Cost effectiveness of momelotinib vs other treatments for myelofibrosis from a US payer perspective

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Introduction

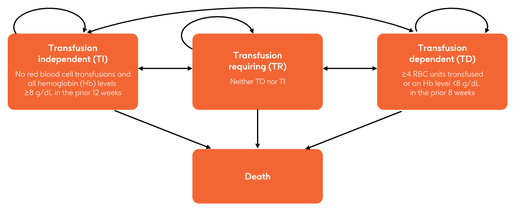
- Janus kinase (JAK) inhibitors are a class of medications that have shown clinical benefit in managing splenomegaly and constitutional symptoms in patients with myelofibrosis (MF)[1]
- A significant proportion of patients with MF develop anemia and become transfusion dependent, which not only is associated with negative quality of life and prognostic impacts but also increases costs and healthcare resource utilization[2,3]
- Momelotinib is a JAK1/JAK2/activin A receptor type I inhibitor recently approved in the US for the treatment of intermediate- or high-risk MF in adults with anemia[4]
  - Evidence in 3 phase 3 trials—SIMPLIFY-1, SIMPLIFY-2, and MOMENTUM—showed that momelotinib offers substantial anemia benefits in addition to effective management of splenomegaly and symptoms in patients with MF[5-7]
- Minimal literature exists evaluating the cost-effectiveness of myelofibrosis treatments in the US
  - Only 1 model has been published comparing ruxolitinib with best available therapy (BAT) in JAK inhibitor–naive patients, with an estimated incremental cost-effectiveness ratio (ICER) of $238,474, suggesting that ruxolitinib is not a cost-effective option vs BAT[8]
- This cost-effectiveness model (CEM) estimated the total costs of and quality-adjusted life-years (QALYs) with momelotinib, pacritinib, and BAT in treating JAK inhibitor–experienced patients with MF and anemia

Methods

Model Overview

- A Markov model was developed to compare costs (in 2023 US $) and QALYs over a 30-year time horizon among US adults with JAK inhibitor–experienced, intermediate- or high-risk MF with anemia (hemoglobin [Hb] <10 g/dL)
  - This population was aligned with that of the phase 3 SIMPLIFY-2 trial of momelotinib vs BAT (88.5% of the BAT arm received ruxolitinib; other BAT options included hydroxyurea, prednisone, erythropoiesis-stimulating agents, no therapy, anagrelide, darbepoetin alfa, aspirin, thalidomide, and dalteparin)[6]
- The model structure consisted of 4 health states, including transfusion status defined based on key secondary endpoints from SIMPLIFY-2 (**Figure 1**)
- The core model comparison was momelotinib vs BAT; in addition, given its relevance as a comparator in the JAK inhibitor–experienced setting in the US but limited public availability of the data needed to estimate transition probabilities, assumptions were made in order to facilitate exploratory comparisons vs pacritinib
  - Comparisons vs fedratinib were not included due to a lack of publicly available data and its greater use in the JAK inhibitor–naive setting
- The base case analysis was conducted from a US commercial payer perspective and assumed a lifetime time horizon of 30 years beginning at a starting average cohort age of 64.7 years (corresponding to a maximum age of 95 years) and a 3% discount rate for all costs and outcomes

Figure 1: **Markov Model Structure**



Model Assumptions

- Patients who discontinued treatment were assumed to receive BAT; patients on BAT were assumed not to discontinue treatment
- Overall survival was assumed not to vary by treatment; patients who were transfusion independent (TI) were assumed to have lower mortality than patients who were transfusion requiring (TR) or transfusion dependent (TD)
- As pacritinib-specific data were unavailable in the literature, additional assumptions related to model inputs for pacritinib are described in the following section

Model Inputs

Clinical

- Health-state transition probabilities were estimated for momelotinib and BAT from SIMPLIFY-2 and assumed to be constant after the trial period; health-state utility values were calculated from EQ-5D-5L questionnaire responses (US value set)
  - Pacritinib was assumed to have transition probabilities and efficacy (patients remaining in/entering the TI state) equal to those of BAT and utility values equal to the treatment-agnostic values from both arms of SIMPLIFY-2
- Adverse event (AE) rates and time to discontinuation for momelotinib and BAT were also based on SIMPLIFY-2; all grade 3/4 AEs that occurred in ≥5% of patients in either treatment arm were included
  - Pacritinib was assumed to have time to discontinuation equal to that of momelotinib; AE rates were derived from an indirect treatment comparison vs momelotinib[9]

Economic

- Treatment-agnostic healthcare resource utilization (HCRU)–related costs in each health state were derived from either of 2 claims analyses (1 Medicare, 1 commercial)[3,10] or via microcosting of resources
- Additional costs included drug acquisition and administration, subsequent treatment (assumed to be BAT), AEs, monitoring, transfusions, and terminal care; no indirect costs were included

