Cost-Effectiveness Analysis of Quizartinib vs Midostaurin for Adult Patients with Newly Diagnosed FLT3-ITD+ Acute Myeloid Leukemia (AML) in Spain

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Concha Martínez Cano, MBA[1], Sudhir Unni, MBA, PhD[2], Efthalia Nikoglou, MBA, MSc, MBE[3], Chuyi Zhang, MSc[4], Anna Maria Vanessa Gittfried, MSc[5]

1. Daiichi Sankyo España, S.A.U., Madrid, Spain; 2. Daiichi Sankyo, Basking Ridge, NJ, USA; 3. Daiichi Sankyo Europe GmbH, Zurich, Switzerland; 4.IQVIA, London, United Kingdom; 5. OPEN Health HEOR & Market Access, Rotterdam, the Netherlands

PURPOSE

- This study assessed the cost-effectiveness of quizartinib versus midostaurin, each combined with standard chemotherapy as induction and consolidation treatment, followed by maintenance monotherapy (up to 36 cycles for quizartinib and 12 for midostaurin; 28-day/cycle), in newly diagnosed FLT3-ITD+ AML patients, from the Spanish National Health System perspective.

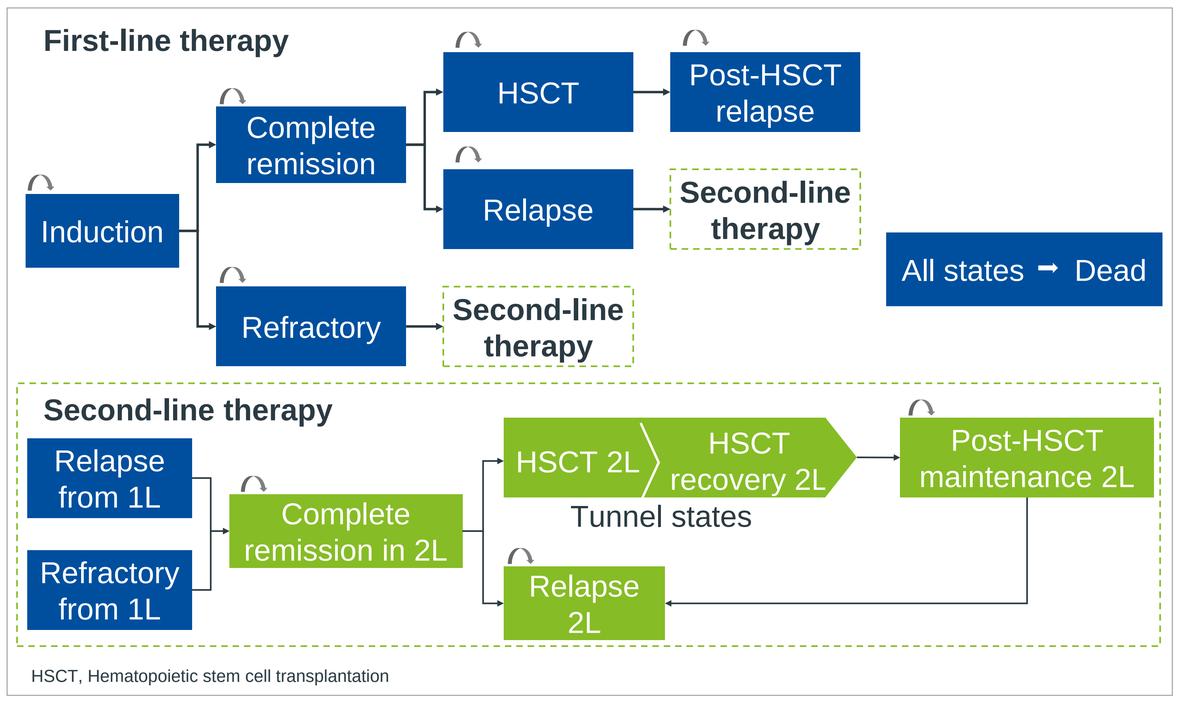
BACKGROUND

- FLT3-ITD+ mutation is a highly prevalent mutation in adults with AML, occurring in approximately 25% of newly diagnosed cases[1].
- FLT3-ITD+ mutation is associated with a poor prognosis, characterized by an increased risk of relapse and reduced long-term survival, even after hematopoietic stem cell transplantation (HSCT)[2,3].
- Quizartinib is an oral, highly potent, second-generation, selective type 2 FLT3 inhibitor. It is indicated for use with standard cytarabine and anthracycline induction, followed by standard cytarabine consolidation chemotherapy and/or HSCT, and then as a single-agent maintenance in adults with newly diagnosed FLT3-ITD+ AML. Quizartinib represents an innovative treatment option for these patients[4].

