A study to investigate the effect of adding venetoclax to treatment with ivosidenib and azacitidine in patients with acute myeloid leukemia (AML) with a specific gene abnormality who have not previously been treated and who are not eligible for intensive chemotherapy.

Estado	Tipo de Participantes	Rangos de Edad
Reclutando	No aportado	Mayores de 64 , Adultos (18-64 años)
Género	**Fases**	**Participantes esperados**
Ambos	Fase III	96
Resultados	**Bajo nivel intervención**	**Enfermedad rara**
Sin resultados	No	No
Cobertura geográfica	**Ámbitos del ensayo**	**Terapia avanzada**
Sin determinar	tratamiento, seguridad, eficacia, farmacocinética, farmacodinamica	NO

Información

Identificador
2024-512753-24-00 (CTIS)

Cod. Protocolo
HOVON 173 AML

Área terapéutica
Enfermedades [C] - Cáncer [C04]|

Enfermedad investigada
Acute Myeloid Leukemia (AML)

Título Científico
HOVON 173 AML: Ivosidenib and Azacitidine With or Without Venetoclax in Adult Patients With Newly Diagnosed IDH1-Mutated AML or MDS/AML Considered Ineligible for Intensive Chemotherapy

Justificación

No aportado

Objetivo Principal

To assess if treatment with venetoclax, in combination with ivosidenib and azacitidine, prolongs event-free survival (EFS) in adult patients with newly diagnosed IDH1-mutated AML ineligible for intensive chemotherapy.

Variables de Evaluación Primaria

EFS in patients with newly diagnosed IDH1-mutated AML, measured from the date of randomization to the date of treatment failure, hematologic relapse from CR/CRh or death from any cause, whichever occurs first. Treatment failure is defined as lack of obtaining either CR or CRh by week 24

Momentos temporales de evaluación primaria

No aportado

Objetivo Secundario

1. To assess if treatment with venetoclax, in combination with ivosidenib and azacitidine, prolongs overall survival (OS) in adult patients with newly diagnosed IDH1-mutated AML ineligible for intensive chemotherapy
2.To assess if treatment with venetoclax, in combination with ivosidenib and azacitidine, increases the combined rate of complete remission (CR) and CR with partial hematologic recovery (CRh) in adult patients with newly diagnosed IDH1-mutated AML ineligible for intensive chemotherapy.
3.To assess if treatment with venetoclax, in combination with ivosidenib and azacitidine, increases the rate of complete remission (CR) in adult patients with newly diagnosed IDH1-mutated AML ineligible for intensive chemotherapy.
4.To evaluate the impact of venetoclax, in combination with ivosidenib and azacitidine, on the combined rate of CR and CR with incomplete hematologic recovery (CRi) in adult patients with newly diagnosed IDH1-mutated AML ineligible for intensive chemotherapy.
5.To assess if treatment with venetoclax, in combination with ivosidenib and azacitidine, increases the rate of CR, CR/CRh, and CR/CRi without measurable residual disease (CRMRD-, CR/CRhMRD-, and CR/CRiMRD-) in adult patients with newly diagnosed IDH1-mutated AML ineligible for intensive chemotherapy.
6.To assess if treatment with venetoclax, in combination with ivosidenib and azacitidine, shortens the time to response (CR, CR/CRh, or CR/CRi) in adult patients with newly diagnosed IDH1-mutated AML ineligible for intensive chemotherapy.
7.To assess if treatment with venetoclax, in combination with ivosidenib and azacitidine, prolongs duration of response (DoR :CR, CR/CRh, or CR/CRi) in adult patients with newly diagnosed IDH1-mutated AML ineligible for intensive chemotherapy.
8.To assess if treatment with venetoclax, in combination with ivosidenib and azacitidine, improves the transfusion independence rate (platelets and RBC) in adult patients with newly diagnosed IDH1-mutated AML ineligible for intensive chemotherapy.
9.To evaluate the pharmacokinetics of ivosidenib and venetoclax .
10.To evaluate the impact of venetoclax, in addition to ivosidenib and azacitidine, on quality of life using the European Organization for Research and Treatment of Cancer (EORTC) QLQ-C30 and EQ-5D-5L in adult patients

