APTIVATE Clinical Trial to Evaluate the Safety, Tolerability, Pharmacokinetics and Pharmacodynamics of Tuspetinib (HM43239) in Patients with Relapsed or Refractory Acute Myeloid Leukemia.

Estado	Tipo de Participantes	Rangos de Edad
Reclutando	No aportado	Mayores de 64 , Adultos (18-64 años)
Género	**Fases**	**Participantes esperados**
Ambos	Fase I , Fase II	218
Resultados	**Bajo nivel intervención**	**Enfermedad rara**
Sin resultados	No	Si
Cobertura geográfica	**Ámbitos del ensayo**	**Terapia avanzada**
Multicéntrico internacional	seguridad, eficacia, farmacocinética, farmacodinamica, dosis	NO

Información

Identificador
2023-503244-14-00 (CTIS)

Cod. Protocolo
HM-FLTI-101

Área terapéutica
Enfermedades [C] - Hematología [C15]|

Enfermedad investigada
Relapsed or Refractory Acute Myeloid Leukemia (AML)<br/

Título Científico
A Phase 1/2, Open-label, Multicenter, Dose Escalation and Expansion Study of the Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of HM43239 in Patients with Relapsed or Refractory Acute Myeloid Leukemia (AML)

Justificación

Phase 1/2, open-label, multicenter, dose- escalation and expansion study<br/

Objetivo Principal

- To determine the recommended phase 2 dose based on safety, efficacy, pharmacokinetics (PK), and pharmacodynamics (PD) consideration.
- To evaluate the safety, tolerability, and PK parameters of HM43239 when administered in patients with relapsed or treatment-refractory (R/R) AML.
- To evaluate the safety, tolerability, and PK parameters of HM43239 in combination with venetoclax when administered in patients with R/R AML.

Variables de Evaluación Primaria

PART A (Dose Escalation) and Part B (Dose Exploration): - Safety and tolerability (determined by monitoring the frequency, duration, and severity of AEs to establish the RP2D) - Pharmacokinetic profile of HM43239 and, if required, its metabolite(s) will be determined in terms of the following variables but not limited to: Cmax, Tmax, AUC0-¿ at C1D1 of Part A, AUCtau, t1/2, CL/F, and Vd/F. PART C (Dose Expansion): - Safety and tolerability of HM43239 in combination with venetoclax<br/

Momentos temporales de evaluación primaria

No aportado

Objetivo Secundario

To investigate anti-leukemic activity of various doses of HM43239 in patients with relapsed or treatment-refractory AML. To investigate anti-leukemic activity of HM43239 in combination with venetoclax in patients with relapsed or treatment-refractory AML.<br/

Variables de Evaluación Secundaria

Efficacy of HM43239 in AML as a single agent or in combination with venetoclax o CR rate o CRc rate (CR + CRh + CRp + CRi) - Best response rate (CRc + PR) - Duration of response - Overall survival (OS) - Event free survival (EFS) - Cumulative incidence of relapse (CIR)<br/

Momentos temporales de evaluación secundaria

No aportado

Criterios de Inclusión

Patient is ¿ 18 years of age (or country's legal age of majority if the legal age is > 18 years) at the time of obtaining informed consent. Patient is defined as having morphologically documented primary or secondary AML by the World Health Organization criteria (2016) and fulfills one of the following: a) Refractory to at least 1 cycle of prior therapy. b) Relapsed after achieving remission with the most recent prior therapy. Patient has an Eastern Cooperative Oncology Group (ECOG) performance status ¿ 2. Patient¿s interval from prior treatment to time of study drug administration is at least 2 weeks for cytotoxic agents (except hydroxyurea given for controlling blast cells), at least 4 weeks for biologic cellular immunotherapies, or at least 5 half-lives for prior experimental agents or immunosuppressive therapy post hematopoietic stem cell transplantation (HSCT). (Upon discussion with the Medical Monitor, shorter than stated washout period may be considered provided that the patient has recovered from any clinically relevant safety issue and recovered to Grade ¿ 1 toxicity from prior therapies). Patient must meet the following criteria as indicated on the clinical laboratory tests: a) Serum aspartate aminotransferase and alanine aminotransferase ¿ 2.5× institutional upper limit of normal (ULN). b) Total serum bilirubin ¿ 1.5× institutional ULN. c) Serum creatinine ¿ 1.5× institutional ULN or an estimated glomerular filtration rate of > 45 mL/min as calculated by the Modification of Diet in Renal Disease equation.<br/

