NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Quizartinib for induction, consolidation and maintenance treatment of newly diagnosed FLT3-ITD-positive acute myeloid leukaemia

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of quizartinib within its marketing authorisation as an induction, consolidation and maintenance therapy for treating newly diagnosed FLT3-ITD-positive acute myeloid leukaemia.

Background

Acute myeloid leukaemia (AML) is a cancer of the blood and bone marrow. It is characterised by the overproduction of early immature myeloid white blood cells (blasts). The abnormal cells build up in the bone marrow and blood and interfere with normal blood cell production. AML progresses quickly over weeks or months and is fatal if not treated. Anaemia, bleeding problems and serious infections are common symptoms of acute myeloid leukaemia. People with AML also feel fatigued which can impact on daily life.

FLT3-ITD-positive is a term used to describe AML cells that have an internal tandem duplication (ITD) mutation in the FLT3 gene. The FLT3 gene plays a role in cell growth and division. FLT3-ITD-positive AML is associated with a poor prognosis, with people having a lower chance of achieving remission and shorter overall survival.[1]

There are around 3,100 new diagnoses of AML on average each year in the UK.[2] Incidence is strongly related to age, with the highest incidence rates being in older people.[2] About 25% of people with AML have the FLT3-ITD mutation.**Error! Bookmark not defined.**

The aim of treatment for AML is to cure it. For people who are fit enough, intensive treatment is available. It is conducted in 2 phases: induction therapy to achieve remission, followed by consolidation therapy to reduce the risk of relapse. For both induction and consolidation therapy, people with a FLT3-ITD mutation are typically offered chemotherapy plus midostaurin (Technology appraisal guidance 523). The most commonly used chemotherapy regimen for the induction phase is cytarabine and daunorubicin.[3,4] Other options include cytarabine with mitoxantrone or idarubicin, or liposomal cytarabine–daunorubicin (Technology appraisal guidance 552). For consolidation, the most commonly used chemotherapy regimens are cytarabine monotherapy or combinations of cytarabine, etoposide, amsacrine and mitoxantrone.[3,4] Alternatively, people may be offered haematopoietic stem cell transplantation if they are in good health.

Following the intensive treatment stage, people who have had a complete remission may be offered long-term maintenance therapy to prevent recurrence of a new episode. Tretament options include monotherapy with midostaurin (Technology appraisal guidance 523) or azacytidine (Technology appraisal guidance 827).

The technology

Quizartinib (Vanflyta, Daiichi Sankyo UK) does not currently have a marketing authorisation in the UK for AML. It has been studied in clinical trials in combination with induction and consolidation chemotherapy, and as maintenance therapy in people with newly diagnosed FLT3-ITD (+) AML.

Intervention(s)	Quizartinib
Population(s)	People with newly diagnosed AML that is FMS-like tyrosine kinase 3 internal tandem duplication (FLT3-ITD) positive.
Comparators	**Induction phase:** • Established clinical management without quizartinib, including but limited to midostaurin with daunorubicin and cytarabine **Consolidation phase:** • Established clinical management without quizartinib, including but limited to midostaurin with cytarabine alone or in combination with other chemotherapy drugs, such as mitoxantrone, etoposide, or amsacrine • Haematopoietic stem cell transplantation **Maintenance phase:** • Midostaurin • Azacitidine
Outcomes	The outcome measures to be considered include: • overall survival • event-free survival • disease-free survival • adverse effects of treatment • health-related quality of life

Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. If the technology is likely to provide similar or greater health benefits at similar or lower cost than technologies recommended in published NICE technology appraisal guidance for the same indication, a cost comparison may be carried out. The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective. The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account. The availability and cost of biosimilar and generic products should be taken into account.
Other considerations	Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.
Related NICE recommendations	**Related technology appraisals:** Oral azacitidine for maintenance treatment of acute myeloid leukaemia after induction therapy (2022) NICE technology appraisal guidance 827. Venetoclax with low dose cytarabine for untreated acute myeloid leukaemia when intensive chemotherapy is unsuitable (2022) NICE technology appraisal guidance 787. Venetoclax with azacitidine for untreated acute myeloid leukaemia when intensive chemotherapy is unsuitable (2022) NICE technology appraisal guidance 765. Liposomal cytarabine–daunorubicin for untreated acute myeloid leukaemia (2018) NICE technology appraisal guidance 552. Gemtuzumab ozogamicin for untreated acute myeloid leukaemia (2018) NICE technology appraisal guidance 545.