with newly diagnosed IDH1-mutated AML ineligible for intensive chemotherapy.
11.To evaluate the impact of venetoclax, in combination with ivosidenib and azacitidine, on cumulative incidence of relapse (CIR) and death (CID) in adult patients with newly diagnosed IDH1-mutated AML ineligible for intensive chemotherapy.
12.To evaluate EFS, OS, DoR, and rates of CR, CR/CRh and CR/CRi by prognostic variables, including clinical variables (e.g., age at randomization, sex, ECOG performance status, white blood cell count), 2022 European LeukemiaNet (ELN) risk groups, and by specific AML genotypes in adult patients with newly diagnosed IDH1-mutated AML ineligible for intensive chemotherapy.
13.To evaluate EFS, OS, rates of CR, CR/CRh, CR/CRi, CRMRD-, CR/CRhMRD-, CR/CRiMRD-, time to response, DoR, CIR, CID in adult patients with newly diagnosed IDH1-mutated MDS/AML ineligible for intensive chemotherapy
14.To evaluate transfusion independence rate (platelets and RBC) and safety objectives as defined below in adult patients with newly diagnosed IDH1-mutated MDS/AML ineligible for intensive chemotherapy.
15.To evaluate the pharmacodynamic effect of ivosidenib.
16.To assess safety of venetoclax, in combination with ivosidenib and azacitidine, in adult patients with newly diagnosed IDH1-mutated AML ineligible for intensive chemotherapy by evaluating incidence and severity of adverse events (AEs) according to Common Terminology Criteria for Adverse Events (CTCAE) version v5.0.
17.To assess time to hematopoietic recovery (absolute neutrophil counts [ANC] 0.5 and 1.0 x 109/L; platelet counts 50 and 100 x 109/L) after each treatment cycle (but at least after each of the first 6 cycles), in adult patients with newly diagnosed IDH1-mutated AML ineligible for intensive chemotherapy.
18.To assess number of patients requiring blood transfusions (platelets and RBC) and the number of units transfused, and the need for hospitalization in adult patients with newly diagnosed IDH1-mutated AML ineligible for intensive chemotherapy

Variables de Evaluación Secundaria

1. OS in patients with newly diagnosed IDH1-mutated AML measured from the date of randomization to the date of death from any cause.
2.Rate of CR/CRh in patients with newly diagnosed IDH1-mutated AML, defined as the proportion of AML patients with CR/CRh at any time-point during on treatment period.
3.Rate of CR in patients with newly diagnosed IDH1-mutated AML defned as the proportion of AML patients with CR at any time-point during protocol treatment
4.Rate of CR/CRi in patients with newly diagnosed IDH1-mutated AML, defined as the proportion of AML patients with CR/CRi at any time point during protocol treatment.
5.Rates of CR, CR/CRh, and CR/CRi without measurable residual disease (CRMRD-, CR/CRhMRD-, and CR/CRiMRD-) in patients with newly diagnosed IDH1-mutated AML, defined as the proportion of AML patients with CRMRD- / CR/CRhMRD- / CR/CRiMRD- at any time point during protocol treatment.
6.Time to achievement of response (CR, CR/CRh, and CR/CRi) in patients with newly diagnosed IDH1-mutated AML, defined as the time from randomization to 1st occurrence of response.
7.Duration of response (CR, CR/CRh, and CR/CRi) in patients with newly diagnosed IDH1-mutated AML, measured from the date of achievement of a response until the date of hematologic relapse or death from any cause.
8.Rate of transfusion independence (platelets and RBC) in patients with newly diagnosed IDH1-mutated AML, defined as the proportion of AML patients who achieved transfusion independence.
9.Ivosidenib and venetoclax plasma concentrations
10.Quality of life in patients with newly diagnosed IDH1-mutated AML as assessed by EORTC QLC-C30 and EQ-5D-5L forms.
11. CIR in adult patients with newly diagnosed IDH1-mutated AML, measured from the date of achievement of a remission (CR/CRh) until the date of hematologic relapse (i.e. not molecular relapse); death without relapse considered as competing risk
12. CID in patients with newly diagnosed IDH1-mutated AML, measured from the date of achievement of a remission (CR/CRh) to death without prior relapse; patients not known to have died will be censored at the date of last contact; relapse is considered as competing risk
13.EFS, OS, DoR and rates of CR, CR/CRh and CR/CRi across different subgroups in patients with newly diagnosed IDH1-mutated AML, where the groups are defined based on prognostic characteristics including clinical variables (e.g., age at randomization, sex, ECOG performance status, white blood cell count), risk category according to 2022

