A Randomized, Open-labelled, Multicenter Trial Evaluating Efficacy and Safety of A Reduced Venetoclax Exposure To Seven Days Versus Standard Continuous Venetoclax Exposure Combined With Azacitidine in Treatment Naïve Subjects with Acute Myeloid Leukemia Who Are Ineligible for Intensive Induction

Estado	**Tipo de Participantes**	**Rangos de Edad**
Reclutando	No aportado	Mayores de 64
Género	**Fases**	**Participantes esperados**
Ambos	Fase III	131
Resultados	**Bajo nivel intervención**	**Enfermedad rara**
Sin resultados	Si	No
Cobertura geográfica	**Ámbitos del ensayo**	**Terapia avanzada**
Sin determinar	seguridad, eficacia, farmacoeconómica	NO

Información

Identificador
2025-521634-29-00 (CTIS)

Cod. Protocolo
CSET 2025/4132

Área terapéutica
·Enfermedades [C] - Hematología [C15]
·Enfermedades [C] - Patologías del sistema inmunitario [C20]

Enfermedad investigada
ONCOLOGY
Acute Myeloid Leukemia

Título Científico

A Randomized, Open-labelled, Multicenter Trial Evaluating Efficacy and Safety of A Reduced Venetoclax Exposure To Seven Days Versus Standard Continuous Venetoclax Exposure Combined With Azacitidine in Treatment Naïve Subjects with Acute Myeloid Leukemia Who Are Ineligible for Intensive Induction (SEVENAZA)

Justificación

No aportado

Objetivo Principal

To demonstrate the non-inferiority of a reduced VEN exposure to 7 days of AZA every 28 days cycle from the first cycle in terms of composite complete remission rate (complete remission + complete remission with incomplete marrow recovery CR/CRi) at any time point during the first 6 cycles compared to conventional continuous 28-day exposure in treatment naïve AML patients.

Variables de Evaluación Primaria

The proportion of subjects with complete remission or complete remission with incomplete marrow recovery (CR/CRi) will be calculated based on current IWG criteria for AML (Cheson et al J Clin Oncol 2003)

Momentos temporales de evaluación primaria

No aportado

Objetivo Secundario

To evaluate OS and EFS (7-day VEN dosing and conventional 28-day dosing). To evaluate early mortality at Day 60 (7-day VEN dosing vs conventional 28-day dosing) To evaluate time to first response and time to best response (7-day VEN dosing and conventional 28-day dosing). To evaluate DoR (7-day VEN dosing and conventional 28-day dosing). To evaluate quality-of-life (according to EQ5D-5L and QLQ-ELD14 questionnaires). To evaluate, in patients who reached CR/CRi, dosing schedule modification, delays (>2 days) or discontinuation (7-day VEN dosing and conventional 28-day dosing). To evaluate toxicity of special interest and healthcare consumption especially in patients who reached CR/CRi (7-day VEN dosing and conventional 28-day dosing). Health economic analysis: cost-minimization analysis and cost-effectiveness analysis (only for included patients treated in France)

Variables de Evaluación Secundaria

Overall survival (OS). Event-Free Survival (EFS). Early mortality rate at Day 60. Time to first response. Time to best response. Duration of response (DoR). Health-Related Quality of Life (HRQoL) assessed by the EORTC QLQ-ELD14 and EuroQol EQ-5D-5L questionnaires Scheme modification will be defined as the proportion of CR/CRi patients that presented treatment modification not authorized by protocol as VEN schedule modification (dose, duration), delay >2 days from the initial Day of the subsequent cycle and/or temporary/definitive VEN discontinuation. Toxicity evaluated by platelet transfusion, febrile neutropenia or severe infection episodes, hospitalization

requirement and hospitalization length stay Incremental costs and QALY and ICER (/QALY) (only for included patients treated in France)

