

Cost of Adverse Events with the Bruton Tyrosine Kinase Inhibitors Ibrutinib and Acalabrutinib in the Treatment of Relapsed/Refractory Chronic Lymphocytic Leukaemia in Brazil

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Why did we perform this research?



- Bruton tyrosine kinase inhibitors (BTKis) are established as first-line therapy and for relapsed/refractory chronic lymphocytic leukaemia (R/R CLL),^{1,2} a typically incurable malignancy that can require long-term treatment³
- Second-generation BTKis, such as acalabrutinib, have reduced off-target effects compared with the first-generation BTKi, ibrutinib⁴
- **To establish the financial implications of these clinical differences, this study assessed the cost of managing adverse events (AEs) with acalabrutinib versus ibrutinib in R/R-CLL in the Brazilian private healthcare context**

Summary

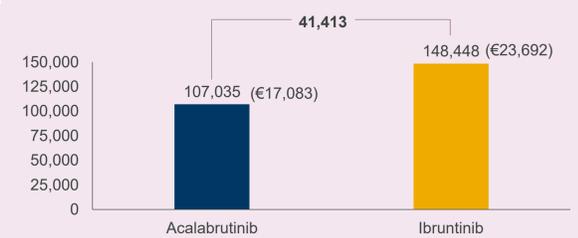


The ELEVATE-RR study⁴ found acalabrutinib to be better tolerated with similar efficacy to ibrutinib in previously treated patients with CLL

The adverse event rates reported in ELEVATE-RR⁴ were combined with available cost data to estimate the financial impact on the private healthcare system in Brazil



Results demonstrated savings with acalabrutinib versus ibrutinib (100 patients)



Key takeaways

- Observed differences in the AE profile of ibrutinib and acalabrutinib can translate into differences in healthcare expenditure from the Brazilian private healthcare perspective
- These benefits should be considered alongside related advantages, particularly reduced discontinuation and longer treatment duration^{4,5}

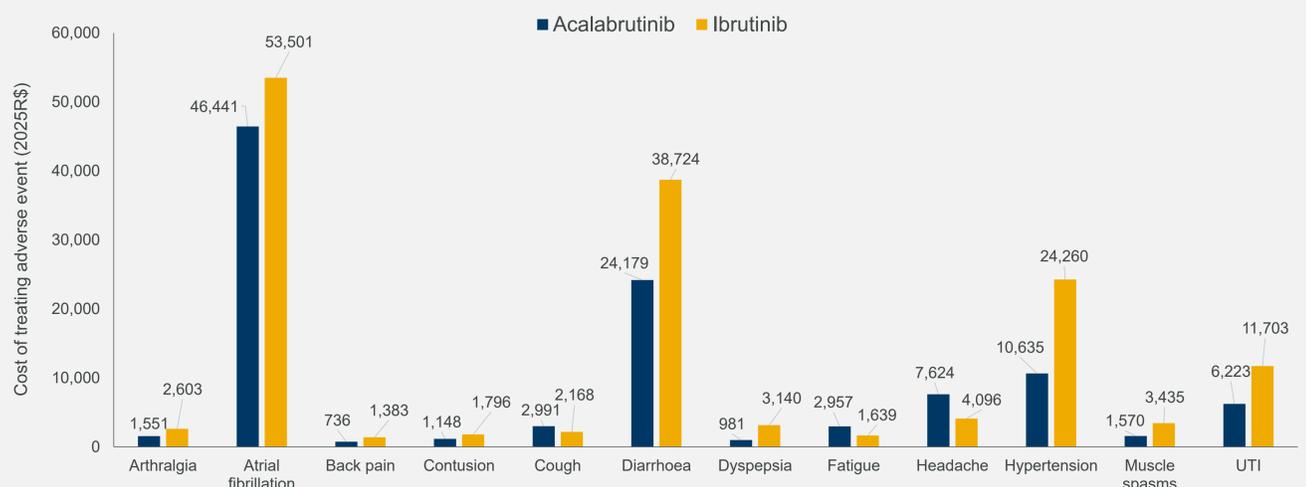
What did we find?

- Considering a population of 100 patients, the total cost of included adverse events was R\$107,035 (€17,083) with acalabrutinib R\$148,448 (€23,692) with ibrutinib a cost-saving of R\$41,413 (€6,610) in favour of acalabrutinib (Table 1, Figure 1)
- These differences were primarily driven by the costs of atrial fibrillation, diarrhoea, hypertension and urinary tract infection (Figure 1)
- Cost savings with acalabrutinib were evident when grade ≤ 2 (R\$28,306 [€4,518]) and grade ≥ 3 adverse events (R\$13,107 [\$2,092]) were considered separately (Table 1)

Table 1. Costs of management according to grade of adverse event (100 patients)

| AEs considered | Cost with acalabrutinib (2025 R\$) | Cost with ibrutinib (2025 R\$) | Incremental cost (2025 R\$) |
|-----------------|------------------------------------|--------------------------------|-----------------------------|
| Grade ≥ 3 | 54,883.85 | 67,991.21 | 13,107.36 |
| Grades ≤ 2 | 52,151.51 | 80,457.17 | 28,305.66 |
| All grades | 107,035.36 | 148,448.38 | 41,413.02 |

Figure 1. Estimated costs per 100 patients



How did we perform this research?