ELN recommendations, as well as specific AML genotypes.
14.EFS, OS, rates of CR, CR/CRh, CR/CRi, CRMRD-, CR/CRhMRD-, CR/CRiMRD-, time to response, DoR, CIR, CID in patients with newly diagnosed IDH1-mutated MDS/AML.
15.Transfusion independence rate and safety endpoints as defined below in patients with newly diagnosed IDH1-mutated MDS/AML.
16.2-HG-plasmaconcentraties
17.Frequency and severity of AE according to CTCAE version 5.0 in patients with newly diagnosed IDH1-mutated AML.
18.Time to hematopoietic recovery (absolute neutrophil counts 0.5 and 1.0 x 109/L; platelets 50 and 100 x 109/L) after each treatment cycle (but at least for each of the first 6 cycles) in patients with newly diagnosed IDH1-mutated AML, defined as the time from the start of the cycle until recovery.
19.Number of patients requiring transfusion (platelet and RBC) and number of units transfused, length of hospital stay, in patients with newly diagnosed IDH1-mutated AML.

Momentos temporales de evaluación secundaria

No aportado

Criterios de Inclusión

1. Patient with newly diagnosed IDH1-mutated AML, or IDH1-mutated MDS/AML according to the 2022 International Consensus Classification. Patients with AML with both IDH1 and IDH2 mutation are eligible as well 10. Men must agree to avoid to father a child (while on therapy and for 6 months after the final study drug administration). 11. Male patient must not donate sperm starting at screening and throughout the study period and for 6 months after the final study drug administration. 12. Able to understand and willing to sign an informed consent form (ICF). 13. Institutional Review Board/Independent Ethics Committee-approved written informed consent as per national regulations must be obtained from the patient prior to any study-related procedures (including consent for withdrawal of prohibited medication, if applicable). 2. Central confirmation of IDH1 mutation in one of the dedicated central genetic laboratories. 3. Age 18 years, no upper age limit. 4. Patient is ineligible for intensive induction chemotherapy by meeting at least 1 of the following criteria: 75 years of age: ineligible for intensive chemotherapy per physicians discretion (with an ECOG performance status 0-2. 18-74 years: patient is not eligible for standard chemotherapy because any of the following co-morbidities: ECOG performance status 2 or 3; Cardiac history of chronic heart failure requiring treatment; or with an ejection fraction 50%; or chronic stable angina; DLCO 65% or FEV1 65%; Creatinine clearance 30 mL/min to <45 ml/min calculated by the Cockcroft Gault formula; Moderate hepatic impairment with total bilirubin > 1.5 to < 3.0 x upper limit of normal (ULN); Any other comorbidity that the local physician assesses to be incompatible with intensive chemotherapy. 5. Patient must have a projected life expectancy of at least 12 weeks (as assessed by the treating physician). 6. Patient must have a white cell blood (WBC) count of < 25 x 109/L. 7. Adequate renal function as evidenced by serum creatinine 2.0 × upper limit of norm (ULN) or creatinine clearance 30 mL/min based on the Cockcroft-Gault glomerular filtration rate (GFR). 8. Adequate hepatic function as evidenced by: Serum total bilirubin 3.0 × ULN unless considered due to Gilberts disease, or leukemic involvement ; Aspartate aminotransferase (AST), alanine aminotransferase (ALT), and alkaline phosphatase (ALP) 3.0 × ULN, unless considered due to leukemic involvement. 9. Female patients: must be of nonchildbearing potential or when of childbearing potential must agree to avoid pregnancy during the study and for 6 months after the final study drug administration; must agree not to breastfeed starting at screening and throughout the study period, and for 2 months and 1 week after the final study drug administration; must agree not to donate ova starting at screening and throughout the study period, and for 6 months after the final study drug administration.

