NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Quizartinib for treating relapsed or refractory acute myeloid leukaemia

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of quizartinib within its marketing authorisation for treating relapsed or refractory FLT3-ITD-positive acute myeloid leukaemia.

Background

Acute myeloid leukaemia is a cancer of the blood and bone marrow. It is characterised by the overproduction of early immature myeloid cells (blasts). Acute myeloid leukaemia is classified into several types. In most types of acute myeloid leukaemia, the cancer cells are immature white blood cells. In acute promyelocytic leukaemia (a subcategory of acute myeloid leukaemia) the abnormal white blood cells are of the neutrophil type and are known as promyelocytes. In other less common types, immature platelets or immature red blood cells form the leukaemia cells. The CD33 antigen is expressed on the blast cells of most types of acute myeloid leukaemia. Anaemia, bleeding problems, serious infections, fatigue, weakness, breathlessness, fever, night sweats, weight loss and bone, joint or muscle pain are common symptoms in acute myeloid leukaemia.

FMS-like tyrosine kinase-3 (FLT3) is a receptor tyrosine kinase, a type of cell-surface receptor, which plays a role in the proliferation, or increase, in the number of certain blood cells. The FLT3 mutation is associated with relatively poor prognosis because of disease relapse.[1] The incidence of acute myeloid leukaemia has increased by 8% in the UK over the last decade. There were 2,662 new diagnoses of acute myeloid leukaemia and 2,168 deaths registered in England in 2016.[1] In the UK in 2013-2015, the majority of new diagnoses were in people aged 85-89 and over.[2]

The aim of treatment for acute myeloid leukaemia is to cure it. For people who are fit enough to have intensive treatment, induction chemotherapy is initially given to achieve a remission. After remission, further cycles of chemotherapy are given to reduce the risk of the leukaemia recurring (consolidation therapy). The treatment of relapsed or refractory AML depends upon several factors such as age, general health, type of leukaemia cells and duration of remission (in case of relapsed AML). For people with good general health, the treatment typically includes chemotherapy and allogeneic stem cell transplant. The aim of chemotherapy is to reduce the leukemic burden before stem cell transplant. Allogeneic stem cell transplant means that stem cells were donated by someone else, usually a sibling whose tissue type closely matches that patient's.

People with relapsed and refractory AML are offered chemotherapy regimens containing high-dose of cytarabine such as fludarabine, cytarabine, idarubicin, and filgrastim (FLAG-Ida). People who cannot tolerate or do not wish to receive high-dose cytarabine are offered intermediate dose cytarabine regimen (IDAC).

People with relapsed and refractory AML also receive supportive care, which includes, blood product replacement, antibiotics, and antifungals. People who cannot have chemotherapy and stem cells transplant, need intermittent hydroxycarbamide to keep peripheral leukaemia cell count under control.

The technology

Quizartinib (Vanflyta, Daiichi Sankyo) is a FMS-like tyrosine kinase-3 (FLT3) inhibitor. It is administered orally. Quizartinib does not currently have a marketing authorisation in the UK for acute myeloid leukaemia. It has been studied as monotherapy in clinical trials in adults aged 18 years or over with relapsed or refractory FMS-like tyrosine kinase-3 internal tandem duplication (FLT3-ITD) positive acute myeloid leukaemia.

Intervention(s)	Quizartinib
Population(s)	People with relapsed or refractory FLT3-ITD positive acute myeloid leukaemia
Comparators	Established clinical management without quizartinib including but not limited to cytarabine based chemotherapy • Fludarabine, cytarabine, idarubicin, and filgrastim (FLAG-Ida) • Intermediate dose cytarabine (IDAC)
Outcomes	The outcome measures to be considered include: • overall survival • progression free survival • time to disease progression • response rates, including haematologic response • blood-transfusion independence • stem cell transplant • infections • 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. 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.
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 and NICE Pathways	Azacitidine for treating acute myeloid leukaemia with more than 30% bone marrow blasts' (2016) NICE Technology Appraisal 399. Review date July 2019. 'Azacitidine for the treatment of myelodysplastic syndromes, chronic myelomonocytic leukaemia and acute myeloid leukaemia' (2011) NICE Technology Appraisal 218. Static list: April 2014. 'Midostaurin for untreated acute myeloid leukaemia' (2018) NICE technology appraisal 523. Review date June 2021. Terminated appraisals 'Decitabine for the treatment of acute myeloid leukaemia' (terminated appraisal) (2012) NICE Technology Appraisal 270. Appraisals in development (including suspended appraisals) 'Gemtuzomab ozogamicin for untreated acute myeloid leukaemia' NICE technology appraisals guidance [ID982]. Publication expected July 2018 'Vosaroxin for treating relapsed or refractory acute myeloid leukaemia' NICE technology appraisals guidance [ID746]. Suspended 2016. Related guidelines 'Haematological cancers: improving outcomes' (2016). NICE Guideline 47. Review date to be confirmed. Related NICE Pathways:

	Blood and bone marrow cancers (2018) NICE pathway
Related National Policy	Clinical commissioning policy: second allogeneic haematopoietic stem cell transplant for relapsed disease (all ages) NHS England 106068/P February 2017 Department of Health and Social Care, NHS Outcomes Framework 2016-2017 (published 2016): Domains 1, 2, 4 and 5. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017

Questions for consultation

Have all relevant comparators for quizartinib been included in the scope? Which treatments are considered to be established clinical practice in the NHS for treating relapsed or refractory acute myeloid leukaemia?

Are the outcomes listed appropriate?

Are there any subgroups of people in whom quizartinib is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Where do you consider quizartinib will fit into the existing Blood and bone marrow cancers (2018) NICE pathway?

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.

Do you consider quizartinib to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might

improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Do you consider that the use of quizartinib can result in any potential significant and 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 Appraisal Committee to take account of these benefits.

To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly.

NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/article/pmg19/chapter/1-Introduction).

NICE has published an addendum to its guide to the methods of technology appraisal (available at https://www.nice.org.uk/Media/Default/About/what-we-do/NICE-guidance/NICE-technology-appraisals/methods-guide-addendum-cost-comparison.pdf), which states the methods to be used where a cost comparison case is made.

- Would it be appropriate to use the cost comparison methodology for this topic?
- Is the new technology likely to be similar in its clinical efficacy and resource use to any of the comparators?
- Is the primary outcome that was measured in the trial or used to drive the model for the comparator(s) still clinically relevant?
- Is there any substantial new evidence for the comparator technology/ies that has not been considered? Are there any important ongoing trials reporting in the next year?

References

1. 1 Small D (2006) FLT3 mutations: biology and treatment. Hematology Am Soc Hematol Educ Program 2006: 178-84.
2. Cancer Research UK (2016) Acute myeloid leukaemia (AML) statistics. Accessed June 2018.
3. Cancer Research UK (2016) Chemotherapy for acute myeloid leukaemia (AML). Accessed June 2018.