# CONFIDENTIAL UNTIL PUBLISHED
# External Assessment Group Report
# Quizartinib for untreated FLT3-ITD-positive acute myeloid leukaemia

## *EAG addendum: Additional analysis requested following the Pre-meeting briefing*


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None


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The views expressed in this report are those of the authors and not necessarily those of the NIHR Evidence Synthesis Programme. Any errors are the responsibility of the authors.

**Note on the text**

All commercial-in-confidence (CIC) data have been [redacted], all depersonalised data (DPD) are [redacted].

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# 1 OVERVIEW

Following the pre-meeting briefing (PMB) for appraisal committee 1 (ACM1) the Committee lead team requested the following additional analysis:

- A scenario analysis assuming the sane relapse rate for quizartinib and midostaurin
- A scenario assuming the clinical equivalence of quizartinib and midostaurin.

The NICE team further requested the following additional information:

- A comparison of  drug acquisition costs for a full course of treatment with quizartinib and midostaurin
- A comparison of annualised drug acquisition costs associated with quizartinib and midostaurin.

# 2 RESULTS OF ADDITIONAL SCENARIO ANALYSIS

Table 1 presents the results of the additional scenario analysis requested by the Committee lead team. These analyses are run on the EAG's updated base case as outlined in the addendum on time on treatment. The scenarios set the efficacy of midostaurin equal to that of quizartinib. Therefore, the total QALYs and costs associated with quizartinib remain unchanged in these scenarios. The EAG considers this approach more appropriate to setting quizartinib equal to midostaurin as the principal uncertainty relates to the relative effectiveness of midostaurin. This also maintains consistency in the estimated cost-effectiveness of quizartinib vs standard chemotherapy.

All results presented in this Section include the PAS discount for quizartinib but exclude commercial arrangements for the comparator treatments. Results inclusive of available commercial arrangements for the comparator treatments are provided in a confidential appendix to this report.

**Table 1 Additional scenario analysis assuming equivalence between quizartinib and midostaurin**

| Scenario | Technology | Total | | Incremental | | Fully incremental ICER |
|---|---|---|---|---|---|---|
| | | Costs | QALYs | Costs | QALYs | |
| **Updated EAG base case inclusive of EAG preferred approach to ToT** | SC regimen | [redacted] | [redacted] | | | |
| | Midostaurin regimen | [redacted] | [redacted] | [redacted] | [redacted] | £163,476 |
| | Quizartinib regimen | [redacted] | [redacted] | [redacted] | [redacted] | £12,863 |
| **Equivalent rate of relapse for midostaurin and quizaertinib** | SC regimen | [redacted] | [redacted] | | | |
| | Midostaurin regimen | [redacted] | [redacted] | [redacted] | [redacted] | £103,773 |
| | Quizartinib regimen | [redacted] | [redacted] | [redacted] | [redacted] | £14,050 |
| **Clinical equivalence of midostaurin and quizaertinib** | SC regimen | [redacted] | [redacted] | | | |
| | Midostaurin regimen | [redacted] | [redacted] | [redacted] | [redacted] | £48,566 |
| | Quizartinib regimen | [redacted] | [redacted] | [redacted] | [redacted] | Dominated |

**Abbreviations**: EAG: Evidence assessment group; ICER: incremental cost-effectiveness ratio; QALY: quality-adjusted life-years; SC, standard chemotherapy; ToT: time on treatment.

## *2.1 EAG comment*

The EAG urges caution when interpreting the equal efficacy scenarios and presents these for illustrative purposes only. There is limited clinical evidence supporting the equivalence of quizartinib and midostaurin. Results from the indirect treatment comparison are subject to considerable uncertainty. As discussed extensively in the evidence assessment report, there are significant methodological challenges with generating unbiased estimates of relevant treatment effect parameters due to the substantial differences between the RATIFY and QuANTUM First trials. Moreover, even if the results of the indirect treatment comparisons are taken at face value, the point estimates generated are associated with wide confidence intervals for all outcome measures.

It is also important to emphasise that the equal efficiency scenarios make several assumptions. Firstly, it assumes quizartinib is received in the post-HSCT setting for up to three years but is associated with no additional benefit. Secondly, patients on quizartinib receive maintenance treatment without HSCT for much longer than those on midostaurin, and this is also assumed to be associated with no benefit. It is unclear whether these assumptions are reasonable. The available evidence does not allow efficacy to be compared across treatment phases, and it is unclear whether maintenance therapy with either quizartinib or midostaurin offers any additional benefit.

# 3 ADDITIONAL INFORMATION ON DRUG ACQUISITION COSTS

**Error! Reference source not found.** presents a comparison of drug acquisition costs associated with quizartinib and midostaurin treatment regimens. The full course of treatment for quizartinib assumes two cycles of induction treatment, four cycles of consolidation treatment and 36 cycles of maintenance treatment. The full course of treatment for midostaurin assumes two cycles of induction treatment, four cycles of consolidation and 12 cycles of maintenance treatment. The annualised costs are presented based on 12 cycles of maintenance treatment.

All results presented in this Section include the PAS discount for quizartinib but exclude commercial arrangements for the comparator treatments. Results inclusive of available commercial arrangements for the comparator treatments are provided in a confidential appendix to this report.

### Table 2 Comparison of drug acquisition costs

| Scenario | Technology | Undiscounted costs |
|---|---|---|
| Cost of a full course of treatment | Midostaurin regimen | £171,518 |
| | Quizartinib regimen | [redacted] |
| Cost of 12 cycles of maintenance treatment | Midostaurin regimen | £134,639 |
| | Quizartinib regimen | [redacted] |