Criterios de Exclusión

1. Subject has previously been treated for AML; a treatment period with hydroxyurea to control WBC counts is allowed; prior treatment with a hypomethylating agent for MDS-EB is not allowed; prior treatment with erythropoiesis-stimulating agents or luspatercept for MDS is allowed. 10. Immediate life-threatening, severe complications of leukemia such as uncontrolled bleeding and/or disseminated intravascular coagulation. 11. Conditions that limit the ingestion or gastrointestinal absorption of orally administered drugs. 12. Patient with a currently active second malignancy. However, patients with the following history/concurrent conditions are allowed: Basal or squamous cell carcinoma of the skin; Carcinoma in situ of the cervix; Carcinoma in situ of the breast; Incidental histologic finding of prostate cancer. 13. Receipt of live, attenuated vaccine within 30 days prior to the study inclusion. 14. Severe neurological or psychiatric disorder interfering with ability to give an informed consent. 15. Contraindication to any of the anti-leukemic agents used (as per SmPC) 16. Participation in other prospective studies with anti-leukemic and/or investigational agents. 17. Patient taking Dabigatran unless they can be transferred to other medications at least 3 days prior to dosing. Patients taking other P-gP transporter-sensitive medications should be properly monitored during the study if they cannot be transferred to other medications. 18. Patients taking known strong cytochrome P450 (CYP) 3A4 inducers unless they can be transferred to other medications within 5 half-lives prior to dosing. 19. The patient is a pregnant or lactating woman, or plans to become pregnant during the study. 2. Acute promyelocytic leukemia (APL) with t(15;17)(q24.1;q21.2); PML-RARA; or one of the other pathognomonic variant chromosomal translocations / fusion genes. 20. Patient who has once been screened and randomized into this HO173 trial but was considered ineligible cannot re-enter this trial at a later date. 3. AML with BCR-ABL1; or myeloid blast crisis of CML. 4. Significant active cardiac disease within 3 months prior to the start of study treatment, including: New York Heart Association (NYHA) class III or IV congestive heart failure; Myocardial infarction; Unstable angina; Severe cardiac arrhythmias; Congenital long QT syndrome of family member with this condition; QTcF >450 msec on screening electrogram for males and >470 msec on screening electrogram for females (mean of triplicate recordings, calculated using Fridericias correction). 5. Familial history of sudden death or polymorphic ventricular arrhythmia 6. Severe obstructive or restrictive ventilation disorder. 7. History of stroke or intracranial hemorrhage within 6 months prior to randomization. 8. Clinical symptoms suggestive of active central nervous system (CNS) leukemia or known CNS leukemia. Evaluation of cerebrospinal fluid (CSF) during screening is only required if there is a clinical suspicion of CNS involvement by leukemia during screening. 9. Active infection, including hepatitis B or hepatitis C or Human Immunodeficiency Virus (HIV) infection, that is uncontrolled prior to first dose of study treatment and may interfere with the study objectives or which could expose the patient to undue risk through the participation in the clinical trial; an infection controlled with an approved antibiotic/ antiviral/ antifungal treatment that is not a strong or moderate CYP3A inducer is allowed. Patients with COVID-19 infection can be enrolled, if the patient has no symptoms and was tested negative twice by PCR test prior to inclusion in the trial.

Calendario

(Última actualización: 02/06/2026)

Autorización	Inicio de Ensayo	Inclusión Primer Paciente	Interrumpido	Reiniciado
08/08/2025	14/01/2026	10/03/2026	No aportado	No aportado

Fin de reclutamiento	Fin prematuro (España)	Fin prematuro (Global)	Fin del ensayo en España	Fin del ensayo global
No aportado	No aportado	No aportado	No aportado	No aportado

Promotor

Hemato-Oncologie voor Volwassenen Nederland (Hovon) Stichting Netherlands

Dr. Molewaterplein 40

Contact Person

HOVON

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Monetary support: N/A

Tipo de promotor: No comercial

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Centros

Activo (15/12/2025)

Hospital Clinic De Barcelona

Barcelona

BARCELONA

Hematology

Activo (19/12/2025)

Hospital Clinico Universitario De Valencia

Valencia

VALENCIA

Hematology

No iniciado (--/--/----)

Hospital De La Santa Creu I Sant Pau

Barcelona

BARCELONA

Hematology

No iniciado (--/--/----)

Institut Catala D'oncologia

Badalona

BARCELONA

Hematology

No iniciado (--/--/----)

Institut Catala D'oncologia

Girona

GERONA

Hematology and hematherapy

Medicamentos

AZACITIDINE
POWDER FOR SUSPENSION FOR INJECTION
SUBCUTANEOUS

-
Principios Activos: N/A

Experimental

Venclyxto 10 mg film-coated tablets
FILM-COATED TABLET
ORAL

Código ATC: L01XX52 - VENETOCLAX
Principios Activos: N/A

Experimental

Venclyxto 100 mg film-coated tablets
FILM-COATED TABLET
ORAL

Código ATC: L01XX52 - VENETOCLAX
Principios Activos: N/A

Experimental

Venclyxto 50 mg film-coated tablets
FILM-COATED TABLET
ORAL

Código ATC: L01XX52 - VENETOCLAX
Principios Activos: N/A

Experimental

AG-120/S95031 250mg film-coated tablet
FILM-COATED TABLET
ORAL USE

-
Principios Activos: N/A

Huérfano
Experimental

Sin resultados

A study to investigate the effect of adding venetoclax to treatment with ivosidenib and azacitidine in patients with acute myeloid leukemia (AML) with a specific gene abnormality who have not previously been treated and who are not eligible for intensive chemotherapy.

