to 2 weeks prior to randomization. Treatment with other TKIs prior to randomization was not permitted. [b]Patients will remain on study for 5 years after the last patient first dose unless they discontinue early due to treatment failure, disease progression, pregnancy, intolerance, or investigator or patient decision. [c]Select items analyzed were fatigue, vomiting, nausea, loose/watery stools, headache, arm/leg swelling, rash, itchy skin, and aching muscles.

RESULTS

- A total of 405 patients were randomized to receive either asciminib (n=201) or IS-TKIs (n=204)
- The median follow-up was 14.3 months in the ASC^{IMA} arm, 13.7 months in IS-TKI^{IMA}, 17.4 months in ASC^{2G}, and 17.0 months in IS-TKI^{2G}
- At the data cutoff, 194 patients receiving asciminib and 195 receiving IS-TKIs had ≥1 PRO assessment during the study (**Figure 2**)
- The completion rates of patients on therapy in both strata were generally balanced for all PRO assessments (**Table 1**)
  - Approximately 40% of patients who received asciminib and those who received an IS-TKI had baseline assessments taken after randomization or treatment; the baseline assessments for these patients were considered missing

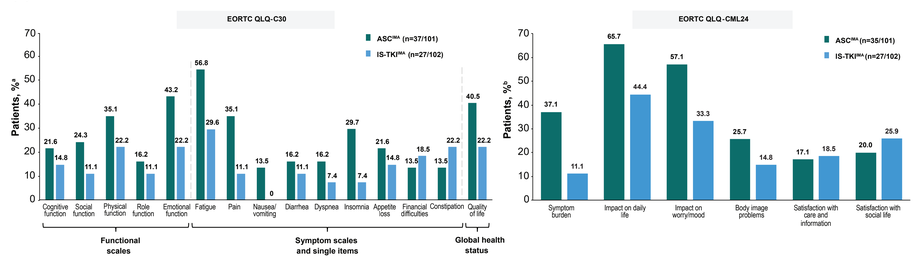
Table 1. Proportion of Patients With Baseline and Week 48 PRO Assessments

Randomized patients, n (%)	ASC^{IMA} (n=101)	IS-TKI^{IMA} (n=102)	ASC^{2G} (n=100)	IS-TKI^{2G} (n=102)
EORTC QLQ-C30	37 (36.6)	27 (26.5)	42 (42.0)	43 (42.2)
EORTC QLQ-CML24	35 (34.7)	27 (26.5)	42 (42.0)	39 (38.2)
PRO-CTCAE	29 (28.7)	28 (27.5)	35 (35.0)	35 (34.3)
FACT-GP5	28 (27.7)	28 (27.5)	35 (35.0)	34 (33.3)
EQ-5D-5L	35 (34.7)	27 (26.5)	41 (41.0)	38 (37.3)

- More patients in the ASC^{IMA} arm, compared with those in the IS-TKI^{IMA} arm, had improvements from baseline across all aspects of QOL, except for financial difficulties (13.5% vs 18.5%) and constipation (13.5% vs 22.2%) per the EORTC QLQ-C30 questionnaire and satisfaction with care and information (17.1% vs 18.5%) and social life (20.0% vs 25.9%) per EORTC QLQ-CML24 (**Figure 3A**)
- More patients (≥5% difference) in the ASC^{2G} arm compared with the IS-TKI^{2G} arm had improvements from baseline across 4 of 12 and 4 of 6 aspects of QOL per EORTC QLQ-C30 and EORTC QLQ-CML24, respectively (**Figure 3B**)
- AEs reported by patients in the ASC^{IMA} arm compared with those in the IS-TKI^{IMA} arm, and the ASC^{2G} arm compared with those in the IS-TKI^{2G} arm, were generally less frequent and less severe, with a lower impact on daily life, as measured by PRO-CTCAE (**Figure 4A-C**)
- A total of 73.6% of patients in the ASC^{IMA} arm and 39.1% in the IS-TKI^{IMA} arm, as well as 64.1% in the ASC^{2G} arm and 50.9% in the IS-TKI^{2G} arm, reported not being bothered at all by treatment-related side effects according to FACT-GP5 (**Figure 5**)
- Similar proportions of patients in the ASC^{IMA} and ASC^{2G} arms compared with IS-TKI^{IMA} and IS-TKI^{2G} arms reported no problems in all dimensions of the EQ-5D-5L system (**Table 2A**)
- There was a slight improvement in EQ-5D-5L VAS for patients in the ASC^{IMA} and ASC^{2G} arms and no improvement in the IS-TKI^{IMA} and IS-TKI^{2G} arms (**Table 2B**)

Figure 3. Improvements in EORTC QLQ-C30 Scores From Baseline to Week 48[a]

