

Health care resource utilization with asciminib and bosutinib among patients with chronic myeloid leukemia in chronic phase previously treated with ≥ 2 tyrosine kinase inhibitors: results from the multicenter, open-label, Phase 3 ASCEMBL trial

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Background

- Chronic myeloid leukemia (CML) typically results from a reciprocal translocation between chromosomes 9 and 22, leading to the formation of a new abnormal (Philadelphia) chromosome encoding the BCR-ABL1 oncoprotein.¹
- The introduction of tyrosine kinase inhibitors (TKIs) has drastically improved prognosis for CML patients; however, there is still an unmet need for those who develop resistance and/or are intolerant to two or more of these drugs (i.e. third line and beyond).²
- Asciminib (ABL001), an agent Specifically Targeting the ABL Myristoyl Pocket (STAMP) to inhibit the enzymatic activity of BCR-ABL1, is currently being compared to bosutinib in ASCEMBL (NCT03106779), an international phase III open-label randomized controlled trial.³
- ASCEMBL met its primary endpoint, with 25.5% of patients randomized to asciminib achieving a major molecular response at 24 weeks compared to 13.2% of patients who received bosutinib; asciminib also demonstrated a favorable safety profile.³
- Beyond differences in efficacy and safety, it is also of interest to decision makers whether the clinical results may translate into differences in health care resource utilization (HCRU) between asciminib and bosutinib.

Objective

- To compare, using descriptive statistics, HCRU among patients with CML in chronic phase (CML-CP) who received asciminib or bosutinib after previously being treated with ≥ 2 TKIs in the ASCEMBL clinical trial.

Materials & Methods

- Adults with CML-CP who had previously been treated with ≥ 2 TKIs were enrolled in ASCEMBL. Patients were randomized in a 2:1 ratio to receive asciminib 40mg twice daily (n=157) or bosutinib 500mg once daily (n=76).
- Measure of resource utilization collected within the trial were:
 - Hospitalizations
 - Emergency room visits (<24 hours)
 - General practitioner visits
 - Specialist visits
 - Urgent care visits
- The reason for each visit (i.e. related to CML, adverse events [AEs] or other reasons) was collected, and for hospitalizations the number of days in ward, the type of ward (hospital unit), and discharge status were also captured.
- Resource utilization assessments were completed by investigators at each scheduled clinical trial visit; however, information with respect to the number of general practitioner, urgent care, specialist or emergency room visits was ascertained from patients.
- Descriptive analyses were performed, stratified by treatment received (asciminib or bosutinib):
 - The proportion of patients in each arm with any HCRU, overall and by category, was first calculated.
 - Median duration of exposure was then estimated for each treatment arm and used to calculate rates of resource use per patient-year on randomized treatment.
 - For each category, the frequency of HCRU was also summarized using descriptive statistics (mean, standard deviation, median, range) along with the distribution of reasons for visits (related to CML, AE, or other reason).
 - Finally, for hospitalizations, length of stay by ward type was summarized using descriptive statistics (mean, standard deviation, median, range).

Results

- As of the 25-May-2020 cut-off, the median duration of exposure was 43.4 and 29.2 weeks in the asciminib and bosutinib arms, respectively.
- One patient in the asciminib arm was excluded from the analysis due to having a different pattern of HCRU compared to other patients, which was for reasons other than CML.
- The proportions of patients with any HCRU as well as by category are presented in **Figure 1**.
 - Proportions were consistently higher for the bosutinib arm compared to the asciminib arm.
- Taking into account differences in exposure time also showed higher rates of HCRU per patient-year with bosutinib versus asciminib (**Figure 2**)
- The frequency of HCRU as well as reasons for visits are shown in **Table 1**.
 - Despite having a lower proportion of patients with any HCRU overall compared to bosutinib, on average patients treated with asciminib tended to utilize more resources, particularly general practitioner (mean 4.1 versus 1.0) and specialist visits (mean 4.1 versus 2.5); however, these differences were driven by the relatively longer time spent on treatment with asciminib versus bosutinib.
 - A higher proportion of total hospital and emergency room visits were due to AEs for bosutinib (35.3% and 75.0%) compared to asciminib (8.6% and 50.0%), but the reverse was observed for general practitioner and specialist visits, although differences were less pronounced.
- Lengths of stay for all hospitalizations and by ward type are summarized in **Table 2**.
 - Length of stay in hospital was also generally higher with bosutinib compared to asciminib, regardless of ward type (e.g. median number of days: 6.5 versus 6.0 in general wards, 19.0 versus 18.0 in intensive care units, and 12.0 versus 3.0 in other care units).