State	Type of participants	Age Ranges
Recruiting	Not provided	Older than 64 , Adults (18-64 years)
Gender	**Phases**	**Expected Participants**
Both	Phase III	96
Results	**Low level of intervention**	**Rare disease**
No results	No	No
Geographic coverage	**Areas of the study**	**Advanced therapy**
Undetermined	treatment, safety, effectiveness, pharmacokinetics, pharmacodynamics	NO

Information

Identifier
2024-512753-24-00 (CTIS)

Protocol Code
HOVON 173 AML

Therapeutic area
Diseases [C] - Cancer [C04]|

Investigated Disease
Acute Myeloid Leukemia (AML)

Scientific Title
HOVON 173 AML: Ivosidenib and Azacitidine With or Without Venetoclax in Adult Patients With Newly Diagnosed IDH1-Mutated AML or MDS/AML Considered Ineligible for Intensive Chemotherapy

Rationale

Not provided

Main Objective

To assess if treatment with venetoclax, in combination with ivosidenib and azacitidine, prolongs event-free survival (EFS) in adult patients with newly diagnosed IDH1-mutated AML ineligible for intensive chemotherapy.

Primary Endpoints

EFS in patients with newly diagnosed IDH1-mutated AML, measured from the date of randomization to the date of treatment failure, hematologic relapse from CR/CRh or death from any cause, whichever occurs first. Treatment failure is defined as lack of obtaining either CR or CRh by week 24

Temporary moments of secondary assessment

Not provided

Secondary Objective

1. To assess if treatment with venetoclax, in combination with ivosidenib and azacitidine, prolongs overall survival (OS) in adult patients with newly diagnosed IDH1-mutated AML ineligible for intensive chemotherapy
2.To assess if treatment with venetoclax, in combination with ivosidenib and azacitidine, increases the combined rate of complete remission (CR) and CR with partial hematologic recovery (CRh) in adult patients with newly diagnosed IDH1-mutated AML ineligible for intensive chemotherapy.
3.To assess if treatment with venetoclax, in combination with ivosidenib and azacitidine, increases the rate of complete remission (CR) in adult patients with newly diagnosed IDH1-mutated AML ineligible for intensive chemotherapy.
4.To evaluate the impact of venetoclax, in combination with ivosidenib and azacitidine, on the combined rate of CR and CR with incomplete hematologic recovery (CRi) in adult patients with newly diagnosed IDH1-mutated AML ineligible for intensive chemotherapy.
5.To assess if treatment with venetoclax, in combination with ivosidenib and azacitidine, increases the rate of CR, CR/CRh, and CR/CRi without measurable residual disease (CRMRD-, CR/CRhMRD-, and CR/CRiMRD-) in adult patients with newly diagnosed IDH1-mutated AML ineligible for intensive chemotherapy.
6.To assess if treatment with venetoclax, in combination with ivosidenib and azacitidine, shortens the time to response (CR, CR/CRh, or CR/CRi) in adult patients with newly diagnosed IDH1-mutated AML ineligible for intensive chemotherapy.
7.To assess if treatment with venetoclax, in combination with ivosidenib and azacitidine, prolongs duration of response (DoR :CR, CR/CRh, or CR/CRi) in adult patients with newly diagnosed IDH1-mutated AML ineligible for intensive chemotherapy.
8.To assess if treatment with venetoclax, in combination with ivosidenib and azacitidine, improves the transfusion independence rate (platelets and RBC) in adult patients with newly diagnosed IDH1-mutated AML ineligible for intensive chemotherapy.
9.To evaluate the pharmacokinetics of ivosidenib and venetoclax .
10.To evaluate the impact of venetoclax, in addition to ivosidenib and azacitidine, on quality of life using the European Organization for Research and Treatment of Cancer (EORTC) QLQ-C30 and EQ-5D-5L in adult patients