METHODS

- A semi-Markov model was developed (*Figure 1*), incorporating first-line and second-line treatments, with a 28-day cycle length.

Figure 1. Eleven-state semi-Markov model structure



HSCT, Hematopoietic stem cell transplantation

- Key clinical parameters were generated from an anchored matching adjusted treatment indirect comparison (MAIC)[4] utilizing clinical trial data from QuANTUM-First (quizartinib)[5] and RATIFY (midostaurin)[6]. To enable a meaningful comparison of survival outcomes, the QuANTUM-First population was reweighted based on treatment effect modifiers (e.g., sex, age, platelet count) to align with the RATIFY population.
- Healthcare resource utilization and direct costs were identified from Spanish databases and public sources (*Table 1*).
- A 3% discount rate was applied to costs and outcomes.
- The one-way sensitivity analysis (OWSA) and the probabilistic sensitivity analysis (with 5,000 iterations) were conducted to test the robustness of the deterministic results.

Table 1. Key model inputs

Parameters	Description	Source
Transition probabilities	Transition matrix between health states	IPD analyses of the QuANTUM-First; published literature
Comparative efficacy inputs	CIR HR, OS HR, CR OR	MAIC analysis of midostaurin vs. quizartinib[4]
Safety inputs	Grade ≥3 AEs reported in ≥5% patients	QuANTUM-First and RATIFY trials
Health utility inputs	Health state utilities	Published literature
Drug acquisition costs (list prices)	Quizartinib tablet 20/30mg Midostaurin tablet 25mg	Consejo General de Colegios Oficiales de Farmacéuticos[7]

AE, Adverse event; CIR, Cumulative incidence of relapse; CR, Complete remission; HR, Hazard ratio; IPD, Individual patient data; MAIC, Matching-adjusted indirect comparison; OR, Odds ratio; OS, Overall survival.

RESULTS

- Over a lifetime horizon, the **base-case results** indicated that quizartinib regimen is a cost-effective treatment option compared to the midostaurin regimen in Spain, with an ICER of €4,239/QALY gained (*Table 2*).

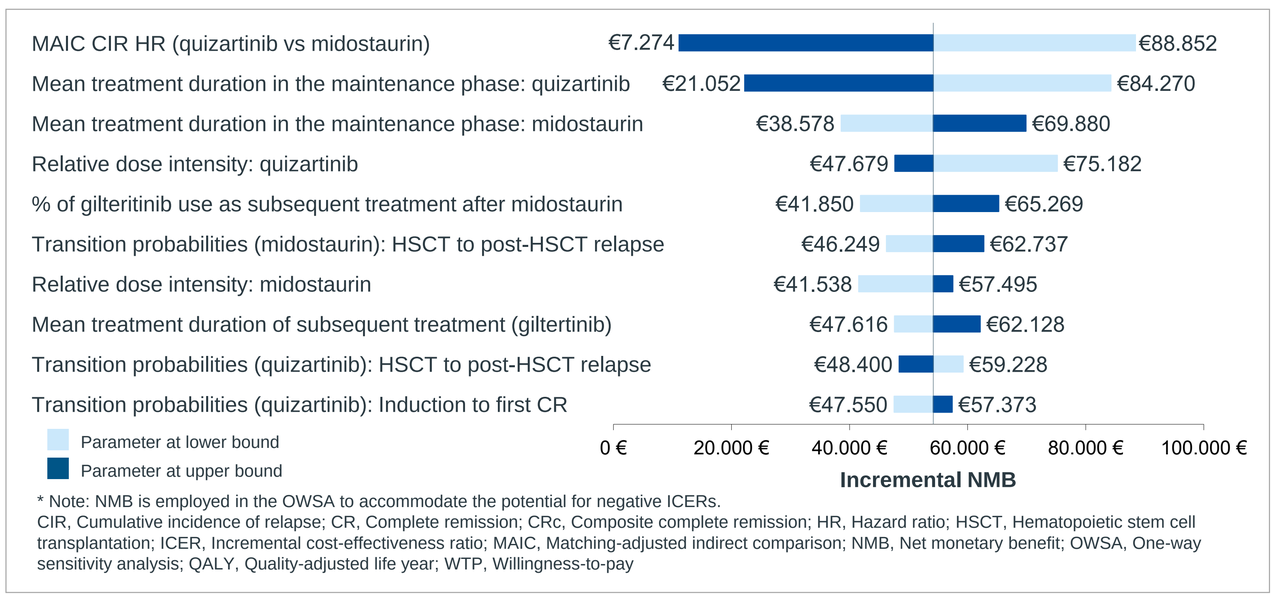
Table 2. Base-case deterministic results based on the drug list prices

Outcomes	Quizartinib	Midostaurin	Incremental
Total costs (€)	219,383	208,321	11,062
Total QALYs	8.36	5.75	2.61
ICER (€/QALY gained)			**4,239**

ICER, Incremental cost-effectiveness ratio; QALY, Quality-adjusted life year.

