Treatment-related costs of ponatinib and asciminib in adult patients with T315I-positive chronic-phase chronic myeloid leukemia (CP-CML) with resistance or intolerance to at least 2 prior kinase inhibitors in the United States

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Background

- Chronic myeloid leukemia (CML) is a rare form of leukemia with an incidence rate of 1.9 per 100,000 men and women per year and an estimated new 8930 cases in 2023[1]
- Approximately 7%–9% of patients with CML progress to third-line therapy, and ~2%–20% develop the T315I mutation[2,3]
- The T315I mutation can occur at any line of therapy and contributes to treatment resistance and poor survival[3-7]
- Ponatinib and asciminib are the only 2 tyrosine kinase inhibitors (TKIs) approved by the US Food and Drug Administration (FDA) for the treatment of T315I-positive CP-CML with resistance or intolerance to at least 2 prior TKIs[8,9]
- Access to these 2 therapies for patients with T315I is important to overcome treatment resistance in CP-CML

Objective

- To assess the treatment-related costs of ponatinib and asciminib in the treatment of T315I-positive CP-CML with resistance or intolerance to at least 2 prior TKIs (referred to as the target population hereafter) over a time horizon of 3 years from the payer perspective—commercial and Medicare—in the US

Methods

- A cost-of-treatment calculator was developed to determine the drug acquisition, monitoring, and adverse event (AE) management costs with ponatinib and asciminib over the 3-year time horizon of analysis
- The median treatment duration of each therapy in the target population was used to determine the percentage of patients who remained on treatment over time, thus accruing the treatment-related costs and was used to calculate treatment-specific constant weekly discontinuation rates using the exponential function shown below
  - Ponatinib's median treatment duration (140.5 weeks) was obtained from individual patient data in the PACE trial (NCT01207440), which informed ponatinib's prescribing information (PI) for the target population[10,11]
  - Asciminib's median treatment duration (108 weeks) was obtained from its PI[9]
  - Assuming a constant treatment discontinuation rate, the percentage of patients who remain on treatment over time is calculated with the following exponential function

$$\%\ \text{patients on treatment by week } t = e^{-\left[\frac{-ln\ (0.5)}{\text{Median treatment duration in weeks}}\right] \times t}$$

- Drug acquisition costs for the commercial perspective were obtained from RED BOOK® **(Table 1)** and were assumed to be the same for the Medicare perspective because ponatinib and asciminib are not included in Medicare Part B for reimbursement[12]

Table 1: Drug acquisition costs

	Ponatinib	Asciminib
Price per pack (WAC in USD)[12]	18,809.00	20,105.28
Pack size[12]	30 tablets	60 tablets
Concentration[12]	45 mg, 30 mg, 15 mg, 10 mg	40 mg, 20 mg
Dose[8,9]	Response-based dosing: 45 mg QD with reduction to 15 mg QD upon achievement of ≤1% *BCR::ABL1*^{IS}	200 twice daily
Drug acquisition cost per day,[a] USD	626.97	3350.88
Drug acquisition cost Per 30 days,[a] USD	18,809.00	100,526.40

[a]Calculated
Abbreviations: USD, US dollar; WAC, wholesale acquisition cost

- Healthcare resource utilization associated with disease management and routine monitoring was obtained from the PIs for ponatinib and asciminib **(Table 2)**[8,9]
- Unit costs of monitoring healthcare resources were based on Current Procedural terminology (CPT®) codes and obtained from public databases **(Table 2)**
  - For the commercial perspective, costs were based on the Practice Management Information Corporation (PMIC) 2023 Medical Fees Directory[13]
  - For the Medicare perspective, costs were based on the US Centers for Medicare & Medicaid Services 2023 clinical diagnostic laboratory fee schedule[14]

Table 2: Routine monitoring healthcare resource utilization and costs

	Frequency of healthcare resource utilization (every 12 months)		Unit cost		
	Ponatinib[8]	Asciminib[9]	CPT code	Commercial[13] (USD)	Medicare[14] (USD)
Complete blood count	15	15	85025	42.00	7.77
Complete metabolic panel	12	4	80053	74.00	10.56
Eye exam	4	0	92012	152.00	90.48
Serum lipase	14	12	81000	16.00	6.89

- Grade 3/4 AEs that occurred in ≥2% of patients who received ponatinib the PACE trial were included in this analysis, which led to the 31 AEs listed in **Table 3**.[10,11] For asciminib, these AE rates were obtained from its PI; however, the PI only reported AEs occurring in ≥10% of patients who received asciminib in study CABL001X2101 (NCT02081378)[9]
  - The inclusion criteria for AEs were considered conservative because they ignore AEs that would have a higher occurrence for asciminib and may therefore underestimate relative treatment AE-related costs in favor of asciminib
- AE costs were obtained from the 2020 Healthcare Cost and Utilization Project and inflated to 2023 for the commercial perspective[15] and from Medicare's fiscal year 2023 Acute Care Hospital Inpatient Prospective Payment System Fee Schedule for Medicaid **(Table 3)**[16]
- For each AE, the cost was estimated as the AE incidence rate multiplied by the corresponding cost of AE management; the total cost of all AEs was estimated for each therapy as the sum of the management costs of all AEs included for cost estimation

Table 3: Grade 3/4 AEs occurring in ≥5% of patients receiving ponatinib and asciminib and unit cost of managing AEs (per event)