with newly diagnosed IDH1-mutated AML ineligible for intensive chemotherapy.
11.To evaluate the impact of venetoclax, in combination with ivosidenib and azacitidine, on cumulative incidence of relapse (CIR) and death (CID) in adult patients with newly diagnosed IDH1-mutated AML ineligible for intensive chemotherapy.
12.To evaluate EFS, OS, DoR, and rates of CR, CR/CRh and CR/CRi by prognostic variables, including clinical variables (e.g., age at randomization, sex, ECOG performance status, white blood cell count), 2022 European LeukemiaNet (ELN) risk groups, and by specific AML genotypes in adult patients with newly diagnosed IDH1-mutated AML ineligible for intensive chemotherapy.
13.To evaluate EFS, OS, rates of CR, CR/CRh, CR/CRi, CRMRD-, CR/CRhMRD-, CR/CRiMRD-, time to response, DoR, CIR, CID in adult patients with newly diagnosed IDH1-mutated MDS/AML ineligible for intensive chemotherapy
14.To evaluate transfusion independence rate (platelets and RBC) and safety objectives as defined below in adult patients with newly diagnosed IDH1-mutated MDS/AML ineligible for intensive chemotherapy.
15.To evaluate the pharmacodynamic effect of ivosidenib.
16.To assess safety of venetoclax, in combination with ivosidenib and azacitidine, in adult patients with newly diagnosed IDH1-mutated AML ineligible for intensive chemotherapy by evaluating incidence and severity of adverse events (AEs) according to Common Terminology Criteria for Adverse Events (CTCAE) version v5.0.
17.To assess time to hematopoietic recovery (absolute neutrophil counts [ANC] 0.5 and 1.0 x 109/L; platelet counts 50 and 100 x 109/L) after each treatment cycle (but at least after each of the first 6 cycles), in adult patients with newly diagnosed IDH1-mutated AML ineligible for intensive chemotherapy.
18.To assess number of patients requiring blood transfusions (platelets and RBC) and the number of units transfused, and the need for hospitalization in adult patients with newly diagnosed IDH1-mutated AML ineligible for intensive chemotherapy

Secondary Endpoints

1. OS in patients with newly diagnosed IDH1-mutated AML measured from the date of randomization to the date of death from any cause.
2.Rate of CR/CRh in patients with newly diagnosed IDH1-mutated AML, defined as the proportion of AML patients with CR/CRh at any time-point during on treatment period.
3.Rate of CR in patients with newly diagnosed IDH1-mutated AML defned as the proportion of AML patients with CR at any time-point during protocol treatment
4.Rate of CR/CRi in patients with newly diagnosed IDH1-mutated AML, defined as the proportion of AML patients with CR/CRi at any time point during protocol treatment.
5.Rates of CR, CR/CRh, and CR/CRi without measurable residual disease (CRMRD-, CR/CRhMRD-, and CR/CRiMRD-) in patients with newly diagnosed IDH1-mutated AML, defined as the proportion of AML patients with CRMRD- / CR/CRhMRD- / CR/CRiMRD- at any time point during protocol treatment.
6.Time to achievement of response (CR, CR/CRh, and CR/CRi) in patients with newly diagnosed IDH1-mutated AML, defined as the time from randomization to 1st occurrence of response.
7.Duration of response (CR, CR/CRh, and CR/CRi) in patients with newly diagnosed IDH1-mutated AML, measured from the date of achievement of a response until the date of hematologic relapse or death from any cause.
8.Rate of transfusion independence (platelets and RBC) in patients with newly diagnosed IDH1-mutated AML, defined as the proportion of AML patients who achieved transfusion independence.
9.Ivosidenib and venetoclax plasma concentrations
10.Quality of life in patients with newly diagnosed IDH1-mutated AML as assessed by EORTC QLC-C30 and EQ-5D-5L forms.
11. CIR in adult patients with newly diagnosed IDH1-mutated AML, measured from the date of achievement of a remission (CR/CRh) until the date of hematologic relapse (i.e. not molecular relapse); death without relapse considered as competing risk
12. CID in patients with newly diagnosed IDH1-mutated AML, measured from the date of achievement of a remission (CR/CRh) to death without prior relapse; patients not known to have died will be censored at the date of last contact; relapse is considered as competing risk
13.EFS, OS, DoR and rates of CR, CR/CRh and CR/CRi across different subgroups in patients with newly diagnosed IDH1-mutated AML, where the groups are defined based on prognostic characteristics including clinical variables (e.g., age at randomization, sex, ECOG performance status, white blood cell count), risk category according to 2022