- **The OWSA** identified the MAIC-derived CIR HR (quizartinib vs midostaurin), and the mean treatment durations during the maintenance phase for both quizartinib and midostaurin as the most impactful drivers of the model outcomes. The OWSA also showed that quizartinib remained the cost-effective option across all tested parameter ranges, assuming a WTP threshold of €25,000 per QALY gained (*Figure 2*).

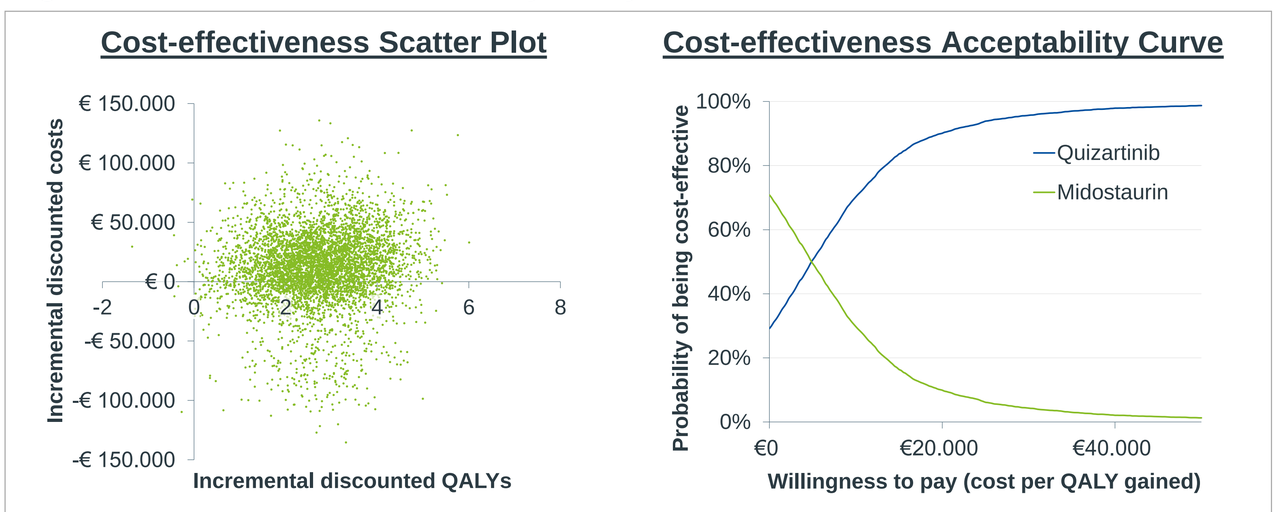
Figure 2. One-way sensitivity analysis results



* Note: NMB is employed in the OWSA to accommodate the potential for negative ICERs.
CIR, Cumulative incidence of relapse; CR, Complete remission; CRc, Composite complete remission; HR, Hazard ratio; HSCT, Hematopoietic stem cell transplantation; ICER, Incremental cost-effectiveness ratio; MAIC, Matching-adjusted indirect comparison; NMB, Net monetary benefit; OWSA, One-way sensitivity analysis; QALY, Quality-adjusted life year; WTP, Willingness-to-pay

- **Probabilistic sensitivity analysis** estimated a mean ICER of €12,276/QALY gained. At a WTP threshold of €25,000/QALY gained, quizartinib had a 94% probability of being cost-effective compared with midostaurin (*Figure 3*). These findings suggest that quizartinib is expected to be cost-effective under commonly accepted WTP thresholds in Spain, with results remaining robust despite uncertainty in model parameters.

Figure 3. Probabilistic sensitivity analysis results



QALY, Quality-adjusted life year.

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ACKNOWLEDGEMENTS

We would like to thank the patients, their families, and caregivers for their participation in the QuANTUM-First study. We also extend our thanks to Katerina Bilitou and Sergio Rico Garcia from Daiichi Sankyo, Inc. for their contributions to the Spanish cost-effectiveness analysis. This study is sponsored by Daiichi Sankyo, Inc. Medical writing support was provided by Chuyi Zhang of IQVIA (London, UK), with funding by Daiichi Sankyo, Inc.