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

Final scope

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 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 high/intermediate dose cytarabine monotherapy or combinations of cytarabine, etoposide, amsacrine and mitoxantrone.[3,4] People may be offered haematopoietic stem cell transplantation if they are in good health.

Following the intensive treatment stage, people who are in 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 oral azacitidine (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 positive AML.

Intervention(s)	Quizartinib
Population(s)	People with newly diagnosed AML that is FMS-like tyrosine kinase 3 internal tandem duplication (FLT3-ITD) positive.
Subgroup	• People who are ineligible for haematopoietic stem cell transplant
Comparators	**Induction phase:** • Established clinical management without quizartinib, including but not limited to midostaurin with daunorubicin and cytarabine **Consolidation phase:** • Established clinical management without quizartinib, including but not limited to midostaurin with cytarabine alone or in combination with other chemotherapy drugs, such as mitoxantrone, etoposide, or amsacrine **Maintenance phase:** • Established clinical management without quizartinib, including but not limited to midostaurin and azacitidine
Outcomes	The outcome measures to be considered include: • overall survival • event-free survival • relapse-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

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.