ELN recommendations, as well as specific AML genotypes.
14.EFS, OS, rates of CR, CR/CRh, CR/CRi, CRMRD-, CR/CRhMRD-, CR/CRiMRD-, time to response, DoR, CIR, CID in patients with newly diagnosed IDH1-mutated MDS/AML.
15.Transfusion independence rate and safety endpoints as defined below in patients with newly diagnosed IDH1-mutated MDS/AML.
16.2-HG-plasmaconcentraties
17.Frequency and severity of AE according to CTCAE version 5.0 in patients with newly diagnosed IDH1-mutated AML.
18.Time to hematopoietic recovery (absolute neutrophil counts 0.5 and 1.0 x 109/L; platelets 50 and 100 x 109/L) after each treatment cycle (but at least for each of the first 6 cycles) in patients with newly diagnosed IDH1-mutated AML, defined as the time from the start of the cycle until recovery.
19.Number of patients requiring transfusion (platelet and RBC) and number of units transfused, length of hospital stay, in patients with newly diagnosed IDH1-mutated AML.

Temporary moments of secondary assessment

Not provided

Inclusion criteria

1. Patient with newly diagnosed IDH1-mutated AML, or IDH1-mutated MDS/AML according to the 2022 International Consensus Classification. Patients with AML with both IDH1 and IDH2 mutation are eligible as well 10. Men must agree to avoid to father a child (while on therapy and for 6 months after the final study drug administration). 11. Male patient must not donate sperm starting at screening and throughout the study period and for 6 months after the final study drug administration. 12. Able to understand and willing to sign an informed consent form (ICF). 13. Institutional Review Board/Independent Ethics Committee-approved written informed consent as per national regulations must be obtained from the patient prior to any study-related procedures (including consent for withdrawal of prohibited medication, if applicable). 2. Central confirmation of IDH1 mutation in one of the dedicated central genetic laboratories. 3. Age 18 years, no upper age limit. 4. Patient is ineligible for intensive induction chemotherapy by meeting at least 1 of the following criteria: 75 years of age: ineligible for intensive chemotherapy per physicians discretion (with an ECOG performance status 0-2. 18-74 years: patient is not eligible for standard chemotherapy because any of the following co-morbidities: ECOG performance status 2 or 3; Cardiac history of chronic heart failure requiring treatment; or with an ejection fraction 50%; or chronic stable angina; DLCO 65% or FEV1 65%; Creatinine clearance 30 mL/min to <45 ml/min calculated by the Cockcroft Gault formula; Moderate hepatic impairment with total bilirubin > 1.5 to < 3.0 x upper limit of normal (ULN); Any other comorbidity that the local physician assesses to be incompatible with intensive chemotherapy. 5. Patient must have a projected life expectancy of at least 12 weeks (as assessed by the treating physician). 6. Patient must have a white cell blood (WBC) count of < 25 x 109/L. 7. Adequate renal function as evidenced by serum creatinine 2.0 × upper limit of norm (ULN) or creatinine clearance 30 mL/min based on the Cockcroft-Gault glomerular filtration rate (GFR). 8. Adequate hepatic function as evidenced by: Serum total bilirubin 3.0 × ULN unless considered due to Gilberts disease, or leukemic involvement ; Aspartate aminotransferase (AST), alanine aminotransferase (ALT), and alkaline phosphatase (ALP) 3.0 × ULN, unless considered due to leukemic involvement. 9. Female patients: must be of nonchildbearing potential or when of childbearing potential must agree to avoid pregnancy during the study and for 6 months after the final study drug administration; must agree not to breastfeed starting at screening and throughout the study period, and for 2 months and 1 week after the final study drug administration; must agree not to donate ova starting at screening and throughout the study period, and for 6 months after the final study drug administration.