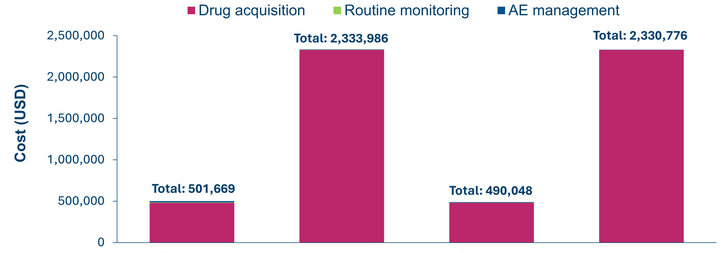
AE	Commercial[15]		Medicare[16]	
	CCSR Code	Mean Cost (USD)	DRG Code	Mean Cost (USD)
Abdominal pain	SYM006	9301.47	391-392	6319.82
Acute coronary syndrome	CIR009	27,070.49	311	4582.85
Acute kidney injury	DIG018	21,321.13	441-443	10,083.65
Anemia	BLD003	14,610.53	811-812	7571.50
Arthralgia	MUS010	9317.39	555-556	6302.84
Cardiac failure congestive	CIR019	15,533.57	291-293	8601.00
Cerebral artery stenosis	CIR023	14,839.70	061-063, 067, 068	13,105.33
Cerebral infarction	CIR020	18,630.53	061-066	9744.26
Constipation	DIG025	17,145.18	391-392	6319.82
Deep vein thrombosis	CIR026	26,497.57	299-301	8155.50
Diarrhea	SYM006	9301.47	391-392	6319.82
Dyspnea	SYM013	10,054.76	204	5552.10
Edema	RSP011	18,866.06	186-188	9042.60
Fatigue	NVS010	9361.95	947-948	6109.69
Headache	SYM007	14,609.47	102-103	6010.15
Hemorrhage	BLD006	19,528.10	377-379	8667.79
Hypertension	CIR007	8863.29	304-305	6000.46
Intermittent claudication	CIR026	26,497.57	299-301	8155.50
Leukocytosis	BLD007	14,610.53	814-816	9135.48
Musculoskeletal pain	MUS010	9317.39	555-556	6302.84
Noncardiac chest pain	CIR012	7879.78	313	4962.18
Pain in extremity	MUS010	9317.39	555-556	6302.84
Pancreatitis	DIG020	12,211.69	438-440	7215.00
Peripheral arterial occlusive disease	CIR026	26,497.57	299-301	8155.50
Peripheral artery stenosis	CIR026	26,497.57	299-301	8155.50
Peripheral artery occlusion	CIR026	26,497.57	299-301	8155.50
Pneumonia	RSP002	12,880.10	193-195	7672.45
Rash	SYM014	8843.13	606-607	7231.39
Sepsis	INF003	21,345.53	870-872	14,466.04
Systemic inflammatory response syndrome	INF003	21,345.53	864	5818.25
Vomiting	SYM004	8267.03	391-392	6319.82

Abbreviations: CCSR, Clinical Classifications Software Refined; DRG, Diagnosis Related Group

Results

- The results of these analysis are presented in **Figure 1**
  - From the commercial perspective, the total treatment-related costs over 3 years were $501,669 for ponatinib and $2,333,986 for asciminib
  - Drug acquisition costs were the main contributor: $480,755 and $2,327,904 for ponatinib and asciminib, respectively
  - Results were consistent from the Medicare perspective

Figure 1: Treatment-related costs over 3 years



	Commercial		Medicare	
	Ponatinib	Asciminib	Ponatinib	Asciminib
Drug acquisition	480,755	2,327,904	480,755	2,327,904
Routine monitoring	4934	2126	1473	459
AE management	15,981	3956	7819	2413

Limitations

- Time on treatment to accrue treatment-related costs over time was based on the median treatment duration reported for ponatinib and asciminib. Kaplan-Meier time-to-treatment discontinuation data could have provided more precise estimates of the percentages of patients who remain on treatment over time. However, because these data would be available only for ponatinib from the individual patient data of the PACE trial, the median treatment duration was used consistently for both comparators.
- Drug acquisition costs, which were the main contributor of the total treatment-related costs for ponatinib and asciminib, were the same for the commercial and Medicare perspectives as both oral products are not reimbursed by Medicare Part B and their acquisition cost is not available
- AE rates for ponatinib were obtained from the PACE trial. In the phase II Optimizing Ponatinib Treatment in CP-CML (OPTIC; NCT02467270) ongoing study evaluating the efficacy and safety of ponatinib, a novel response-based dose-reduction strategy starting at 45 mg and reducing to 15 mg upon achievement of clinical benefit (defined as *BCR::ABL1*^{IS} ≤1%) has demonstrated long-term manageable safety, including a low rate of exposure-adjusted arterial occlusive events rates and an optimal benefit-risk ratio.[17] Thus, the response-based strategy has the potential to reduce the cost of AE management associated with ponatinib and presented in this study.

Conclusions

- Over a 3-year horizon of analysis of the payer perspective in the US, total treatment-related costs for patients with T315I-positive CP-CML are nearly 5-fold lower with ponatinib versus asciminib
- The treatment-related costs associated with ponatinib and asciminib may be considered during treatment selection and formulary decision-making

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Disclosures

LH and **LER:** employment and stock ownership (Takeda)

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