NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Quizartinib for treating relapsed or refractory acute myeloid leukaemia

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of quizartinib within its marketing authorisation for treating relapsed or refractory FLT3-ITD mutation-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. 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. Mutations in the FLT3 gene occurs in around 30% of patients with AML. FLT3 mutations can be either internal tandem duplications (FLT3-ITD mutations) or point mutations of the tyrosine kinase domain (FLT3-TKD mutations). The FLT3-ITD 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 years old.[2] Around 60% of patients with mutations in the FLT3 gene will relapse within the first 2 years of induction therapy.

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 may be offered treatment combinations containing lower doses of cytarabine.

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) mutation-positive acute myeloid leukaemia.

Intervention	Quizartinib
Population	People with relapsed or refractory FLT3-ITD mutation-positive acute myeloid leukaemia
Comparators	Established clinical management without quizartinib including but not limited to cytarabine based chemotherapy
Outcomes	The outcome measures to be considered include: • overall survival • event-free survival • disease-free survival • response rates, including remission • stem cell transplant • 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	**Related Technology Appraisals** '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. **Terminated appraisals** 'Decitabine for the treatment of acute myeloid leukaemia' (terminated appraisal) (2012) NICE Technology Appraisal 270. **Appraisals in development (including suspended appraisals)** '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

References

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.