

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Ivosidenib with azacitidine for untreated IDH1-positive acute myeloid leukaemia

Final scope

Remit/evaluation objective

To appraise the clinical and cost effectiveness of ivosidenib (with azacitidine) within its marketing authorisation for untreated IDH1-positive acute myeloid leukaemia when intensive induction chemotherapy is unsuitable.

Background

Acute myeloid leukaemia (AML) is a cancer of the blood and bone marrow. It is characterised by the overproduction of early immature myeloid cells (blasts). AML progresses quickly over weeks or months and is fatal if not treated. Anaemia, bleeding problems and serious infections are common symptoms of AML. People with AML also feel fatigued, which can affect daily life.

There are around 3,100 new diagnoses of AML in the UK every year.¹ The incidence rate is highest in people aged 85 to 89.¹ The 5-year survival rate for AML is 15%.² Isocitrate dehydrogenase 1 (IDH1) mutations are detected in 6% to 10% of people with AML and the mutation has been associated with a poorer prognosis.³

The aim of treatment for AML is to cure it. People who are fit enough can have intensive treatment. It is done in 2 phases: induction chemotherapy to reduce the number of blast cells, then consolidation chemotherapy to reduce the risk of recurrence. For people with good general health, the treatment options are intensive chemotherapy and allogeneic haematopoietic stem cell transplant (HSCT).

Over half of patients with AML are ineligible for intensive chemotherapy and stem cell transplants because of factors such as age or comorbidities. Other treatment options for these people include azacitidine, low dose cytarabine and venetoclax.

[NICE technology appraisal guidance 218](#) recommends azacitidine for adults who are not eligible for HSCT and have AML with 20% to 30% blasts and multilineage dysplasia, according to the World Health Organization classification.

[NICE technology appraisal guidance 765](#) recommends venetoclax with azacitidine for untreated AML in adults when intensive chemotherapy is unsuitable.

[NICE technology appraisal guidance 787](#) recommends venetoclax with low dose cytarabine for untreated AML in adults when intensive chemotherapy is unsuitable, if they have over 30% bone marrow blasts.

The technology

Ivosidenib (Tibsovo, Servier Laboratories) does not currently have a marketing authorisation in the UK for untreated IDH1-positive AML. It is being studied in a clinical trial in combination with azacitidine compared with placebo plus azacitidine in

adults with untreated AML and an IDH1 mutation when intensive induction chemotherapy is unsuitable.

Intervention(s)	Ivosidenib with azacitidine
Population(s)	Adults with untreated IDH1-positive AML when intensive induction chemotherapy is unsuitable
Comparators	<ul style="list-style-type: none"> • venetoclax with azacitidine • venetoclax with low dose cytarabine (if over 30% bone marrow blasts) • azacitidine (if not eligible for HSCT and have AML with 20% to 30% blasts and multilineage dysplasia) • low dose cytarabine
Outcomes	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> • overall survival • event-free survival • disease-free survival • response rates, including remission • blood transfusion dependence • rate of complete remission and complete remission with partial haematologic recovery • adverse effects of treatment • health-related quality of life.

Economic analysis	<p>The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year.</p> <p>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.</p> <p>Costs will be considered from an NHS and Personal Social Services perspective.</p> <p>The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account. The availability of any managed access arrangement for the intervention will be taken into account.</p> <p>The use of ivosidenib with azacitidine is conditional on the presence of the IDH1 mutation. The economic modelling should include the costs associated with diagnostic testing for IDH1 in people with AML who would not otherwise have been tested. A sensitivity analysis should be provided without the cost of the diagnostic test. See section 4.8 of the guidance development manual.</p>
Other considerations	<p>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.</p>
Related NICE recommendations	<p>Related technology appraisals:</p> <p>Venetoclax with low dose cytarabine for untreated acute myeloid leukaemia when intensive chemotherapy is unsuitable (2022) NICE technology appraisal guidance 787</p> <p>Venetoclax with azacitidine for untreated acute myeloid leukaemia when intensive chemotherapy is unsuitable (2022) NICE technology appraisal guidance 765</p> <p>Azacitidine for the treatment of myelodysplastic syndromes, chronic myelomonocytic leukaemia and acute myeloid leukaemia (2011) NICE technology appraisal guidance 218</p> <p>Related technology appraisals in development:</p> <p>Cedazuridine–decitabine for untreated acute myeloid leukaemia unsuitable for intensive chemotherapy. NICE technology appraisal guidance [ID6135]. Publication date to be confirmed.</p>

	<p>Related NICE guidelines:</p> <p>Haematological cancers: improving outcomes (2016) NICE guideline NG47</p> <p>Related quality standards:</p> <p>Haematological cancers (2017) NICE quality standard 150</p>
<p>Related National Policy</p>	<p>The NHS Long Term Plan (2019) NHS Long Term Plan</p> <p>NHS England (2023) Prescribed Specialised Services Manual Chapter 105 – Specialist cancer services (adults)</p> <p>NHS Digital (2022) NHS Outcomes Framework Indicators March 2022 release (England)</p>

References

1. Cancer Research UK: [acute myeloid leukaemia \(AML\) statistics](#). Accessed April 2023.
2. Cancer Research UK: [survival for acute myeloid leukaemia \(AML\)](#). Accessed April 2023.
3. Montesinos P, Recher C, Vives S, et al. (2022) [Ivosidenib and azacitidine in IDH1-mutated acute myeloid leukemia](#). New England Journal of Medicine 386(16): 1519–1531.