Impact of indirect treatment comparison (ITC) methodology on cost-effectiveness of quizartinib in newly diagnosed FLT3-ITD+ acute myeloid leukemia (AML) in Canada and the United Kingdom (UK)

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PURPOSE

- This study assessed the impact of using two ITC approaches on the cost-effectiveness of quizartinib regimen in adults with newly diagnosed FLT3-ITD+ AML compared with midostaurin regimen from the perspective of Canadian and UK public payers.

CONCLUSION

- Quizartinib represents a cost-effective treatment for patients with newly diagnosed FLT3-ITD+ AML compared to the midostaurin regimen in both Canada and the UK. The use of different ITC methods (MAIC and ML-NMR) did not impact this conclusion.

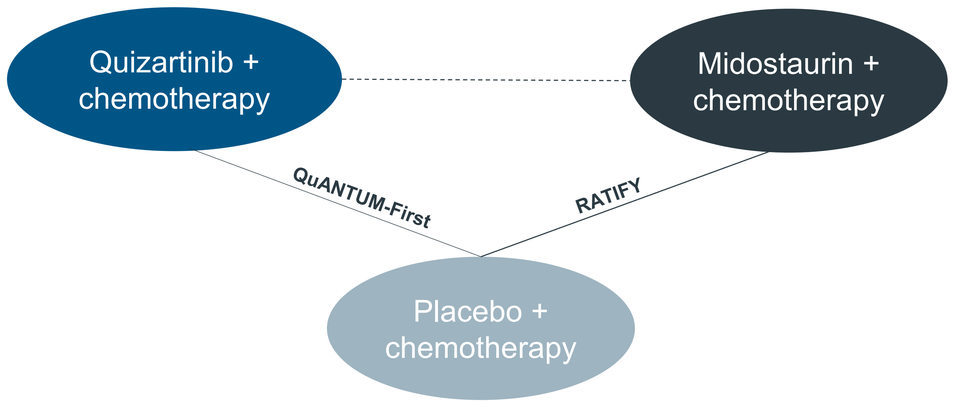
BACKGROUND

- Health technology assessments (HTA) worldwide often require estimates of comparative effectiveness for all relevant treatments to inform reimbursement decisions. When direct evidence from head-to-head studies is not available, ITCs are often used to generate evidence[1].
- **Quizartinib** is an oral, highly potent, second-generation, selective type 2 FLT3 inhibitor[2], **approved for reimbursement** in adults with newly diagnosed FLT3-ITD+ AML in Canada and the UK.
- This study compared the impact of using **two different ITC approaches** on results of a cost-effectiveness (CE) analysis conducted in **Canadian and UK settings**.