Sensitivity Analyses

- One-way sensitivity analyses (OWSAs) and probabilistic sensitivity analyses (PSAs) were conducted to assess the robustness of results to changes in model parameters
  - Outcomes included total cost difference (Δ total cost) for and incremental net monetary benefit (iNMB) of momelotinib and pacritinib, each vs BAT, across a range of willingness-to-pay (WTP) thresholds ($50,000, $100,000, and $150,000 per QALY gained)
  - PSA simulations (5000) were used to generate mean total costs, QALYs, and ICERs vs BAT
- Additional details on model assumptions and inputs can be found by scanning the **QR code**

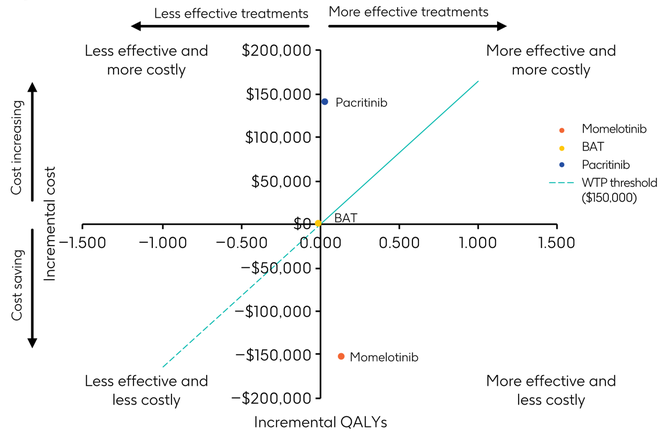
Discussion

- These results are specific to the JAK inhibitor–experienced population with anemia and may differ in the overall population and/or in the JAK inhibitor–naive setting
- This study is limited by data availability, as minimal data exist on transition probabilities and utility costs for pacritinib and other potential comparators; additional data are needed in order to calibrate the comparative efficacy data
- Potential sources of bias include sourcing for model inputs, as these were limited to available clinical trial data and indirect treatment comparisons, resulting in assumptions (such as efficacy and discontinuation in the pacritinib arm) that may be modified as more data become available
- Utility values were only available for the overall population and were assumed to apply to the anemic subpopulation, which may affect QALY calculations for each comparator

Results

- For the JAK inhibitor–experienced population, total per-patient costs, LYs, and QALYs in the base case Medicare cost scenario are summarized in **Figure 2** and **Table 1**; trends consistent with these Medicare scenario results also were observed in the base case commercial and microcosting scenarios (**QR code**)
  - Momelotinib was preferred over BAT in terms of costs ($165,938 savings) and QALYs (0.14 more); pacritinib was costlier than BAT ($132,948 more) but had incrementally more QALYs (0.04 more)
  - Momelotinib was in the lower right quadrant of the cost-effectiveness plane, suggesting that it is both cost saving and effective

Figure 2: **Cost-Effectiveness Plane (Medicare Cost Basis)**



The blue line indicates the WTP threshold ($150,000). Quadrants below the horizontal line are cost saving; quadrants to the right of the vertical line are clinically beneficial. Thus, therapies in the lower right quadrant are more effective and have decreased costs.

Table 1: **Base Case Results (Medicare Cost Basis)**

Comparator	Total costs	Total LYs	Total QALYs	Δ Total cost	Δ QALYs	iNMB[a]
Momelotinib	$881,223	2.90	2.210	−$165,938	0.144	$187,571
BAT	$1,047,161	2.83	2.066	0 (reference)	0	0
Pacritinib	$1,180,108	2.83	2.106	$132,948	0.040	−$126,964

[a] iNMB was calculated at a WTP threshold of $150,000 as: "(Δ QALYs * 150,000) − Δ Total cost."

- In OWSAs of momelotinib vs BAT, Δ total cost and iNMB were most sensitive to costs of ruxolitinib, the proportion of patients receiving subsequent ruxolitinib treatment, and costs of momelotinib (**Figure 3**)
  - Total cost differences for momelotinib ranged from $266,095 to $65,781 less than BAT, while iNMBs ranged from $87,414 to $287,727
- In OWSAs and iNMB analyses of pacritinib vs BAT, Δ total cost and iNMB were most sensitive to costs of pacritinib and ruxolitinib, followed by the proportion of patients receiving subsequent ruxolitinib treatment (**Figure 4**)

Figure 3: **OWSAs of Momelotinib (Medicare Cost Basis): (A) Δ Total Cost vs BAT and (B) iNMB vs BAT**

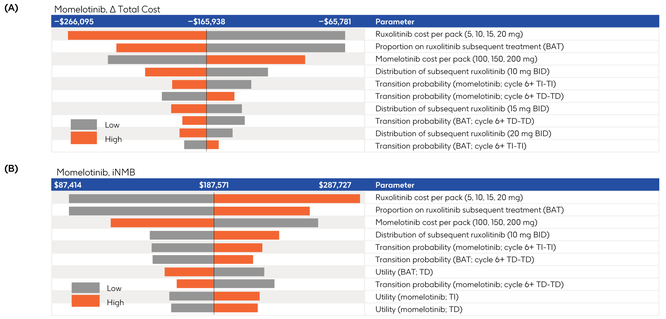
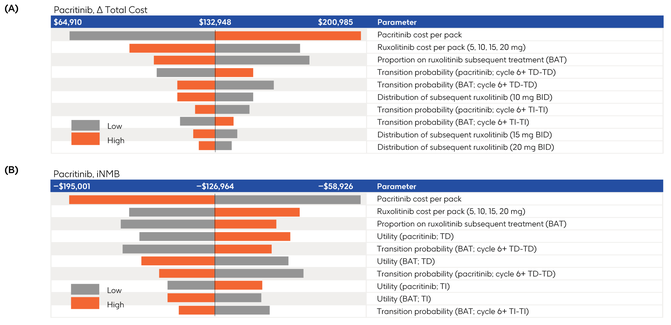