Model inputs – adverse event rates

- ELEVATE-RR, a phase III, randomised, multicenter, open-label, non-inferiority study assessed the efficacy and tolerability of acalabrutinib and ibrutinib in patients with previously treated RR CLL⁴
 - The study reported rates of adverse events that occurred in $\geq 10\%$ (any grade) or $\geq 5\%$ (grade ≥ 3) of patients in either treatment arm⁴
 - Median treatment exposure was 38.3 months with acalabrutinib and 35.5 months with ibrutinib

Our analysis included those adverse events for which a statistically significant difference between arms was reported for all adverse events or grade ≥ 3 adverse events (Table 2)

Model inputs – costs

- The cost of treating adverse events was estimated using a micro costing approach
 - Expected healthcare utilisation to treat a particular adverse event was identified and validated with clinical experts (this included consideration of medical appointments/consultations, hospital stay, investigational procedures/tests and clinical intervention)

- Costs associated with these procedures were extracted from available Brazilian data^{6–9} (Table 3)
- All costs were uplifted to 2025 R\$¹⁰

Limitations

- Definitive AE costs are lacking in Brazil and costs of management may vary across different hospitals
- Rates of adverse events observed in clinical trials may not reflect rates encountered in clinical practice

Table 2. Frequency of included adverse events

| Adverse event | Rate all severities of adverse events | | Rate grade ≥ 3 adverse events | | Rate grade ≤ 2 adverse events | |
|-------------------------|---------------------------------------|-----------|------------------------------------|-----------|------------------------------------|-----------|
| | Acalabrutinib | Ibrutinib | Acalabrutinib | Ibrutinib | Acalabrutinib | Ibrutinib |
| Arthralgia | 15.8% | 22.8% | 0.0% | 0.8% | 15.8% | 22.0% |
| Atrial fibrillation | 9.0% | 15.6% | 4.5% | 3.4% | 4.5% | 12.2% |
| Back pain | 7.5% | 12.9% | 0.0% | 0.8% | 7.5% | 12.1% |
| Contusion | 11.7% | 18.3% | 0.0% | 0.4% | 11.7% | 17.9% |
| Cough | 28.9% | 21.3% | 0.8% | 0.4% | 28.1% | 20.9% |
| Diarrhoea | 34.6% | 46.0% | 1.1% | 4.9% | 33.5% | 41.1% |
| Dyspepsia | 10.0% | 32.0% | 0.0% | 0.0% | 10.0% | 32.0% |
| Fatigue | 20.3% | 16.7% | 3.4% | 0.0% | 16.9% | 16.7% |
| Headache | 34.6% | 20.2% | 1.5% | 0.0% | 33.1% | 20.2% |
| Hypertension | 8.6% | 22.8% | 4.1% | 8.7% | 4.5% | 14.1% |
| Muscle spasms | 16.0% | 35.0% | 0.0% | 0.8% | 16.0% | 34.2% |
| Urinary tract infection | 8.3% | 13.7% | 1.1% | 2.3% | 7.2% | 11.4% |

Table 3. Costs of treating adverse events by severity

| Adverse event | Cost of treatment (2025 R\$) | |
|-------------------------|------------------------------|----------------|
| | Grade ≥ 3 | Grade ≤ 2 |
| Arthralgia | 555.27 | 98.14 |
| Atrial fibrillation | 8,228.03 | 2,092.27 |
| Back pain | 244.31 | 98.14 |
| Contusion | 98.14 | 98.14 |
| Cough | 291.62 | 98.14 |
| Diarrhoea | 2,551.85 | 637.96 |
| Dyspepsia | 98.14 | 98.14 |
| Fatigue | 381.83 | 98.14 |
| Headache | 608.27 | 202.76 |
| Hypertension | 2,185.42 | 372.11 |
| Muscle spasms | 98.14 | 98.14 |
| Urinary tract infection | 3,315.04 | 357.78 |

What are the implications for payors?

- Observed differences in the AE profile of first- and second-generation BTKis can translate into quantifiable differences in healthcare expenditure
- These costs should be considered in decisions regarding reimbursement/funding of treatments for CLL

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