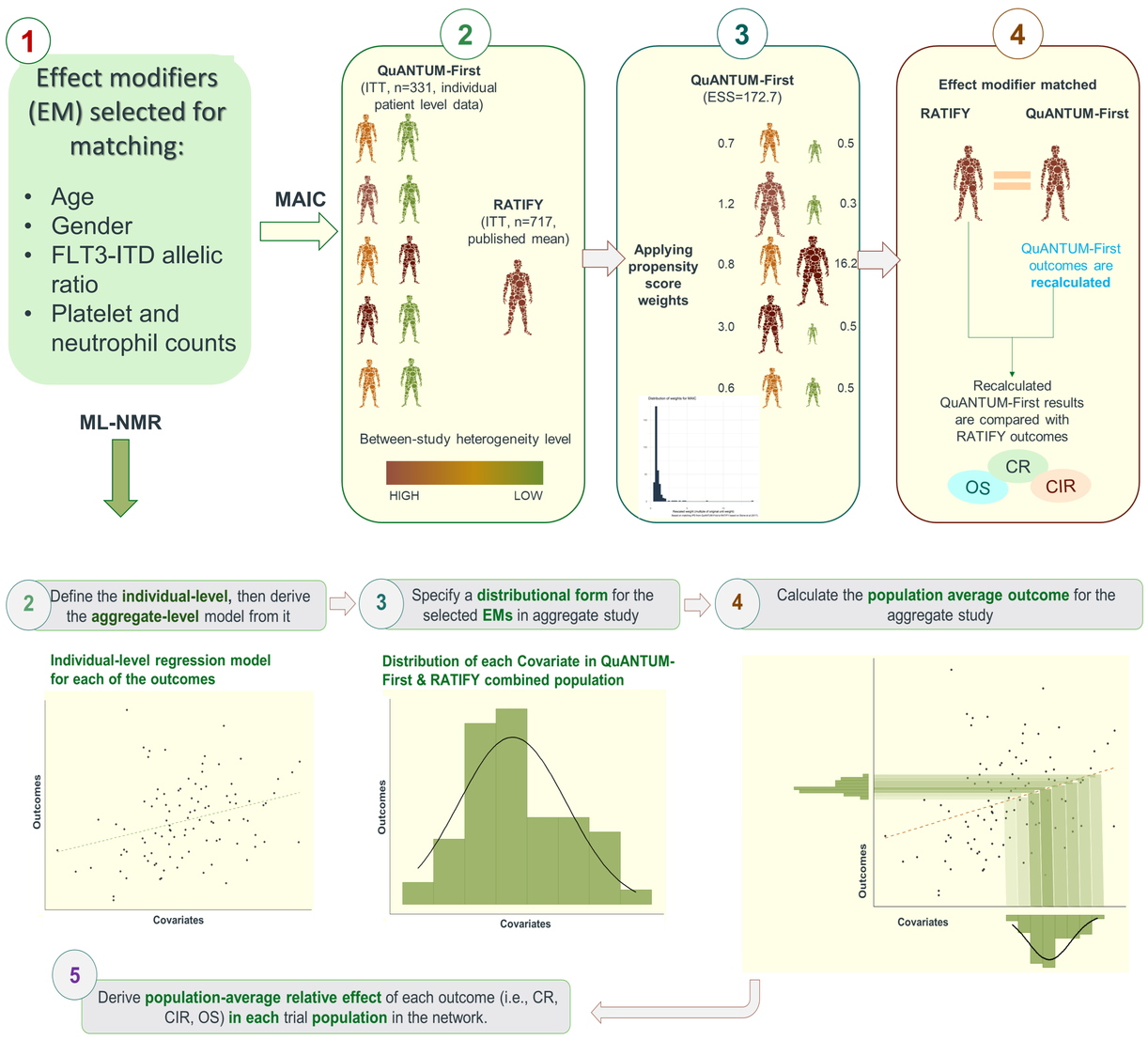
METHODS

- A **semi-Markov model** was developed consisting of **11 health states**, incorporating first-line and second-line treatments, with a 28-day cycle length.
- Relative efficacy for key clinical parameters such as complete remission (CR), relapse after complete remission (CIR) and overall survival (OS) were informed by two approaches: an **anchored matching-adjusted indirect comparison (MAIC)** and an **ML-NMR** using data from QuANTUM-First (quizartinib)[2] and RATIFY (midostaurin)[3] trials.

Figure 1. Network of evidence



- Figures 2 and 3 below provide more details on **MAIC** and **ML-NMR**.



CIR, Cumulative incidence of relapse; CR, Complete remission; EM, Effect modifier; ESS, Effective sample size; HR, Hazard ratio; IPD, Individual patient data; MAIC, Matching-adjusted indirect comparison; ML-NMR, multilevel network meta-regression; OR, Odds ratio; OS, Overall survival.

- Descriptions and sources of key model inputs are summarised in *Table 1*. Of note, the **main model driver** (CIR HR) was consistent across both approaches: hazard ratio (95% CI): **0.42** (0.20 to 0.91) in **MAIC** and **0.49** (0.23 to 0.997) in **ML-NMR**, supporting a treatment benefit for quizartinib regimen vs. midostaurin regimen, regardless of the ITC approach adopted.
- Key outcomes included total costs, total quality-adjusted life years (QALYs), and incremental cost-effectiveness ratio (ICER). The base case (deterministic) was from the Canadian and UK public payer perspective.

