Erasmus School of Health Policy & Management

EE398

Cost-Utility Analysis and Budget Impact Analysis for Pirtobrutinib versus Idelalisib plus Rituximab as Third-Line Treatment in Relapsed or Refractory Chronic Lymphocytic Leukaemia Patients in the Netherlands

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At the current list price, pirtobrutinib is not cost-effective versus IdelaR in the Netherlands (ICER €262,702/QALY); a 45% price reduction is needed to reach €80,000/QALY threshold

Background

- Chronic lymphocytic leukaemia (CLL) is the most common type of leukaemia in the Netherlands, with 1,219 new cases in 2025.[1]
- After relapse on or after a covalent BTK inhibitor (cBTKi), median overall survival falls to 11-29 months.[2] Idelalisib + rituximab (IdelaR) is the Dutch standard of care.[3]
- Pirtobrutinib, a non-covalent BTKi, prolonged PFS versus investigator's choice (IdelaR or BR) in the phase 3 BRUIN CLL-321 trial (median 14.0 vs 8.7 months).[4]
- Pirtobrutinib is in the Dutch *sluis* (lock) for expensive medicines; ZIN's assessment is ongoing (advice expected autumn 2026).[5] No Dutch economic evaluation has been published.

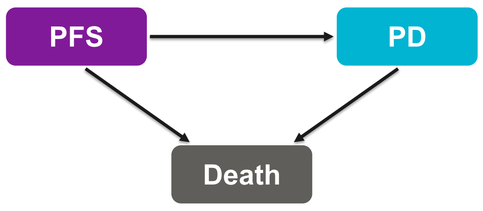
Objective

To assess the cost-utility and 3-year budget impact of pirtobrutinib versus IdelaR in R/R CLL after cBTKi from a societal perspective in the Netherlands, and the price at which pirtobrutinib would be cost-effective.

Methods

Table 1: Model inputs and sources

Parameter	Base case	Source
Model	3-state partitioned survival model, 28-day cycles, initial cohort of 1,000 patients	-
Horizon	15 years (lifetime)	-
Perspective	Dutch setting, societal perspective, including unrelated future medical costs	ZIN 2024[6]
Discounting	Costs 3% per annum, effects 1.5% per annum	ZIN 2024[6]
Survival data	Digitised KM curves, pseudo-IPD, 7 distributions fitted	BRUIN[4], Hoyle - Henley[7]
Selected curves	PFS: Gamma (pirtobrutinib), Gompertz (IdelaR), OS: Weibull (pirtobrutinib)	AIC, visual fit
Costs	Drugs, administration, monitoring, AEs, BSC, end of life, societal (€ 2026)	Kompas[8], Costing manual[9]
Utilities	PFS 0.85, PD 0.67, disutilities for 6 grade ≥3 AEs	References[10-12]
Analyses	DSA, PSA (1,000 iterations), 8 scenarios, EVPI, 3-year BIA (200 patients/year)	ZIN 2024[6]



Crossover adjustment: 76% of comparator-arm patients with progression crossed over to pirtobrutinib, inflating comparator OS.
IdelaR OS was therefore derived from pirtobrutinib OS using the trial-reported IPCW-adjusted HR of 0.87 (95% CI 0.51-1.50).[4]

Results

Pirtobrutinib costs €262,702 per QALY gained

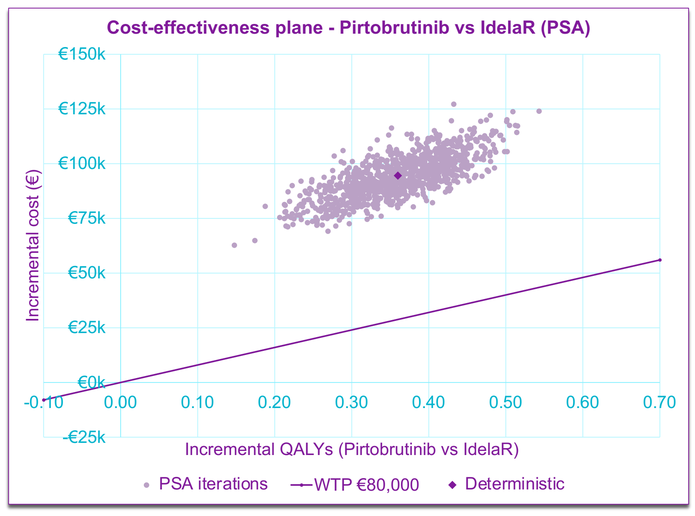
Table 2: Base-case results per patient (15 years)