Exclusion criteria

1. Subject has previously been treated for AML; a treatment period with hydroxyurea to control WBC counts is allowed; prior treatment with a hypomethylating agent for MDS-EB is not allowed; prior treatment with erythropoiesis-stimulating agents or luspatercept for MDS is allowed. 10. Immediate life-threatening, severe complications of leukemia such as uncontrolled bleeding and/or disseminated intravascular coagulation. 11. Conditions that limit the ingestion or gastrointestinal absorption of orally administered drugs. 12. Patient with a currently active second malignancy. However, patients with the following history/concurrent conditions are allowed: Basal or squamous cell carcinoma of the skin; Carcinoma in situ of the cervix; Carcinoma in situ of the breast; Incidental histologic finding of prostate cancer. 13. Receipt of live, attenuated vaccine within 30 days prior to the study inclusion. 14. Severe neurological or psychiatric disorder interfering with ability to give an informed consent. 15. Contraindication to any of the anti-leukemic agents used (as per SmPC) 16. Participation in other prospective studies with anti-leukemic and/or investigational agents. 17. Patient taking Dabigatran unless they can be transferred to other medications at least 3 days prior to dosing. Patients taking other P-gP transporter-sensitive medications should be properly monitored during the study if they cannot be transferred to other medications. 18. Patients taking known strong cytochrome P450 (CYP) 3A4 inducers unless they can be transferred to other medications within 5 half-lives prior to dosing. 19. The patient is a pregnant or lactating woman, or plans to become pregnant during the study. 2. Acute promyelocytic leukemia (APL) with t(15;17)(q24.1;q21.2); PML-RARA; or one of the other pathognomonic variant chromosomal translocations / fusion genes. 20. Patient who has once been screened and randomized into this HO173 trial but was considered ineligible cannot re-enter this trial at a later date. 3. AML with BCR-ABL1; or myeloid blast crisis of CML. 4. Significant active cardiac disease within 3 months prior to the start of study treatment, including: New York Heart Association (NYHA) class III or IV congestive heart failure; Myocardial infarction; Unstable angina; Severe cardiac arrhythmias; Congenital long QT syndrome of family member with this condition; QTcF >450 msec on screening electrogram for males and >470 msec on screening electrogram for females (mean of triplicate recordings, calculated using Fridericias correction). 5. Familial history of sudden death or polymorphic ventricular arrhythmia 6. Severe obstructive or restrictive ventilation disorder. 7. History of stroke or intracranial hemorrhage within 6 months prior to randomization. 8. Clinical symptoms suggestive of active central nervous system (CNS) leukemia or known CNS leukemia. Evaluation of cerebrospinal fluid (CSF) during screening is only required if there is a clinical suspicion of CNS involvement by leukemia during screening. 9. Active infection, including hepatitis B or hepatitis C or Human Immunodeficiency Virus (HIV) infection, that is uncontrolled prior to first dose of study treatment and may interfere with the study objectives or which could expose the patient to undue risk through the participation in the clinical trial; an infection controlled with an approved antibiotic/ antiviral/ antifungal treatment that is not a strong or moderate CYP3A inducer is allowed. Patients with COVID-19 infection can be enrolled, if the patient has no symptoms and was tested negative twice by PCR test prior to inclusion in the trial.

Calendar

(Last Update: 02/06/2026)

Authorization	Start of Trial	First patient inclusion	Halted	Restarted
08/08/2025	14/01/2026	10/03/2026	Not aported	Not aported

End of recruitment	Premature end (Spain)	Premature End (Global)	Trial end (Spain)	Trial end (Global)
Not aported	Not aported	Not aported	Not aported	Not aported

Sponsor

Hemato-Oncologie voor Volwassenen Nederland (Hovon) Stichting Netherlands

Dr. Molewaterplein 40

Contact Person

HOVON

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hovon@erasmusmc.nl

Monetary support: N/A

Sponsor type: No commercial

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Sites

Active (15/12/2025)

Hospital Clinic De Barcelona

Barcelona

BARCELONA

Hematology

Active (19/12/2025)

Hospital Clinico Universitario De Valencia

Valencia

VALENCIA

Hematology

not initialized (--/--/----)

Hospital De La Santa Creu I Sant Pau

Barcelona

BARCELONA

Hematology

not initialized (--/--/----)

Institut Catala D'oncologia

Badalona

BARCELONA

Hematology

not initialized (--/--/----)

Institut Catala D'oncologia

Girona

GERONA

Hematology and hematherapy

Medication

AZACITIDINE
POWDER FOR SUSPENSION FOR INJECTION
SUBCUTANEOUS

-

Active Principles: N/A

Experimental

Venclyxto 10 mg film-coated tablets
FILM-COATED TABLET
ORAL

ATC code: L01XX52 - VENETOCLAX
Active Principles: N/A

Experimental

Venclyxto 100 mg film-coated tablets
FILM-COATED TABLET
ORAL

ATC code: L01XX52 - VENETOCLAX
Active Principles: N/A

Experimental

Venclyxto 50 mg film-coated tablets
FILM-COATED TABLET
ORAL

ATC code: L01XX52 - VENETOCLAX
Active Principles: N/A

Experimental

AG-120/S95031 250mg film-coated tablet
FILM-COATED TABLET
ORAL USE

-

Active Principles: N/A

Orphan Experimental

No results