Treatment Response and Safety of Ponatinib and Asciminib in Patients with Chronic Myeloid Leukemia: A National Veterans Health Administration Analysis

U.S. Department of Veterans Affairs

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Introduction

- Patients with chronic myeloid leukemia (CML) resistant or intolerant to multiple tyrosine kinase inhibitors (TKIs) face limited treatment options.
- Ponatinib, a third-generation TKI, has demonstrated efficacy, particularly in patients with T315I mutation.
- Asciminib, a first-in-class STAMP (Specifically Targeting the ABL Myristoyl Pocket) inhibitor, binds to BCR-ABL1 kinase, preventing it from interacting with its natural substrate, ATP.
- Direct comparative data on the efficacy and safety of ponatinib versus asciminib in CML patients remain limited.

Objective

- This national VHA study comparatively evaluates the outcomes efficacy (response rate, survival) and safety of ponatinib versus ascinimib in the treatment of CML.

Methods

- **Retrospective cohort study** through VA Corporate Data Warehouse
- Adult patients **(≥18 years)** with chronic-phase chronic myeloid leukemia (CML-CP) treated with either ponatinib or asciminib, or both between **2012-2024**.
- Eligibility criteria:
  - Confirmed diagnosis of CML
  - Documented prior TKI resistance or intolerance
  - Availability of baseline and follow-up clinical data
- **74 patients** were included:
  - **Ponatinib: n = 41**
  - **Asciminib: n = 25**
  - **Ponatinib and asciminib: n = 8**
- Sociodemographic data, including age, sex, and comorbidities such as heart disease, diabetes, and hypertension, collected to assess baseline comparability.

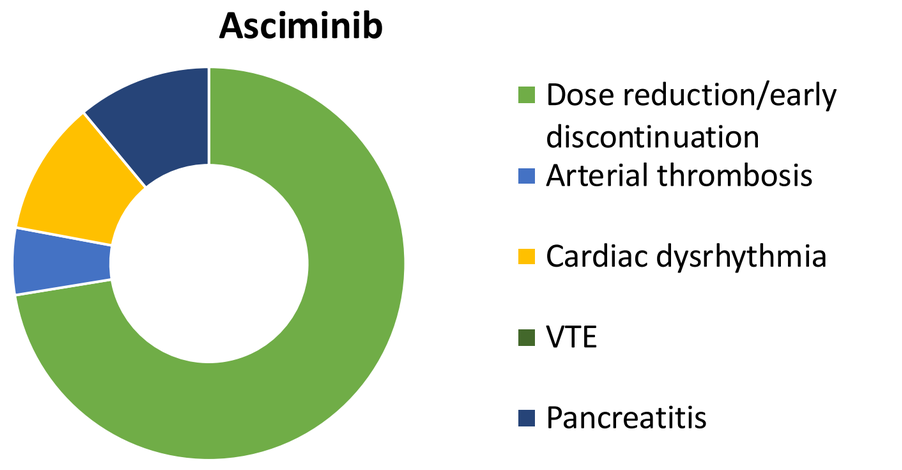
Results

Table 1. Baseline Characteristics of Patients Treated with Ponatinib or Asciminib

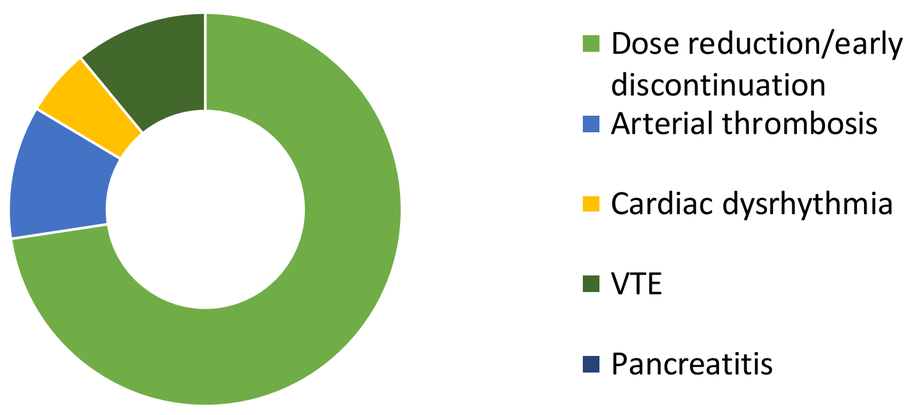
Characteristic	Ponatinib (n = 49)	Asciminib (n = 33)	Total Unique (N = 82)
Number of unique VA sites	38	25	63
Median age at therapy start, years (range)	67, 39 - 45	74, 49 - 90	72, 39 - 89
Male, %	90%	97%	93%
Race, % (n)			
White	65 (32)	73 (24)	68 (56)
Black or African American	18 (9)	18 (6)	18 (15)
Asian	2 (1)	0 (0)	1 (1)
Other	8 (4)	3 (1)	6 (5)
Unknown/Not reported	6 (3)	6 (2)	6 (5)
Ethnicity, % (n)			
Hispanic or Latino	12 (6)	6 (2)	10 (8)
Non-Hispanic	86 (42)	94 (31)	89 (73)
Unknown/Not reported	2 (1)	0 (0)	1 (1)
Social Deprivation Index (SDI)			
0–25	8	7	15
26–50	14	9	23
51–75	10	10	20
76–100	15	6	21
RUCA (rurality) breakdown, % (n)			
Rural (R)	24 (12)	42 (14)	32 (26)
Highly rural (H)	0 (1)	0 (1)	2 (1)
BMI > 25, %	63 (31)	73 (24)	67 (55)
Comorbidities, % (n)			
Hypertension or hyperlipidemia	78 (38)	85 (28)	80 (66)
Diabetes mellitus	39 (19)	45 (15)	41 (34)
History of smoking	29 (14)	36 (12)	32 (26)
Heart disease	29 (14)	52 (17)	38 (31)

Safety Profiles:

Asciminib



Ponatinib



Significant factors associated with Overall Survival (OS):

Factor	HR	CI	p-value
BMI (per unit increase)	0.94	0.89–0.995	0.046
Accelerated/ blast phase	3.29	1.58–6.90	0.0015
Hispanic vs. NHW	2.77	0.97–7.02	0.04

***Drug choice (asciminib vs ponatinib)**: Not associated with OS after adjusting for LOT and age

Factors associated with Progression-Free Survival (PFS):

Factor	HR	CI	p-value
BMI (per unit increase)	0.94	0.89–0.99	0.036
Accelerated/ blast phase	2.75	1.35–5.56	0.005
LOT therapy	1.40	1.02–1.93	0.037

***Choice of drug** was **not associated** with PFS: HR 0.95, 95% CI 0.44–2.15, p = 0.90

Molecular Response

- **MMR:** Choice of drug not associated (OR 1.57, 95% CI 0.42–6.37, p = 0.51)
- **MR5:** Ponatinib had higher rates (OR 3.74, 95% CI 1.10–14.3, p = 0.04)

Conclusions

- **Choice of drug (asciminib vs ponatinib) was not associated with OS, PFS, or MMR.**
- **Disease biology (accelerated/BP)** and **clinical factors** were primary drivers of survival outcomes.
- Ponatinib was associated with **higher MR5 rates**, while asciminib showed **comparable response at the MMR level**.
- Ponatinib carried risks of arterial/venous events, whereas asciminib was more often associated with pancreatitis and discontinuations.

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