Figure 1: Healthcare resource utilization overall and by category while on randomized treatment

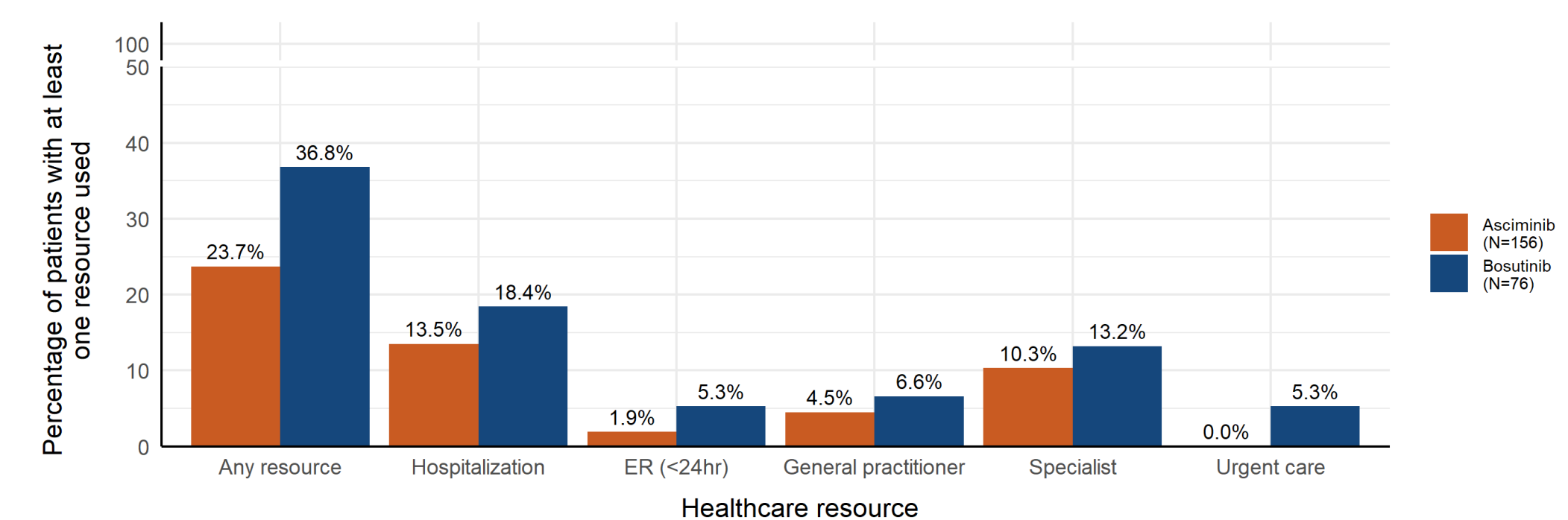
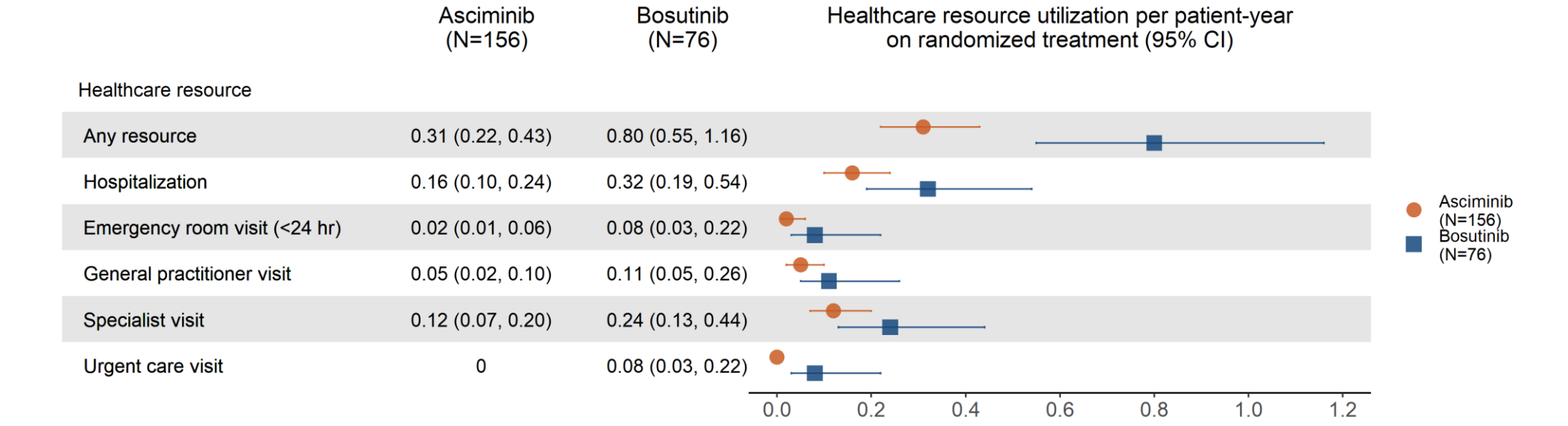


