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Poster CML-754

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

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KEY FINDINGS & CONCLUSIONS

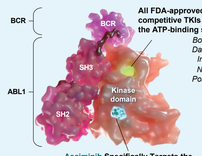
- In the week 48 ASC4FIRST PRO analysis, asciminib was associated with improved HRQOL and reduced symptom burden compared with IS-TKIs, suggesting better tolerability with asciminib
  - Per the EORTC QLQ-C30 and EORTC QLQ-CML24 questionnaires, more patients in the ASC^{MA} arm than the IS-TKI^{IMA} arm 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 the EORTC QLQ-C30, resulting in an additional response option, indicated no substantial impact on conclusions (data not shown)
  - Based on the PRO-CTCAE, patients in the ASC^{MA} 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 the FACT-GP5
  - A similar proportion of patients in the ASC^{MA} and ASC^{2G} arms, compared with the IS-TKI^{IMA} and IS-TKI^{2G} arms reported no problems with anxiety/depression, mobility, pain/discomfort, self-care, and usual activities per the EQ-5D-5L
- These results align with the overall trend in PROs observed with asciminib in the ASCEMBL clinical trial[1]
- Findings from the week 48 PRO 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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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[2-5]
- 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).[6] **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[7-11]
- 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[11,12]
- 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[10,14,15]

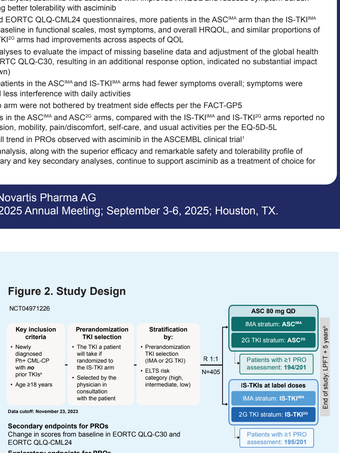


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METHODS

- ASC4FIRST is a phase 3, randomized, multicenter, open-label trial in adults with newly diagnosed CML-CP in which patients were randomly assigned 1:1 to receive asciminib 80 mg QD 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)[11] (**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) in the functional scale represented improved level of functioning
  - An increase in score (>5 points from baseline) in the global health status/QOL represented improved QOL
  - A decrease in score (>5 points from baseline) in a symptom scale/item represented improved symptom burden
- The exploratory endpoints were assessed longitudinally using the PRO-CTCAE, FACT-GP5, and EQ-5D-5L
- Patients completed PRO questionnaires on electronic devices (ePRO); the EORTC QLQ-C30 and EORTC QLQ-CML24 were completed at baseline and within 2 days prior to scheduled study visits, and the PRO-CTCAE and FACT-GP5 were completed at baseline and weekly until week 24 or every 4 weeks until 12 weeks after end of treatment

Figure 2. Study Design



From Hochhaus A, *et al. N Engl J Med.* 2024;391:885-898. Copyright © 2024 Massachusetts Medical Society. Reprinted with permission from Massachusetts Medical Society.
[a]Either imatinib, bosutinib, dasatinib, or nilotinib is allowed for ≤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

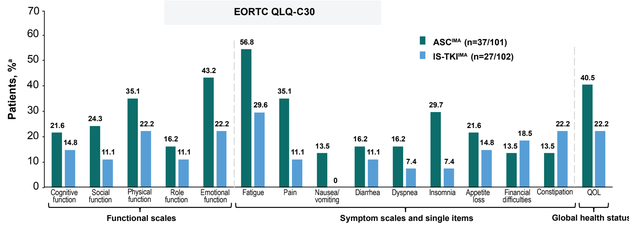
- A total of 405 patients were randomized to receive either asciminib (n=201) or IS-TKIs (n=204)
- The median follow-up was 14.3 months in the ASC^{MA} arm, 13.7 months in the IS-TKI^{IMA} arm, 17.4 months in the ASC^{2G} arm, and 17.0 months in the IS-TKI^{2G} arm
- At the data cutoff, 194 patients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

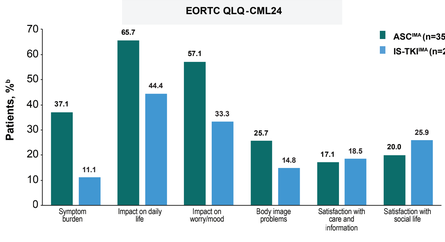
Table 1. Patients With Baseline and Week 48 PRO Assessments

Patients, n (%)	ASC^{MA} (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)

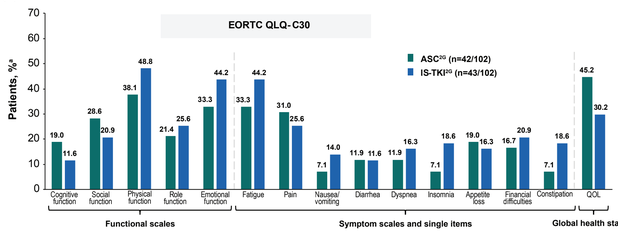
Figure 3. Improvements in EORTC QLQ-C30 Scores From Baseline to Week 48[a]