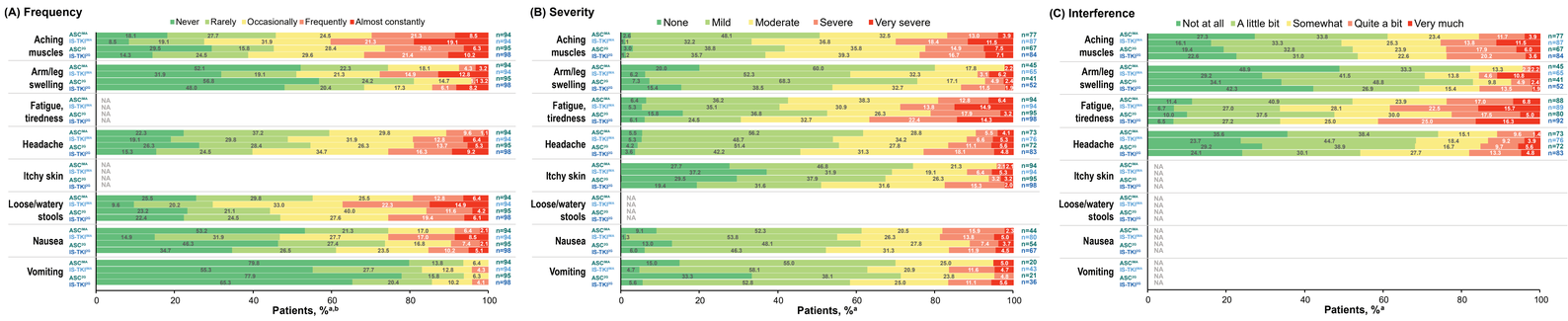
(A) ASC^{IMA} vs IS-TKI^{IMA}



(B) ASC^{2G} vs IS-TKI^{2G}

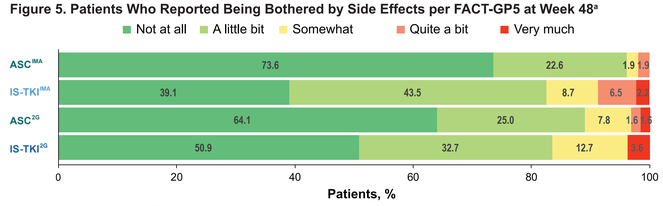
[a] In patients with assessments at baseline and at week 48 in ASC4FIRST. Improvements in EORTC QLQ-C30 items were defined as an increase in score of >5 points from baseline for functional scales and global health status/QOL and a decrease of >5 points from baseline for symptom scales.[19]
[b] In patients with assessments at baseline and at week 48 in ASC4FIRST. Improvements in EORTC QLQ-CML24 items were defined as an increase in score of >5 points from baseline.[20]

Figure 4. PRO-CTCAE Maximum Scores Among All Reported Postbaseline Values Up to Week 48



[a]Maximum is among all reported postbaseline values up to week 48 per patient. n is the number of patients with nonmissing values up to week 48 for the specific AE and attribute (frequency, interference and severity). [b] Presence of rash was reported by 58.5% of patients in the ASC^{IMA} arm and 60.6% in IS-TKI^{IMA}, as well as 64.2% in ASC^{2G} and 75.5% in IS-TKI^{2G}.

Figure 5. Patients Who Reported Being Bothered by Side Effects per FACT-GP5 at Week 48[a]



[a] In patients with nonmissing values at the specified time point for the attribute.

Table 2A. Patient Health Experiences per EQ-5D-5L Descriptive System at Week 48[a]

	ASC^{IMA}			IS-TKI^{IMA}			ASC^{2G}			IS-TKI^{2G}		
Randomized patients, %[a]	No problems	Slight-moderate problems	Severe-extreme problems	No problems	Slight-moderate problems	Severe-extreme problems	No problems	Slight-moderate problems	Severe-extreme problems	No problems	Slight-moderate problems	Severe-extreme problems
Anxiety/ depression	69.8	27.0	3.2	62.2	33.3	4.4	64.8	33.8	1.4	65.1	30.2	4.8
Mobility	73.0	22.2	4.8	68.9	31.1	0	87.3	11.3	1.4	87.3	11.1	1.6
Pain/ discomfort	63.5	36.5	0	51.1	46.7	2.2	70.4	25.4	4.2	69.8	30.2	0
Self-care	95.2	4.8	0	95.6	4.4	0	98.6	1.4	0	96.8	3.2	0
Usual activities	76.2	17.5	6.3	64.4	35.6	0	80.3	18.3	1.4	84.1	15.9	0

[a]Patients with nonmissing values at the specified time point for the AE and the attribute.

Table 2B. Change From Baseline for EQ-5D-5L VAS at Week 48

Randomized patients, %	ASC^{IMA}	IS-TKI^{IMA}	ASC^{2G}	IS-TKI^{2G}
n[a]	35	27	41	38
Mean (SD)	5.6 (17.0)	−2.1 (20.8)	4.7 (9.7)	−0.7 (17.9)
Median (range)	1.0 (−21.0 to 79.0)	−1.0 (−48.0 to 73.0)	2.0 (−17.0 to 40.0)	0 (−48.0 to 69.0)

[a]Patients who completed the questionnaire.

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Abbreviations

2G, second generation; ABL1, Abelson tyrosine kinase 1; AE, adverse event; ASC, asciminib; ATP, adenosine triphosphate; BCR, breakpoint cluster region; BID, twice daily; CML, chronic myeloid leukemia; CP, chronic phase; CTCAE, Common Terminology Criteria for Adverse Events; ELTS, EUTOS long-term survival score; EORTC, European Organisation for Research and Treatment of Cancer; EUTOS, European Treatment and Outcome Study; FACT, Functional Assessment of Cancer Therapy; FDA, Food and Drug Administration; HRQOL, health-related quality of life; IMA, imatinib; IS-TKI, investigator-selected tyrosine kinase inhibitor; LPFT, last patient first treatment; NA, not applicable; Ph+, Philadelphia chromosome positive; PRO, patient-reported outcome; QD, once daily; QOL, quality of life; R, randomized; SD, standard deviation; TKI, tyrosine kinase inhibitor; VAS, visual analog scale.