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 or ML-NMR analyses of midostaurin vs. quizartinib
Safety inputs	Grade ≥3 AEs reported in ≥5% patients	QuANTUM-First and RATIFY trials
Health utility inputs	Health state utilities	Published literature
Healthcare costs	Drug acquisition, disease and AE management	Canadian and UK databases, literature, expert opinion
Discount rate	Applied to both costs and outcomes	Canada: 1.5%; UK: 3.5%

RESULTS

- Over a lifetime horizon, the gains in QALYs for quizartinib were **considerably higher** than for midostaurin and were **clinically meaningful** regardless of approach (*Table 2*).

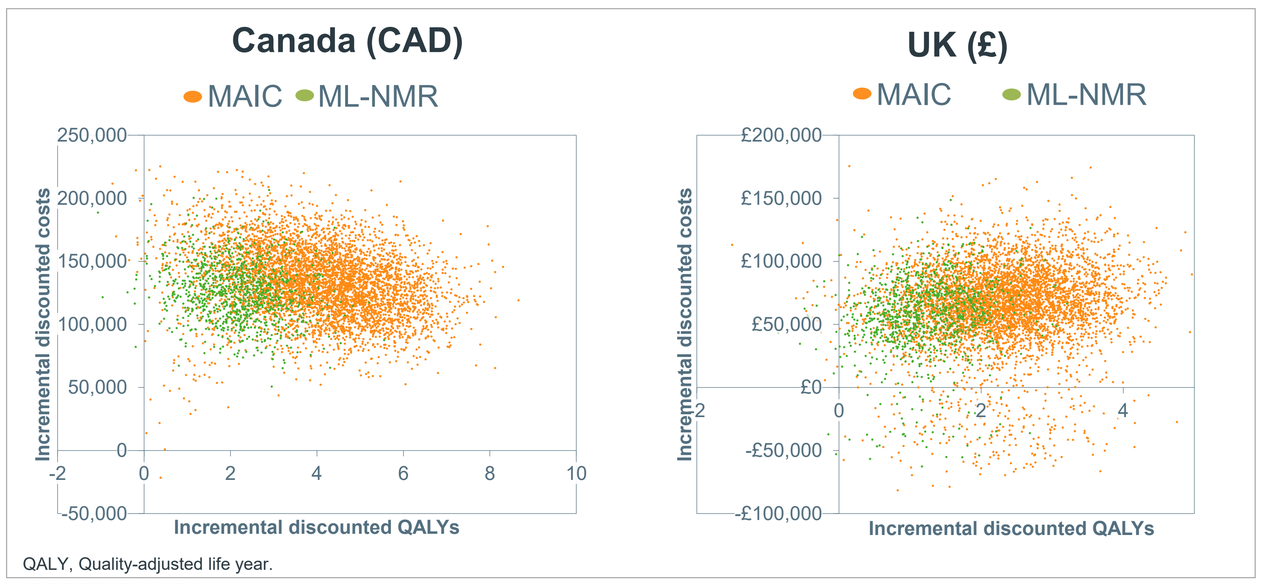
Table 2. Base Case Deterministic Results (at list prices)

Outcomes	Canada	UK
Incremental total costs		
MAIC	CAD138,234	£65,328
ML-NMR	CAD127,715	£56,676
Incremental total QALYs		
MAIC	3.87	2.18
ML-NMR	2.20	1.24
ICER		
MAIC	CAD 35,729	£30,015
ML-NMR	CAD 58,179	£45,732

ICER, Incremental cost-effectiveness ratio; MAIC, Matching-adjusted indirect comparison; ML-NMR, multilevel network meta-regression; QALY, Quality-adjusted life year;

- On the probabilistic sensitivity analysis, in comparison to the midostaurin regimen and using the list prices, most iterations were in the North-Eastern quadrant: 94.7% (MAIC) and 93.2% (ML-NMR) in the UK and ~100% for both types of ITC in Canada (*Figure 4*).
- When confidential net prices are applied, the introduction of quizartinib as a therapeutic option represents a **cost-effective use of public payer resources** in both Canada and UK.

Figure 4. Cost-effectiveness scatterplots



QALY, Quality-adjusted life year.

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