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	Tipo de Participantes	Rangos de Edad
Reclutando	No aportado	Mayores de 64 , Adultos (18-64 años)
Género	**Fases**	**Participantes esperados**
Ambos	Fase III	22
Resultados	**Bajo nivel intervención**	**Enfermedad rara**
Sin resultados	No	No
Cobertura geográfica	**Ámbitos del ensayo**	**Terapia avanzada**
Sin determinar	seguridad, eficacia, farmacocinética, farmacodinamica, farmacoeconómica	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 Symdrome (MDS)
Myelodysplastic Symdrome (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	Inicio de Ensayo	Inclusión Primer Paciente	Interrumpido	Reiniciado
02/12/2024	08/05/2025	19/05/2025	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 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

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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'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	Type of participants	Age Ranges
Recruiting	Not provided	Older than 64 , Adults (18-64 years)
Gender	**Phases**	**Expected Participants**
Both	Phase III	22
Results	**Low level of intervention**	**Rare disease**
No results	No	No
Geographic coverage	**Areas of the study**	**Advanced therapy**
Undetermined	safety, effectiveness, pharmacokinetics, pharmacodynamics, pharmacoeconomic	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 Symdrome (MDS)
Myelodysplastic Symdrome (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.
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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	Start of Trial	First patient inclusion	Halted	Restarted
02/12/2024	08/05/2025	19/05/2025	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

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

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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'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