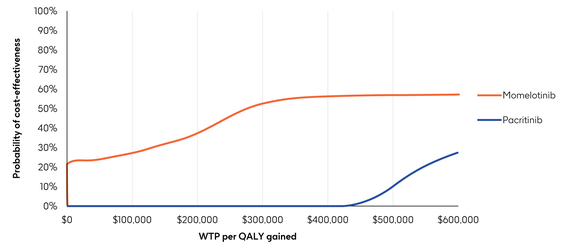
Figure 4: **OWSAs of Pacritinib (Medicare Cost Basis): (A) Δ Total Cost vs BAT and (B) iNMB vs BAT**



- PSAs were generally aligned with deterministic results, demonstrating cost-effectiveness probabilities of momelotinib across all WTP thresholds; pacritinib did not achieve cost-effectiveness until the WTP threshold was ≥$401,000 (**Figure 5**)

WTP threshold of $50,000 per QALY gained	WTP threshold of $100,000 per QALY gained	WTP threshold of $150,000 per QALY gained
Probability of momelotinib cost-effectiveness: 24.2%	Probability of momelotinib cost-effectiveness: 27.6%	Probability of momelotinib cost-effectiveness: 32.2%

Figure 5: **Cost-Effectiveness Acceptability Curves**

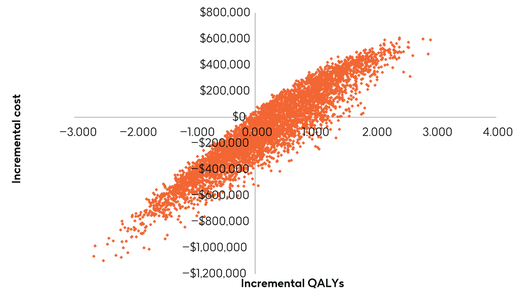


- PSAs of momelotinib showed mean total costs of $820,228 and mean total QALYs of 1.944, with mean incremental savings vs BAT of $104,909 and mean incremental QALYs of 0.167 (**Table 2**)
  - In contrast, pacritinib was associated with mean total costs of $1,058,420 and mean total QALYs of 1.821, resulting in mean incremental costs and QALYs of $133,283 and 0.044, respectively, relative to BAT (**Table 2**)
- The ICERs for momelotinib vs BAT from each PSA simulation are shown in the cost-effectiveness cloud (**Figure 6**; each point represents one simulation), illustrating the impact of varying model parameters to account for uncertainty on the results

Table 2: **PSA Results**

	Total costs and QALYs vs BAT		Incremental costs and QALYs vs BAT	
	Mean	95% CI	Mean	95% CI
Momelotinib				
Total costs	$820,228	$565,637-$1,047,199	−$104,909	−$677,663 to $442,660
Total QALYs	1.944	0.883-3.136	0.167	−1.540 to 1.890
Pacritinib				
Total costs	$1,058,420	$573,936-$1,547,935	$133,283	−$608,756 to $852,611
Total QALYs	1.821	0.688-3.050	0.044	−1.732 to 1.806

Figure 6: **Cost-Effectiveness Cloud vs BAT**



Conclusions

- These results suggest that momelotinib is cost-effective for treating JAK inhibitor–experienced patients with MF and anemia compared with BAT
  - Momelotinib was associated with lower costs and increased QALYs
  - Total cost difference was most sensitive to ruxolitinib costs when ruxolitinib was used as part of a BAT regimen, with momelotinib costing at least $65,781 less than BAT
- This study also suggests that momelotinib may be more cost-effective than pacritinib, given the higher costs and minimal QALY gain with pacritinib vs BAT, although this comparison should be considered exploratory given the model assumptions required for pacritinib
- This analysis represents the first US-based cost-effectiveness study focusing on momelotinib and pacritinib vs BAT in a JAK inhibitor–experienced population, complementing existing clinical trial results and supporting the use of momelotinib as a cost-effective option in this population

Abbreviations

AE, adverse event; BAT, best available therapy; CEM, cost-effectiveness model; Hb, hemoglobin; HCRU, healthcare resource utilization; ICER, incremental cost-effectiveness ratio; iNMB, incremental net monetary benefit; JAK, Janus kinase; MF, myelofibrosis; OWSA, one-way sensitivity analysis; PSA, probabilistic sensitivity analysis; QALY, quality-adjusted life-year; RBC, red blood cell; TD, transfusion dependent; TI, transfusion independent; TR, transfusion requiring; WTP, willingness-to-pay.

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Digital poster

Supplemental data

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