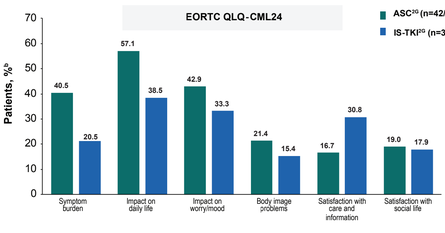
(A) ASC^{IMA} vs IS-TKI^{IMA}





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

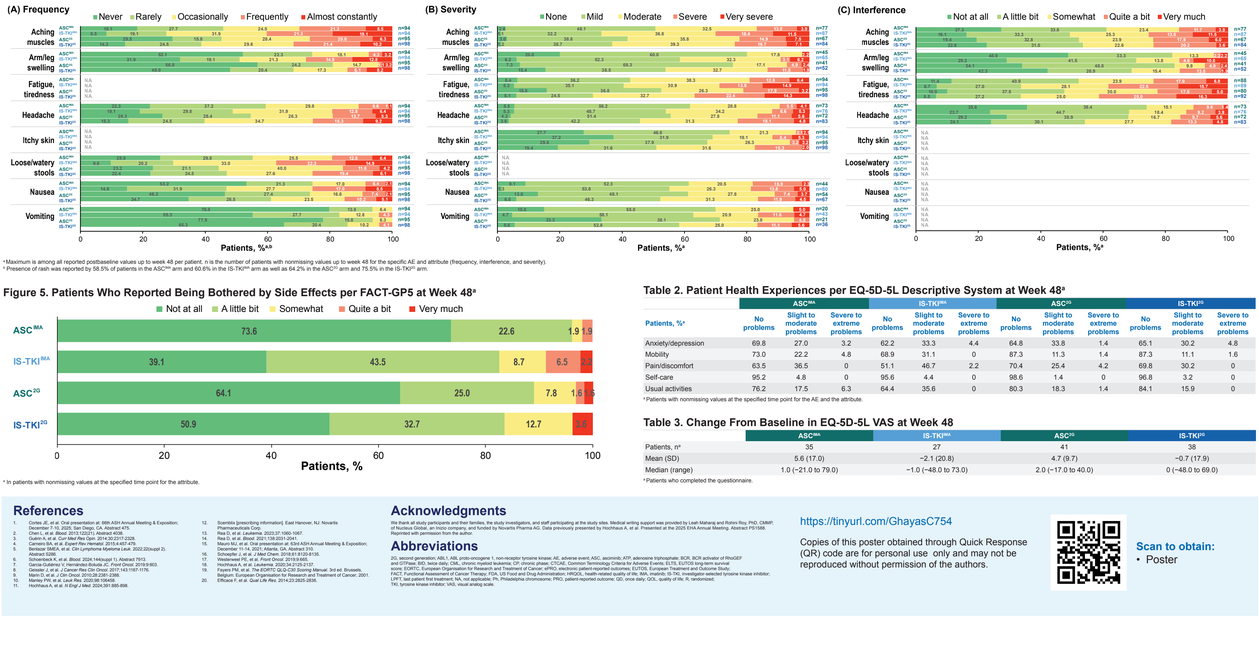




[a] In patients with assessments at baseline and in week 48 in ASC4FIRST. Improvements in EORTC QLQ-C30 items were defined as an increase in score of >5 points from baseline for functional scales and global health status/QOL and a decrease of >5 points from baseline for symptom scales.[19]
[b] In patients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

- More patients in the ASC^{MA} arm than 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 and satisfaction with care and information (17.1% vs 18.5%) and social life (20.0% vs 25.9%) per the EORTC QLQ-CML24 (**Figure 3A**)
- More patients (≥5% difference) in the ASC^{2G} arm than the IS-TKI^{2G} arm had improvements from baseline across 4 of 12 and 4 of 6 aspects of QOL per the EORTC QLQ-C30 and EORTC QLQ-CML24, respectively (**Figure 3B**)
- AEs reported by patients in the ASC^{MA} 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 the PRO-CTCAE (**Figure 4**)
- A total of 73.6% of patients in the ASC^{MA} 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 the FACT-GP5.(**Figure 5**)
- Similar proportions of patients in the ASC^{MA} and ASC^{2G} arms compared with the IS-TKI^{IMA} and IS-TKI^{2G} arms reported no problems in all dimensions of the EQ-5D-5L (**Table 2**)
- There was a slight improvement in EQ-5D-5L VAS in patients in the ASC^{MA} and ASC^{2G} arms and no improvement in the IS-TKI^{IMA} and IS-TKI^{2G} arms (**Table 3**)

Figure 4. PRO-CTCAE Maximum Scores in 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^{MA} arm and 60.6% in the IS-TKI^{IMA} arm as well as 64.2% in the ASC^{2G} arm and 75.5% in the IS-TKI^{2G} arm.

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

	ASC^{MA}			IS-TKI^{IMA}			ASC^{2G}			IS-TKI^{2G}		
Patients, %[a]	No problems	Slight to moderate problems	Severe to extreme problems	No problems	Slight to moderate problems	Severe to extreme problems	No problems	Slight to moderate problems	Severe to extreme problems	No problems	Slight to moderate problems	Severe to 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 3. Change From Baseline in EQ-5D-5L VAS at Week 48

	ASC^{MA}	IS-TKI^{IMA}	ASC^{2G}	IS-TKI^{2G}
Patients, 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, Abl proto-oncogene 1, non-receptor tyrosine kinase; AE, adverse event; ASC, asciminib; ATP, adenosine triphosphate; BCR, BCR activator of RhoGEF and GTPase; BID, twice daily; CML, chronic myeloid leukemia; CP, chronic phase; CTCAE, Common Terminology Criteria for Adverse Events; ELTS, ELTS5 long-term survival score; EORTC, European Organisation for Research and Treatment of Cancer; EQ-5D-5L, EuroQol 5-dimension 5-level; FACT-GP5, Functional Assessment of Cancer Therapy; FDA, US 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; PRO, patient-reported outcome; QD, once daily; QOL, quality of life; R, randomized; TKI, tyrosine kinase inhibitor; VAS, visual analog scale.

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