NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Ivosidenib with azacitidine for untreated IDH1-positive acute myeloid leukaemia ID6198

Draft scope

Draft 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

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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	• azacitidine alone for adults who are not eligible for HSCT and have AML with 20% to 30% blasts and multilineage dysplasia • low dose cytarabine • venetoclax with low dose cytarabine if people have over 30% bone marrow blasts • venetoclax with azacitidine • cedazuridine–decitabine (subject to NICE evaluation)
Outcomes	The outcome measures to be considered include: • 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	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. 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.

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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:** 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. 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 unsuitable for intensive chemotherapy. NICE technology appraisal guidance [ID6135]. Publication date to be confirmed. **Related NICE guidelines:** Haematological cancers: improving outcomes (2016) NICE guideline NG47. **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 (2023) Prescribed Specialised Services Manual Chapter 105 – Specialist cancer services (adults) NHS Digital (2022) NHS Outcomes Framework Indicators March 2022 release (England)

Questions for consultation

Have all relevant comparators for ivosidenib with azacitidine been included in the scope?

Should best supportive care be a comparator? If so, how should it be defined?

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Is low dose cytarabine a relevant comparator?

Would people with untreated IDH1-positive AML, for whom intensive induction chemotherapy is unsuitable, be able to have an HSCT?

Are the outcomes listed appropriate?

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

Is IDH1 routinely tested for in clinical practice?

What proportion of people with AML have the IDH1 mutation?

Where do you consider ivosidenib with azacitidine will fit into the existing care pathway for untreated IDH1-positive AML when intensive chemotherapy is unsuitable?

Would ivosidenib with azacitidine be a candidate for managed access?

Do you consider that the use of ivosidenib with azacitidine can result in any potential substantial health-related benefits that are unlikely to be included in the quality-adjusted life year (QALY) calculation?

Please identify the nature of the data that you understand to be available to enable the committee to take account of these benefits.

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 ivosidenib will be licensed;
- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, for example 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.

NICE intends to evaluate this technology through its Single Technology Appraisal process. (Information on NICE's health technology evaluation processes is available at https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-technology-appraisal-guidance/changes-to-health-technology-evaluation).

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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.

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