	Costs	QALYs	LYs
Pirtobrutinib	€306,907	2.66	3.62
IdelaR	€212,322	2.30	3.24
Incremental	€94,586	0.36	0.39

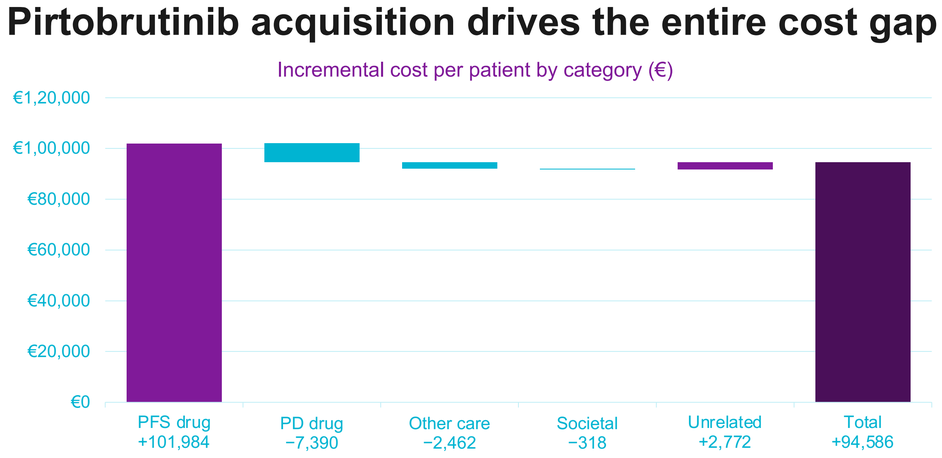
€262,702/QALY

above the €80,000/QALY threshold

PSA: mean ICER €261,995/QALY;
0 of 1,000 iterations reported ICER below €80,000/QALY

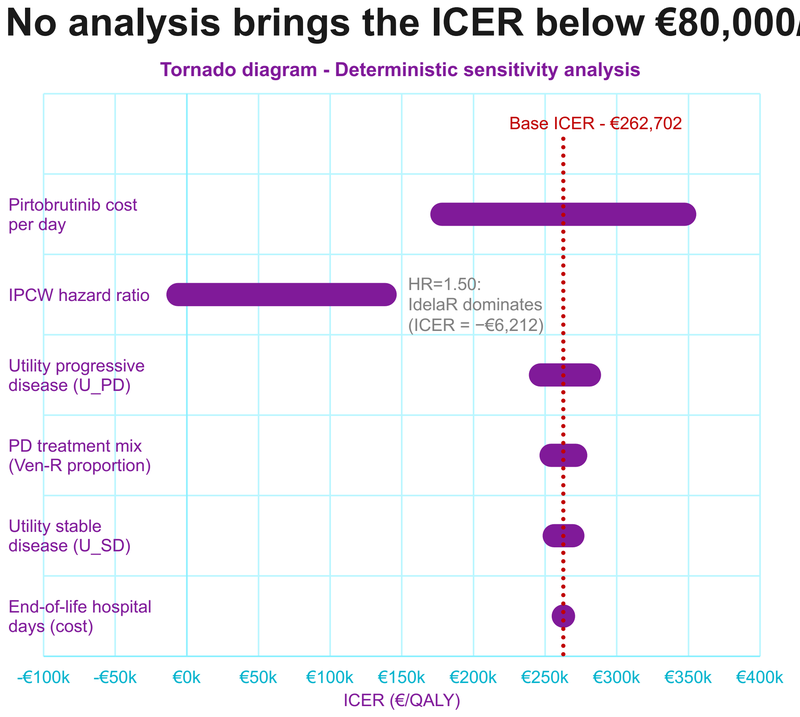


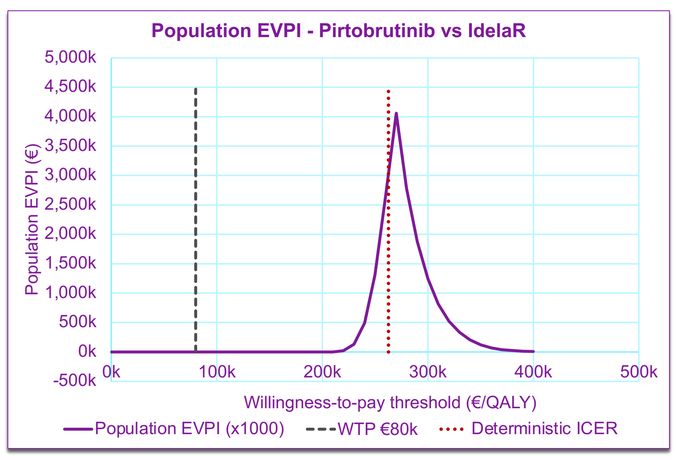
Pirtobrutinib acquisition drives the entire cost gap



