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Health Technology Briefing
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Gilteritinib maintenance therapy for FLT3-ITD mutated acute myeloid leukaemia

Company/Developer	Astellas Pharma Ltd

☐ New Active Substance ☒ Significant Licence Extension (SLE)

NIHRIO ID: 18312	NICE ID: 10582	UKPS ID: 667073

Licensing and Market Availability Plans

Currently in phase III clinical trials

Summary

Gilteritinib is in clinical development as maintenance therapy for patients with FMS-like tyrosine kinase 3 internal tandem duplication (FLT3-ITD) acute myeloid leukaemia (AML) who have received a haematopoietic stem cell transplant (HSCT) and are in first complete remission (CR1). AML is a type of cancer of the white blood cells which are important in fighting infections and controlling tissue damage. HSCT aims to cure AML, but the disease often comes back. FLT3-ITD mutations in AML are common and are associated with a poor prognosis. Maintenance treatments continue after the patient is in remission following HSCT to stop any remaining cancerous cells from spreading and surviving. The aim of maintenance treatment is to increase relapse-free and overall survival times. There are currently no recommended treatment options for maintenance treatment in patients with FLT3-ITD AML who have undergone HSCT.

Gilteritinib is a small molecule inhibitor, that blocks the action of FLT3. It works by stopping cells that over express the FLT 3 receptor from signalling, growing, and can induce cell death. Gilteritinib will be administered orally, once daily. If licensed, gilteritinib will offer a maintenance therapy for FLT3-ITD AML patients in CR1 who have undergone HSCT.

Proposed Indication

Maintenance treatment following haematopoietic stem cell transplant (HSCT) in adult patients with FMS-like tyrosine kinase 3 internal tandem duplication (FLT3-ITD) mutated acute myeloid leukaemia (AML), where patient has achieved first morphologic complete remission.[1]

Technology

Description

Gilteritinib (Xospata) is a small molecule drug that is a selective FLT3 inhibitor. Gilteritinib inhibits the signalling and proliferation of cells that exogenously express FLT3 mutations and can induce apoptosis in leukaemic cells expressing FLT3-ITD.[2-4] FLT3 can be found on the surface of cancer cells in AML and is involved in stimulating the cells to multiply uncontrollably. Blocking FLT3 is expected to slow down development of the disease.[5]
In the phase III trial (NCT02997202), patients with FLT3-ITD AML in first complete remission (CR1) following HSCT will receive gilteritinib once daily via oral administration.[1]

Key Innovation

FLT3-ITD is a negative prognostic marker for AML and prognosis of relapsed AML after HSCT is generally poor due to a lack of effective treatments.[6,7] The goal of maintenance therapy is to improve overall survival rates and reduce the risk of relapse. If licensed, gilteritinib will offer a post-HSCT maintenance treatment option for patients with FLT3-ITD AML, who currently have limited options and are at high risk of relapse.[8]

Regulatory & Development Status

Gilteritinib currently has Marketing Authorisation in the EU/UK as monotherapy for the treatment of adult patients who have relapsed or refractory AML with a FLT3 mutation.[3]

Gilteritinib as a monotherapy is in phase I/II clinical development for AML with FLT3-ITD mutations in children, young adults, and adolescents.[9] Gilteritinib is also in phase III clinical development in combination with induction and consolidation chemotherapy for newly diagnosed FLT3 AML patients eligible for high intensity chemotherapy.[10]

Patient Group

Disease Area and Clinical Need

Leukaemia is a cancer of the white blood cells with AML specifically affecting the patients myeloid cells which are important in fighting infections and controlling tissue damage.[11,12] Genetic mutations involved in haematopoiesis results in a clonal expansion of undifferentiated myeloid precursors (blasts) in the peripheral blood and bone marrow resulting in ineffective erythropoiesis and bone marrow failure.[13] Mutations in the FLT3 gene occur in approximately 30% of AML cases, with ITD representing the most common type of FLT3 mutation. FLT3-ITD is a common driver mutation that presents with a high leukemic burden and confers a poor prognosis in patients with AML.[7] Symptoms of AML usually develop rapidly, becoming worse over time and can include frequent infections, fatigue, weakness, breathlessness, and unusual/ frequent bruising or bleeding.[11] Risk factors of developing AML include: age, with most cases seen in those aged 85-89; smoking; obesity; exposure to radiation or benzene; genetic conditions such as

Fanconi anaemia; Down's syndrome; previous treatment with chemotherapy drugs; and autoimmune conditions such as rheumatoid arthritis.[14]

In England (2017), there were 4,102 patients diagnosed with AML and 2,497 deaths registered where AML was the underlying cause.[15] AML accounts for less than 1% of all new cancer cases in the UK each year, but 2% of cancer deaths (2016-18).[16] [17] The five-year relative survival rate in England for AML is 14% for men and 16% for women.[18] The age standardised incidence rate of AML in England is 6.2 and 4.1 per 100,000 amongst males and females respectively.[19] In England (2021-22), there were 53,971 finished consultant episodes (FCEs) and 50,789 admissions for AML (ICD-10 code C92.0), which resulted in 44,564 day cases and 109,522 FCE bed days.[20]

Recommended Treatment Options

There are currently no NICE recommended maintenance treatments following HSCT for patients with FLT3-ITD mutated AML who are in first complete remission.

Clinical Trial Information

Trial	**MORPHO**; NCT02997202, 2016-001061-83; A Multi-center, Randomized, Double-blind, Placebo-controlled Phase III Trial of the FLT3 Inhibitor Gilteritinib Administered as Maintenance Therapy Following Allogeneic Transplant for Patients With FLT3/ITD AML **Phase III –** Active, not recruiting **Primary completion date:** July 2025 **Location(s):** 8 EU countries, UK, USA, Australia, and others
Trial Design	Randomised, parallel assignment, double-blind, quadruple-masked, placebo-controlled
Population	N=356; patients diagnosed with FLT3-ITD mutated AML who have undergone HSCT; aged 18 years and older.
Intervention(s)	Gilteritinib, oral administration once daily
Comparator(s)	Matched placebo
Outcome(s)	Primary outcome measure: • Relapse-free survival [Time frame: 96 months] See trial record for full list of other outcomes
Results (efficacy)	-
Results (safety)	-

Estimated Cost

Gilteritinib is already marketed in the UK for the treatment of adult patients who have relapsed or refractory acute AML with a FLT3 mutation. The hospital indicative cost of gilteritinib is £14,188.00 for a pack of 84 x 40mg tablets.[3,21]

Relevant Guidance

NICE Guidance

No relevant guidance identified.

NHS England (Policy/Commissioning) Guidance

- NHS England. 2013/14 NHS Standard Contract for Cancer: Chemotherapy (Adult). B15/S/a.
- NHS England. Clinical Commissioning Policy: Haematopoietic Stem Cell Transplantation. NHSCB/B04/P/a. April 2013.

Other Guidance

- European Leukaemia Network. Diagnosis and management of AML in adults: 2022 recommendations from an international expert panel. 2022.[22]
- European Society for Medical Oncology. Acute myeloid leukaemia in adult patients: ESMO clinical practice guidelines for diagnosis, treatment, and follow-up. 2020.[23]
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