Momentos temporales de evaluación secundaria

No aportado

Criterios de Inclusión

Subject must have confirmation of AML by WHO 2022 criteria and be ineligible for treatment with a standard cytarabine and anthracycline induction regimen due to age or co-morbidities. Subject must voluntarily sign and date an informed consent, approved by an Independent Ethics Committee (IEC)/Institutional Review Board (IRB), prior to the initiation of any screening or study specific procedures. Patients must be affiliated to a social security system or beneficiary of the same (only for France) Patients shall be eligible to undergo Azacitidine and Venetoclax treatment and BM aspiration. Patients who do not consent to a BM aspiration will not be eligible (diagnosis and follow up) Subject must be 60 years of age. Subject must have a projected life expectancy of at least 12 weeks. Subject must be considered ineligible for induction therapy defined by the following: 75 years of age OR 60 to 74 years of age with at least one of the following co-morbidities: ECOG Performance Status of 2 or 3; Cardiac history of CHF requiring treatment or Ejection Fraction 50% or chronic stable angina; DLCO 65% or FEV1 65%; Severe Renal impairement: Creatinine clearance 30 mL/min to < 45 ml/min Moderate hepatic impairment with total bilirubin > 1.5 to 3.0 × ULN Any other comorbidity that the physician judges to be incompatible with intensive chemotherapy must be reviewed and approved by the coordinator before study enrollment Subject must have an Eastern Cooperative Oncology Group (ECOG) Performance status (Appendix 4): 0 to 2 for subject 75 years of age. 0 to 3 for subject 60 to 74 years of age. Subject must have adequate renal function as demonstrated by a creatinine clearance 30 mL/min; calculated by the Cockcroft Gault formula. Subject must have adequate liver function as demonstrated by: Aspartate aminotransferase (AST) 3.0 × ULN* alanine aminotransferase (ALT) 3.0 × ULN* bilirubin 1.5 × ULN* * Unless considered to be due to leukemic organ involvement. Subjects who are < 75 years of age may have a bilirubin of 3.0 × ULN Female subjects must be either postmenopausal (amenorrhea for at least 12 months with no alternative medical reasons) or surgically sterile (bilateral oophorectomy, bilateral salpingectomy or hysterectomy). Non-sterile male subjects must use contraceptive methods with partner(s) prior to beginning study drug administration and continuing up to 90 days after the last dose of study drug. Male subjects must agree to refrain from sperm donation from initial study drug administration until 90 days after the last dose of study drug.

Criterios de Exclusión

Subject has received treatment with the following: - Hypomethylating agent, venetoclax and/or any chemo-therapeutic agent for Myelodysplastic syndrome (MDS). - Chimeric Antigen Receptor (CAR)-T cell therapy. - Experimental therapies for MDS or Acute Myeloid Leukemia (AML). - Current participation in another research or observational study Subject has acute promyelocytic leukemia Subject has known active CNS involvement with AML. Known human immunodeficiency virus HIV Known hepatitis B or C infection with the exception of those with an undetectable viral load within 3 months. Subject has a cardiovascular disability status of New York Heart Association Class 2. Class 2 is defined as cardiac disease in which patients are comfortable at rest but ordinary physical activity results in fatigue, palpitations, dyspnea, or anginal pain. Subject has chronic respiratory disease that requires continuous oxygen, or significant history of renal, neurologic, psychiatric, endocrinologic, metabolic, immunologic, hepatic, cardiovascular disease, or any other medical condition that in the opinion of the investigator would adversely affect his/her participating in this study. NB: patients with IDH1-mutant AML will not be formally excluded from the study. However, investigators are strongly encouraged to prefer treatment combining Azacitidine and Ivosidenib (AGILE phase III trial). Subject has a malabsorption syndrome or other condition that precludes enteral route of administration. Subject exhibits evidence of other clinically significant uncontrolled systemic infection requiring

therapy (viral, bacterial or fungal). Subject has a history of other malignancies prior to study entry, with the exception of: Adequately treated in situ carcinoma of the cervix uteri or carcinoma in situ of breast; Basal cell carcinoma of the skin or localized squamous cell carcinoma of the skin; Previous malignancy confined and surgically resected (or treated with other modalities) with curative intent and considered in remission for 3 years. Subject has a white blood cell count > 25 × 109/L. (Hydroxyurea is permitted to meet this criterion.) Subject has hypersensitivity to the active substances of any of the excipients Patient under guardianship or deprived of his liberty by a judicial or administrative decision or incapable of giving its consent. Subject has history of myeloproliferative neoplasm [MPN], including myelofibrosis, essential thrombocythemia, polycythemia vera, chronic myeloid leukemia (CML) with or without BCR-ABL1 translocation and AML with BCR-ABL1 translocation. Subject has favorable risk cytogenetics such as t(8;21), inv(16), t(16;16) or t(15;17) as per the NCCN Guidelines Version 2, 2016 for Acute Myeloid Leukemia.

Calendario

(Última actualización: 03/09/2026)

Autorización	Inicio de Ensayo	Inclusión Primer Paciente	Interrumpido	Reiniciado
13/02/2026	02/03/2026	02/03/2026	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

Institut Gustave Roussy France

114 Rue Edouard Vaillant

Contact Person

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Monetary support: N/A

Tipo de promotor: No comercial

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Centros

Activo (26/03/2026)

Hospital Clinico Universitario De Valencia

Valencia

VALENCIA

ONCOLOGIA

Activo (29/04/2026)

Hospital General Universitario De Albacete

Albacete

ALBACETE

ONCOLOGIA

Activo (22/04/2026)

Hospital General Universitario Dr. Balmis

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ALICANTE

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MADRID

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Activo (26/03/2026)

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Cordoba

CÓRDOBA

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Activo (02/03/2026)

Hospital Universitario Y Politecnico La Fe

Valencia

VALENCIA

ONCOLOGIA

Activo (24/03/2026)

Hospital Universitario 12 De Octubre

Madrid

MADRID

ONCOLOGIA

Activo (26/03/2026)

University Hospital Virgen Del Rocio S.L.