	Midostaurin for untreated acute myeloid leukaemia (2018) NICE technology appraisal guidance 523. Azacitidine for treating acute myeloid leukaemia with more than 30% bone marrow blasts (2016) NICE technology appraisal guidance 399. Azacitidine for the treatment of myelodysplastic syndromes, chronic myelomonocytic leukaemia and acute myeloid leukaemia (2011) NICE technology appraisal guidance 218. **Related technology appraisals in development:** Cedazuridine-decitabine for untreated acute myeloid leukaemia when intensive chemotherapy is unsuitable [ID6135]. Publication date to be confirmed. Talacotuzumab for untreated acute myeloid leukaemia. NICE technology appraisal guidance [ID1262] Publication to be confirmed. Gilteritinib for maintenance treatment of FLT3-mutation-positive acute myeloid leukaemia after stem cell transplant [ID6243] Suspended Histamine dihydrochloride with interleukin-2 for maintenance treatment of acute myeloid leukaemia [ID1627] Suspended Ivosidenib with azacitidine for untreated IDH1-positive acute myeloid leukaemia [ID6198] Publication to be confirmed **Related NICE guidelines:** COVID-19 rapid guideline: delivery of systemic anticancer treatments (2020) NICE guideline NG161. Review date not stated. Haematological cancers: improving outcomes (2016) NICE guideline NG47. Review date not stated **Related quality standards:** Haematological cancers (2017) NICE quality standard 150
Related National Policy	The NHS Long Term Plan (2019) NHS Long Term Plan NHS England (2018) Manual for prescribed specialised services 2018/19 Chapter 105 – Specialist cancer services (adults) NHS England (November 2018) Clofarabine for refractory or relapsed acute myeloid leukaemia (AML) as a bridge to stem cell transplantation (all ages). Clinical Commissioning Policy. Reference 170080P

	NHS England (2013) 2013/14 NHS Standard Contract for Cancer: Chemotherapy (Adult). B15/S/a Department of Health Cancer research and treatment Department of Health (2016) NHS Outcomes Framework 2016 to 2017: Domains 3, 4 and 5. Department of Health (2014) The national cancer strategy: 4th annual report

Questions for consultation

Where do you consider quizartinib will fit into the existing care pathway for untreated FLT3-ITD-positive AML?

Have all relevant comparators for quizartinib been included in the scope at all three treatment stages (induction, consolidation and maintenance)?

Is the technology likely to be similar in its clinical effectiveness and resource use to midostaurin? Or in what way is it different to midostaurin?

Will the intervention be used to treat the same population as midostaurin?

Is FLT3-ITD routinely tested for in clinical practice?

Approximately what proportion of people in complete remission following consolidation therapy would be offered a maintenance treatment? What factors would influence this decision?

Would quizartinib be a candidate for managed access?

Do you consider that the use of quizartinib can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits.

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which quizartinib will be licensed;

- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;

- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the committee to identify and consider such impacts.

NICE intends to evaluate this technology through its Single Technology Appraisal process. (Information on NICE's health technology evaluation processes is available at https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-technology-appraisal-guidance/changes-to-health-technology-evaluation).

References

1 Daver, N., Schlenk, R. F., Russell, N. H., & Levis, M. J. (2019). Targeting FLT3 mutations in AML: review of current knowledge and evidence. Leukemia, 33(2), 299-312.

2 Cancer Research UK: Acute myeloid leukaemia (AML) statistics. Accessed April 2023.

3 RM Partners, South East London Cancer Alliance, North Central and East London Cancer Alliance. Pan-London Haemato-Oncology Clinical Guidelines. Part 2: Acute Myeloid Leukaemia (2020). https://www.selca.nhs.uk/application/files/5916/4319/6737/Pan_London_Acute_Myeloid_Leukaemia_guidelines.pdf Accessed June 2023.

4 BMJ best practice. Acute myeloid leukaemia. https://bestpractice.bmj.com/topics/en-gb/274 Accessed June 2023.