- Acquisition during PFS (+€101,984) exceeds the total increment; later-line savings are small

No analysis brings the ICER below €80,000/QALY





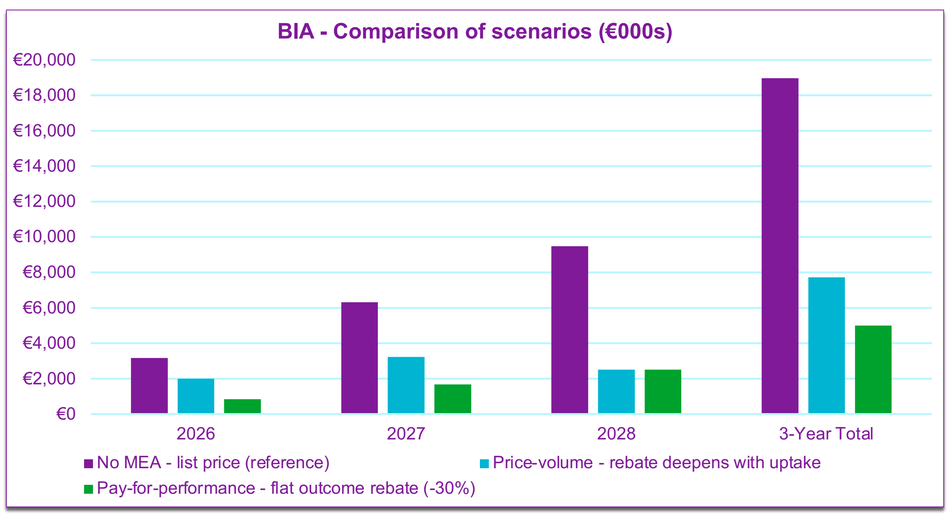
- All 8 scenarios exceed the threshold (€255,004 - €781,700/QALY)
- Price and the IPCW HR dominate the DSA
- EVPI is €0 at €80,000/QALY: more evidence will not change the decision at list price. It peaks near the ICER (~€4.1m, 1,000 patients)

A 45% price reduction is needed to reach the threshold

−45%

From €320 to €176 per day

list price reduction required to reach €80,000/QALY threshold



- Even with MEAs, net spend rises by €5.0m - €7.7m over 3 years

Abbreviations: AE: adverse event; BIA: budget impact analysis; BR: bendamustine + rituximab; BSC: best supportive care; BTKi: Bruton tyrosine kinase inhibitor; CLL: Chronic lymphocytic leukaemia; DSA/PSA: deterministic/probabilistic sensitivity analysis; EVPI: expected value of perfect information; HR: hazard ratio; ICER: incremental cost-effectiveness ratio; IPCW: inverse probability of censoring weighting; KM: Kaplan-Meier; LY: life-year; MEA: managed entry agreement; OS: overall survival; PD: progressed disease; PFS: progression-free survival; QALY: quality-adjusted life-year; R/R: relapsed/refractory; ZIN: Zorginstituut Nederland.

Conclusions

At list price, pirtobrutinib is not cost-effective versus IdelaR in Dutch R/R CLL; a ~45% price reduction or an outcome-based managed entry agreement would be required for reimbursement

- Uncertainty lies in long-term OS under crossover; needs re-assessment once mature OS data becomes available
- Budget impact: €19.0m over 3 years at current list price; €5.0m - €7.7m under MEAs

Limitations

- 17-month median follow-up extrapolated to 15 years
- No trial-reported HRQoL available; hence utilities taken from literature
- Crossover-adjusted comparator OS is uncertain (IPCW HR 0.87, CI 0.51 - 1.50)

Future research

- Analyses using mature OS or real-world data for better extrapolation
- Comparison with venetoclax-based regimens as it is an alternate treatment regimen in The Netherlands

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