Sevilla

SEVILLA

ONCOLOGIA

Medicamentos

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

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

Experimental

Vidaza 25 mg/ml powder for suspension for injection
SUSPENSION FOR INJECTION
INTRAVENOUS/SUBCUTANEOUS/INTRAMUSCULAR

Código ATC: L01BC07 - AZACITIDINA
Principios Activos: N/A

Experimental

Sin resultados

A Randomized, Open-labelled, Multicenter Trial Evaluating Efficacy and Safety of A Reduced Venetoclax Exposure To Seven Days Versus Standard Continuous Venetoclax Exposure Combined With Azacitidine in Treatment Naïve Subjects with Acute Myeloid Leukemia Who Are Ineligible for Intensive Induction

State	Type of participants	Age Ranges
Recruiting	Not provided	Older than 64
Gender	**Phases**	**Expected Participants**
Both	Phase III	131
Results	**Low level of intervention**	**Rare disease**
No results	Yes	No
Geographic coverage	**Areas of the study**	**Advanced therapy**
Undetermined	safety, effectiveness, pharmacoeconomic	NO

Information

Identifier
2025-521634-29-00 (CTIS)

Protocol Code
CSET 2025/4132

Therapeutic area
·Diseases [C] - Hemic and Lymphatic Diseases [C15]
·Diseases [C] - Immune System Diseases [C20]

Investigated Disease
ONCOLOGY
Acute Myeloid Leukemia

Scientific Title

A Randomized, Open-labelled, Multicenter Trial Evaluating Efficacy and Safety of A Reduced Venetoclax Exposure To Seven Days Versus Standard Continuous Venetoclax Exposure Combined With Azacitidine in Treatment Naïve Subjects with Acute Myeloid Leukemia Who Are Ineligible for Intensive Induction (SEVENAZA)

Rationale

Not provided

Main Objective

To demonstrate the non-inferiority of a reduced VEN exposure to 7 days of AZA every 28 days cycle from the first cycle in terms of composite complete remission rate (complete remission + complete remission with incomplete marrow recovery CR/CRi) at any time point during the first 6 cycles compared to conventional continuous 28-day exposure in treatment naïve AML patients.

Primary Endpoints

The proportion of subjects with complete remission or complete remission with incomplete marrow recovery (CR/CRi) will be calculated based on current IWG criteria for AML (Cheson et al J Clin Oncol 2003)

Temporary moments of secondary assessment

Not provided

Secondary Objective

To evaluate OS and EFS (7-day VEN dosing and conventional 28-day dosing). To evaluate early mortality at Day 60 (7-day VEN dosing vs conventional 28-day dosing) To evaluate time to first response and time to best response (7-day VEN dosing and conventional 28-day dosing). To evaluate DoR (7-day VEN dosing and conventional 28-day dosing). To evaluate quality-of-life (according to EQ5D-5L and QLQ-ELD14 questionnaires). To evaluate, in patients who reached CR/CRi, dosing schedule modification, delays (>2 days) or discontinuation (7-day VEN dosing and conventional 28-day dosing). To evaluate toxicity of special interest and healthcare consumption especially in patients who reached CR/CRi (7-day VEN dosing and conventional 28-day dosing). Health economic analysis: cost-minimization analysis and cost-effectiveness analysis (only for included patients treated in France)

Secondary Endpoints

Overall survival (OS). Event-Free Survival (EFS). Early mortality rate at Day 60. Time to first response. Time to best response. Duration of response (DoR). Health-Related Quality of Life (HRQoL) assessed by the EORTC QLQ-ELD14 and EuroQol EQ-5D-5L questionnaires Scheme modification will be defined as the proportion of CR/CRi patients that presented treatment modification not authorized by protocol as VEN schedule modification (dose, duration), delay >2 days from the initial Day of the subsequent cycle and/or temporary/definitive VEN discontinuation. Toxicity evaluated by platelet transfusion, febrile neutropenia or severe infection episodes, hospitalization

requirement and hospitalization length stay Incremental costs and QALY and ICER (/QALY) (only for included patients treated in France)

