

A Phase 3, multicenter, open label, randomized, non-comparative two-arm study of ivosidenib monotherapy (IVO) and azacitidine monotherapy (AZA) in adult patients with hypomethylating agent (HMA) naive myelodysplastic syndromes (MDS) with an IDH1 mutation (PyramIDH study).

Estado Reclutando	Tipo de Participantes No aportado	Rangos de Edad Mayores de 64 , Adultos (18-64 años)
Género Ambos	Fases Fase III	Participantes esperados 22
Resultados Sin resultados	Bajo nivel intervención No	Enfermedad rara No
Cobertura geográfica Sin determinar	Ámbitos del ensayo seguridad, eficacia, farmacocinética, farmacodinámica, farmacoeconómica	Terapia avanzada NO

Información

Identificador 2023-510155-37-00 (CTIS)	Cod. Protocolo S095031-178
--	--------------------------------------

Área terapéutica

Enfermedades [C] - Hematología [C15]

Enfermedad investigada

Hypomethylating agent (HMA) naive myelodysplastic syndromes
Myelodysplastic Syndrome (MDS)
Myelodysplastic Syndrome (MDS)

Título Científico

A phase 3, multicenter, open label, randomized, non-comparative two-arm study of ivosidenib (IVO) monotherapy

and azacitidine (AZA) monotherapy in adult patients with hypomethylating agent (HMA) naive myelodysplastic syndromes (MDS) with an isocitrate dehydrogenase-1 (IDH1) mutation (PyramIDH study).

Justificación

No aportado

Objetivo Principal

To assess the efficacy of IVO monotherapy in participants with HMA naive MDS with an IDH1m

Variables de Evaluación Primaria

Complete remission (CR) + Partial remission (PR) by 4 months as per IWG 2006 criteria.

Momentos temporales de evaluación primaria

No aportado

Objetivo Secundario

To assess the efficacy of IVO monotherapy in participants with HMA naive MDS with an IDH1m.
To assess the efficacy of IVO monotherapy in participants with HMA naive MDS based on QOL and health economic outcome measures
To evaluate the PK and PD of ivosidenib administered as monotherapy
To assess the safety and tolerability of IVO in participants with HMA naive MDS

Variables de Evaluación Secundaria

Overall Response (OR) rate per IWG 2023 criteria defined as CR (or CR equivalent) + PR + CRL + CRh + hematological improvement (HI).
Event-free survival (EFS) defined as the date of randomization to the date of first documented confirmed relapse/progression/death, whichever occurs first.
Overall Survival (OS) defined as the time from randomization to the date of death due to any cause. Participants who are alive at the analysis cutoff date will be censored at the date they were last known to be alive.
Duration of CR and PR among participants who achieve CR + PR per IWG 2006 criteria.
Time to CR and PR defined as time from the date of the randomization to the date of CR+PR, among participants who achieve CR+PR based on IWG 2006 Response Criteria.
Acute myeloid leukemia (AML) transformation rate
Time to transfusion independence (TTTI) defined as time from date of randomization to date transfusion independence (TI) is first observed (Day 1 of a 56 days period without a transfusion), among participants who are baseline transfusion dependent and have achieved post-baseline TI. In the event a participant had more than one 56-day period, which met TI criteria, the earliest period will be used in analysis.

Duration of transfusion independence (DOTI) among participants who have achieved post-baseline TI, DOTI will be calculated as the time from the date TI is first observed (Day 1 of a 56-day period without a transfusion) until the day before the participants had a subsequent transfusion.

Transfusion independence rate

Quality of Life in Myelodysplasia Scale (QUALMS) scores range from 0 to 100, with a higher score representing a better QOL.

Change from baseline in health economic outcomes measures based on EQ-5D-5L score. Health economic outcomes measures as assessed by the 5-level EuroQol five dimensions questionnaire (EQ-5D-5L) scores range from 5 to 25 with a higher number representing a worse health status.

Number of participants who proceed to hematopoietic stem cell transplantation (HSCT).

Ivosidenib plasma concentration and 2-HG plasma concentrations for participants receiving Ivosidenib monotherapy.

Number of participants achieving CR and PR by 6 months as per IWG 2006 criteria.

Number of participants achieving CR and PR by 6 months as per IWG 2023 criteria.

Number of participants achieving CR and PR by 4 months as per IWG 2023 criteria.

Number of adverse events (AEs) and serious adverse events (SAEs).

Health economic outcomes measures as assessed by the 5-level EuroQol five dimensions questionnaire (EQ-5D-5L) scores range from 5 to 25 with a higher number representing a worse health status.

Momentos temporales de evaluación secundaria

No aportado

Criterios de Inclusión

Diagnosis of HMA naive IDH1 R132 mutated MDS defined according to World Health Organization (WHO) criteria (5th edition): - Moderate high, high and very high-risk MDS per IPSS-M score will be eligible regardless of blood counts and with blast counts 0-19%. - Low and moderate low-risk MDS per IPSS-M score must: o Have cytopenias related to MDS, defined as: <100 platelets/L, or absolute neutrophil count (ANC) <1000/mm³, or Hgb <10g/dL AND o Have a blast count between 5-19% AND o Be eligible for HMA therapy (very low risk participants are to be excluded). Locally or centrally confirmed IDH1 R132 C/G/H/L/S mutation.