Figure 2: Rate of healthcare resource utilization per patient-year on randomized treatment



Abbreviations: CI, confidence interval; ER, emergency room.

Table 1: Frequency and reasons for healthcare resource utilization while on randomized treatment, by category

	Asciminib N=156	Bosutinib N=76
Hospitalizations		
Number of subjects with at least one hospitalization - n (%)	21 (13.5)	14 (18.4)
Frequency/duration of exposure – n (median, weeks)	35 (54.6)	17 (21.4)
Number per subject	Mean (SD) 1.7 (0.97) Median (range) 1.0 (1-4)	1.2 (0.58) 1.0 (1-3)
Reason - n (%)	AE related to CML therapy CML Other reason	6 (35.3) 0 11 (64.7)
Emergency room visits (<24 hours)		
Number of subjects with at least one emergency room visit (<24 hr) - n (%)	3 (1.9)	4 (5.3)
Frequency/duration of exposure – n (median, weeks)	4 (60.1)	4 (22.7)
Number per subject	Mean (SD) 1.3 (0.58) Median (range) 1.0 (1-2)	1.0 (0.00) 1.0 (1-1)
Reason for hospitalization - n (%)	AE related to CML therapy CML Other reason	3 (75.0) 0 1 (25.0)
General practitioner visits		
Number of subjects with at least one general practitioner visit - n (%)	7 (4.5)	5 (6.6)
Frequency/duration of exposure – n (median, weeks)	29 (54.6)	5 (69.1)
Number per subject	Mean (SD) 4.1 (6.59) Median (range) 2.0 (1-19)	1.0 (0.00) 1.0 (1-1)
Reason - n (%)	AE related to CML therapy CML Other reason	0 0 5 (100)
Specialist visits		
Number of subjects with at least one specialist visit - n (%)	16 (10.3)	10 (13.2)
Frequency/duration of exposure – n (median, weeks)	66 (57.4)	25 (50.9)
Number per subject	Mean (SD) 4.1 (3.77) Median (range) 3.5 (1-14)	2.5 (2.37) 1.0 (1-8)
Reason - n (%)	AE related to CML therapy CML Other reason	2 (8.0) 0 23 (92.0)
Urgent care visits		
Number of subjects with at least one urgent care visit - n (%)	0	4 (5.3)
Frequency/duration of exposure – n (median, weeks)	0 (–)	4 (24.1)
Number per subject	Mean (SD) -- Median (range) --	1.0 (0.00) 1.0 (1-1)
Reason - n (%)	AE related to CML therapy CML Other reason	2 (50.0) 0 4