Temporary moments of secondary assessment

Not provided

Inclusion criteria

Subject must have confirmation of AML by WHO 2022 criteria and be ineligible for treatment with a standard cytarabine and anthracycline induction regimen due to age or co-morbidities. Subject must voluntarily sign and date an informed consent, approved by an Independent Ethics Committee (IEC)/Institutional Review Board (IRB), prior to the initiation of any screening or study specific procedures. Patients must be affiliated to a social security system or beneficiary of the same (only for France) Patients shall be eligible to undergo Azacitidine and Venetoclax treatment and BM aspiration. Patients who do not consent to a BM aspiration will not be eligible (diagnosis and follow up) Subject must be 60 years of age. Subject must have a projected life expectancy of at least 12 weeks. Subject must be considered ineligible for induction therapy defined by the following: 75 years of age OR 60 to 74 years of age with at least one of the following co-morbidities: ECOG Performance Status of 2 or 3; Cardiac history of CHF requiring treatment or Ejection Fraction 50% or chronic stable angina; DLCO 65% or FEV1 65%; Severe Renal impairement: Creatinine clearance 30 mL/min to < 45 ml/min Moderate hepatic impairment with total bilirubin > 1.5 to 3.0 × ULN Any other comorbidity that the physician judges to be incompatible with intensive chemotherapy must be reviewed and approved by the coordinator before study enrollment Subject must have an Eastern Cooperative Oncology Group (ECOG) Performance status (Appendix 4): 0 to 2 for subject 75 years of age. 0 to 3 for subject 60 to 74 years of age. Subject must have adequate renal function as demonstrated by a creatinine clearance 30 mL/min; calculated by the Cockcroft Gault formula. Subject must have adequate liver function as demonstrated by: Aspartate aminotransferase (AST) 3.0 × ULN* alanine aminotransferase (ALT) 3.0 × ULN* bilirubin 1.5 × ULN* * Unless considered to be due to leukemic organ involvement. Subjects who are < 75 years of age may have a bilirubin of 3.0 × ULN Female subjects must be either postmenopausal (amenorrhea for at least 12 months with no alternative medical reasons) or surgically sterile (bilateral oophorectomy, bilateral salpingectomy or hysterectomy). Non-sterile male subjects must use contraceptive methods with partner(s) prior to beginning study drug administration and continuing up to 90 days after the last dose of study drug. Male subjects must agree to refrain from sperm donation from initial study drug administration until 90 days after the last dose of study drug.

Exclusion criteria

Subject has received treatment with the following: - Hypomethylating agent, venetoclax and/or any chemo-therapeutic agent for Myelodysplastic syndrome (MDS). - Chimeric Antigen Receptor (CAR)-T cell therapy. - Experimental therapies for MDS or Acute Myeloid Leukemia (AML). - Current participation in another research or observational study Subject has acute promyelocytic leukemia Subject has known active CNS involvement with AML. Known human immunodeficiency virus HIV Known hepatitis B or C infection with the exception of those with an undetectable viral load within 3 months. Subject has a cardiovascular disability status of New York Heart Association Class 2. Class 2 is defined as cardiac disease in which patients are comfortable at rest but ordinary physical activity results in fatigue, palpitations, dyspnea, or anginal pain. Subject has chronic respiratory disease that requires continuous oxygen, or significant history of renal, neurologic, psychiatric, endocrinologic, metabolic, immunologic, hepatic, cardiovascular disease, or any other medical condition that in the opinion of the investigator would adversely affect his/her participating in this study. NB: patients with IDH1-mutant AML will not be formally excluded from the study. However, investigators are strongly encouraged to prefer treatment combining Azacitidine and Ivosidenib (AGILE phase III trial). Subject has a malabsorption syndrome or other condition that precludes enteral route of administration. Subject exhibits evidence of other clinically significant uncontrolled systemic infection requiring

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Calendar

(Last Update: 03/09/2026)

Authorization	Start of Trial	First patient inclusion	Halted	Restarted
13/02/2026	02/03/2026	02/03/2026	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

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Contact Person

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Monetary support: N/A

Sponsor type: No commercial

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Active (26/03/2026)

University Hospital Virgen Del Rocio S.L.

Sevilla

SEVILLA

ONCOLOGIA

Medication

Venclyxto 100 mg film-coated tablets

FILM-COATED TABLET

ORAL

ATC code: L01XX52 - VENETOCLAX

Active Principles: N/A

Experimental

Vidaza 25 mg/ml powder for suspension for injection

SUSPENSION FOR INJECTION

INTRAVENOUS/SUBCUTANEOUS/INTRAMUSCULAR

ATC code: L01BC07 - AZACITIDINA

Active Principles: N/A

Experimental

No results