Criterios de Exclusión

Received prior anticancer/disease modifying treatment for MDS (including HMAs, cytotoxic chemotherapy, investigational agents, bcl-2 inhibitor based-regimens, hematopoietic stem cell transplant (HSCT), IDH1 inhibitors). For LR-MDS patients, prior treatment with growth factors, luspatercept, lenalidomide, and imetelstat are allowed. > 20% blasts by morphology or immunohistochemistry on screening bone marrow aspirate.

Calendario

(Última actualización: 30/04/2026)

Autorización 02/12/2024	Inicio de Ensayo 08/05/2025	Inclusión Primer Paciente 19/05/2025	Interrumpido No aportado	Reiniciado No aportado
Fin de reclutamiento No aportado	Fin prematuro (España) No aportado	Fin prematuro (Global) No aportado	Fin del ensayo en España No aportado	Fin del ensayo global No aportado

Promotor

Institut De Recherches Internationales Servier IRIS France

22 Route 128

Contact Person

Clinical Studies Department

33155726000

scientificinformation@servier.com

Monetary support: N/A

Tipo de promotor: Comercial

Ceim

CEIm de la Comunidad Foral de Navarra

C/ Irunlarrea, 3 31008 Pamplona

ceic@cfnavarra.es

Centros

Activo (13/05/2025)	Clinica Universidad De Navarra Pamplona NAVARRA Hematology
No iniciado (---/---/----)	Clinica Universidad De Navarra Madrid MADRID Hematology
Activo (16/12/2025)	Hospital Germans Trias I Pujol Badalona BARCELONA Hematology
Activo (04/06/2025)	Hospital Universitario De Salamanca Salamanca SALAMANCA Hematology
Activo (14/05/2025)	Hospital Universitario Virgen De La Macarena Sevilla SEVILLA Hematology
Activo (08/05/2025)	Hospital Universitario Y Politecnico La Fe Valencia VALENCIA Hematology
No iniciado (---/---/----)	Institut Catala D&#39;oncologia Badalona BARCELONA Hematology
Activo (16/07/2025)	Vall D Hebron Institute Of Oncology Barcelona BARCELONA Hematology

Medicamentos

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

Principios Activos: N/A

Experimental

Vidaza 25 mg/ml powder for suspension for injection

SUSPENSION FOR INJECTION
INTRAVENOUS (IV) OR SUBCUTANEOUS (SC)

Código ATC: L01BC07 - AZACITIDINA

Principios Activos: N/A

Experimental

Sin resultados

A Phase 3, multicenter, open label, randomized, non-comparative two-arm study of ivosidenib monotherapy (IVO) and azacitidine monotherapy (AZA) in adult patients with hypomethylating agent (HMA) naive myelodysplastic syndromes (MDS) with an IDH1 mutation (PyramIDH study).

State
Recruiting

Type of participants
Not provided

Age Ranges
Older than 64 , Adults (18-64 years)

Gender
Both

Phases
Phase III

Expected Participants
22

Results
No results

Low level of intervention
No

Rare disease
No

Geographic coverage
Undetermined

Areas of the study
safety, effectiveness, pharmacokinetics,
pharmacodynamics, pharmacoeconomic

Advanced therapy
NO

Information

Identifier
2023-510155-37-00 (CTIS)

Protocol Code
S095031-178

Therapeutic area
Diseases [C] - Hemic and Lymphatic Diseases [C15]

Investigated Disease
Hypomethylating agent (HMA) naive myelodysplastic syndromes
Myelodysplastic Syndrome (MDS)
Myelodysplastic Syndrome (MDS)

Scientific Title
A phase 3, multicenter, open label, randomized, non-comparative two-arm study of ivosidenib (IVO) monotherapy

and azacitidine (AZA) monotherapy in adult patients with hypomethylating agent (HMA) naive myelodysplastic syndromes (MDS) with an isocitrate dehydrogenase-1 (IDH1) mutation (PyramIDH study).

Rationale

Not provided

Main Objective

To assess the efficacy of IVO monotherapy in participants with HMA naive MDS with an IDH1m

Primary Endpoints

Complete remission (CR) + Partial remission (PR) by 4 months as per IWG 2006 criteria.

Temporary moments of secondary assessment

Not provided

Secondary Objective

To assess the efficacy of IVO monotherapy in participants with HMA naive MDS with an IDH1m.
To assess the efficacy of IVO monotherapy in participants with HMA naive MDS based on QOL and health economic outcome measures
To evaluate the PK and PD of ivosidenib administered as monotherapy
To assess the safety and tolerability of IVO in participants with HMA naive MDS

Secondary Endpoints

Overall Response (OR) rate per IWG 2023 criteria defined as CR (or CR equivalent) + PR + CRL + CRh + hematological improvement (HI).
Event-free survival (EFS) defined as the date of randomization to the date of first documented confirmed relapse/progression/death, whichever occurs first.
Overall Survival (OS) defined as the time from randomization to the date of death due to any cause. Participants who are alive at the analysis cutoff date will be censored at the date they were last known to be alive.
Duration of CR and PR among participants who achieve CR + PR per IWG 2006 criteria.
Time to CR and PR defined as time from the date of the randomization to the date of CR+PR, among participants who achieve CR+PR based on IWG 2006 Response Criteria.
Acute myeloid leukemia (AML) transformation rate
Time to transfusion independence (TTTI) defined as time from date of randomization to date transfusion independence (TI) is first observed (Day 1 of a 56 days period without a transfusion), among participants who are baseline transfusion dependent and have achieved post-baseline TI. In the event a participant had more than one 56-day period, which met TI criteria, the earliest period will be used in analysis.