Table 2: Length of stay by ward type

	Asciminib N=156	Bosutinib N=76
All hospitalizations		
Number of subjects with at least one hospitalization - n (%)	21 (13.5)	14 (18.4)
Length of stay	Mean (SD) 9.5 (10.74) Median (range) 5.0 (1-47)	10.7 (10.23) 7.0 (1-35)
Emergency room		
Number of subjects with a hospitalization spent in emergency room - n (%)	1 (0.6)	5 (6.6)
Hospitalizations with time spent in emergency room - n (%)	1 (2.9)	6 (35.3)
Length of stay	Mean (SD) 1.0 (NA) Median (range) 1.0 (1-1)	1.5 (1.22) 1.0 (1-4)
General ward		
Number of subjects with a hospitalization spent in general ward - n (%)	14 (9.0)	10 (13.2)
Hospitalizations with time spent in general ward - n (%)	25 (71.4)	12 (70.6)
Length of stay	Mean (SD) 9.4 (10.49) Median (range) 6.0 (1-47)	10.2 (9.15) 6.5 (2-32)
Intensive care unit		
Number of subjects with a hospitalization spent in intensive care unit - n (%)	2 (1.3)	2 (2.6)
Hospitalizations with time spent in intensive care unit - n (%)	2 (5.7)	2 (11.8)
Length of stay	Mean (SD) 18.0 (18.38) Median (range) 18.0 (5-31)	19.0 (22.63) 19.0 (3-35)
Other care unit		
Number of subjects with a hospitalization spent in other care unit - n (%)	5 (3.2)	1 (1.3)
Hospitalizations with time spent in other care unit - n (%)	7 (19.4)	1 (5.9)
Length of stay	Mean (SD) 7.3 (10.55) Median (range) 3.0 (2-31)	12.0 (NA) 12.0 (12-12)

Abbreviations: AE, adverse event; CML, chronic myeloid leukemia; SD, standard deviation.

Limitations

- The main limitation of this analysis was the short duration of follow-up over which HCRU may occurred; this led to a relatively small number of patients in both arms experiencing an "event" (i.e. having any form of HCRU), which makes it difficult to draw conclusions regarding any potential differences between treatments.
 - The small numbers of observations also meant the relative frequency of HCRU and length of stay in hospital were heavily influenced by select patients. For example, only two and one instances of hospitalization in patients treated with bosutinib resulted in stays in an intensive care unit and other care unit, respectively. Duration of exposure also differed between the arms, with patients on asciminib tending to be treated for longer, which provided more opportunity for HCRU compared to patients on bosutinib.
- Another limitation stemmed from the self-reported nature of much of the HCRU data collected within ASCEMBL.
 - During regular assessments, investigators relied on participants to accurately recall their general practitioner, urgent care, specialist and emergency room visits. This may have introduced bias in the event that, for example, instances of HCRU were incorrectly not classified as such by participants.
- Finally, patterns of HCRU as observed in the trial setting may not align with what will be seen in routine clinical practice.
 - There is a large body of literature on the limitations associated with the collection of HCRU in clinical trials.⁴ For example, clinical experience with patient management for a novel experimental therapy (e.g. asciminib) is less compared to an established standard of care (e.g. bosutinib), contributing to differences in patterns of HCRU in clinical trials which may not be observed once the former has become more widely established.

Conclusion

- These results suggest that HCRU may be lower for CML-CP patients treated with asciminib compared with bosutinib in terms of overall numbers of patients accessing services and length of stay in hospital.
- Additional follow-up from the ASCEMBL trial as well as future data from real world usage, pending regulatory approval, will be needed to validate these findings.

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