Duration of transfusion independence (DOTI) among participants who have achieved post-baseline TI, DOTI will be calculated as the time from the date TI is first observed (Day 1 of a 56-day period without a transfusion) until the day before the participants had a subsequent transfusion.

Transfusion independence rate

Quality of Life in Myelodysplasia Scale (QUALMS) scores range from 0 to 100, with a higher score representing a better QOL.

Change from baseline in health economic outcomes measures based on EQ-5D-5L score. Health economic outcomes measures as assessed by the 5-level EuroQol five dimensions questionnaire (EQ-5D-5L) scores range from 5 to 25 with a higher number representing a worse health status.

Number of participants who proceed to hematopoietic stem cell transplantation (HSCT).

Ivosidenib plasma concentration and 2-HG plasma concentrations for participants receiving Ivosidenib monotherapy.

Number of participants achieving CR and PR by 6 months as per IWG 2006 criteria.

Number of participants achieving CR and PR by 6 months as per IWG 2023 criteria.

Number of participants achieving CR and PR by 4 months as per IWG 2023 criteria.

Number of adverse events (AEs) and serious adverse events (SAEs).

Health economic outcomes measures as assessed by the 5-level EuroQol five dimensions questionnaire (EQ-5D-5L) scores range from 5 to 25 with a higher number representing a worse health status.

Temporary moments of secondary assessment

Not provided

Inclusion criteria

Diagnosis of HMA naive IDH1 R132 mutated MDS defined according to World Health Organization (WHO) criteria (5th edition): - Moderate high, high and very high-risk MDS per IPSS-M score will be eligible regardless of blood counts and with blast counts 0-19%. - Low and moderate low-risk MDS per IPSS-M score must: o Have cytopenias related to MDS, defined as: <100 platelets/L, or absolute neutrophil count (ANC) <1000/mm³, or Hgb <10g/dL AND o Have a blast count between 5-19% AND o Be eligible for HMA therapy (very low risk participants are to be excluded). Locally or centrally confirmed IDH1 R132 C/G/H/L/S mutation.

Exclusion criteria

Received prior anticancer/disease modifying treatment for MDS (including HMAs, cytotoxic chemotherapy, investigational agents, bcl-2 inhibitor based-regimens, hematopoietic stem cell transplant (HSCT), IDH1 inhibitors). For LR-MDS patients, prior treatment with growth factors, luspatercept, lenalidomide, and imetelstat are allowed. > 20% blasts by morphology or immunohistochemistry on screening bone marrow aspirate.

Calendar

(Last Update: 30/04/2026)

Authorization 02/12/2024	Start of Trial 08/05/2025	First patient inclusion 19/05/2025	Halted Not aported	Restarted Not aported
End of recruitment Not aported	Premature end (Spain) Not aported	Premature End (Global) Not aported	Trial end (Spain) Not aported	Trial end (Global) Not aported

Sponsor

Institut De Recherches Internationales Servier IRIS France
22 Route 128

Contact Person

Clinical Studies Department

33155726000

scientificinformation@servier.com

Monetary support: N/A

Sponsor type: Commercial

Ceim

CEIm de la Comunidad Foral de Navarra

C/ Irunlarrea, 3 31008 Pamplona

ceic@cfnavarra.es

Sites

Active (13/05/2025)	Clinica Universidad De Navarra Pamplona NAVARRA Hematology
not initialized (---/---/----)	Clinica Universidad De Navarra Madrid MADRID Hematology
Active (16/12/2025)	Hospital Germans Trias I Pujol Badalona BARCELONA Hematology
Active (04/06/2025)	Hospital Universitario De Salamanca Salamanca SALAMANCA Hematology
Active (14/05/2025)	Hospital Universitario Virgen De La Macarena Sevilla SEVILLA Hematology
Active (08/05/2025)	Hospital Universitario Y Politecnico La Fe Valencia VALENCIA Hematology
not initialized (---/---/----)	Institut Catala D&#39;oncologia Badalona BARCELONA Hematology
Active (16/07/2025)	Vall D Hebron Institute Of Oncology Barcelona BARCELONA Hematology

Medication

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

Active Principles: N/A

Experimental

Vidaza 25 mg/ml powder for suspension for injection
SUSPENSION FOR INJECTION
INTRAVENOUS (IV) OR SUBCUTANEOUS (SC)

ATC code: L01BC07 - AZACITIDINA

Active Principles: N/A

Experimental

No results