Criterios de Exclusión

Patient was diagnosed as acute promyelocytic leukemia. Patient has known BCR-ABL-positive leukemia. Patient has an active malignancy requiring therapy other than AML or myelodysplastic syndrome. Patient has persistent non-hematological toxicities of ¿ Grade 2 (Common Terminology Criteria for Adverse Events v4.03), with symptoms and objective findings, from prior AML treatment (including chemotherapy, kinase inhibitors, immunotherapy, experimental agents, radiation, or surgery). Patient has had HSCT and meets any of the following: a) Has undergone HSCT within the 2-month period prior to the first study dose b) Has clinically significant graft-versus-host-disease requiring treatment c) Has ¿ Grade 2 persistent non-hematological toxicity related to the transplant d) Has a donor lymphocytes infusion (DLI) ¿ 30 days prior to the first study dose or during the first 2 cycles of treatment in the study. Patient has meningeal or central nervous system (CNS) involvement with leukemia or other CNS disease related to underlying and secondary effects of malignancy. Patient has any condition which, in the investigator's opinion, makes the patient unsuitable for study participation. Patient has a history of Grade 3 or 4 non-hematologic toxicity related to a tyrosine kinase inhibitor.<br/

Calendario

(Última actualización: 09/10/2023)

Autorización	Inicio de Ensayo	Inclusión Primer Paciente	Interrumpido	Reiniciado
16/06/2023	11/08/2023	28/08/2023	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

Aptose Biosciences Inc. United States

12770 High Bluff Drive Suite 120

Contact Person

Zoey Liu-Imanuel

+18589262730

zimanuel@aptose.com

Monetary support: N/A

Tipo de promotor: Comercial

Centros

Activo (28/06/2023)

Fir Huvh Fundacio Institut De Recerca Hospital Universitari Vall De Hebron

Barcelona

BARCELONA

Hematology

Activo (15/06/2023)

Hospital Clinic De Barcelona

Barcelona

BARCELONA

Hematology

Activo (28/06/2023)

Hospital Clinico Universitario De Valencia

Valencia

VALENCIA

Hematology

Activo (11/07/2023)

Hospital De La Santa Creu I Sant Pau

Barcelona

BARCELONA

Hematology

Activo (29/06/2023)

Hospital General Universitario De Alicante

Alicante

ALICANTE

Hematology

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

Hospital General Universitario Gregorio Maranon

Madrid

MADRID

Hematology

Activo (06/10/2023)

Hospital Universitario Central De Asturias

Oviedo

ASTURIAS

Hematology

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

Hospital Universitario De Salamanca

Salamanca

SALAMANCA

Hematology

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

Hospital Universitario Fundacion Jimenez Diaz

Madrid

MADRID

Hematology

Activo (26/06/2023)

Hospital Universitario Quironsalud Madrid

Pozuelo De Alarcon

MADRID

Hematology

Activo (17/07/2023)

Hospital Universitario Y Politecnico La Fe

Valencia

VALENCIA

Hematology

Medicamentos

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

Tuspetinib
FILM COATED TABLET
ORAL

-
Principios Activos: N/A

Experimental

Tuspetinib
FILM COATED TABLET
ORAL

-
Principios Activos: N/A

Experimental

Sin resultados

APTIVATE Clinical Trial to Evaluate the Safety, Tolerability, Pharmacokinetics and Pharmacodynamics of Tuspetinib (HM43239) in Patients with Relapsed or Refractory Acute Myeloid Leukemia.

State	**Type of participants**	**Age Ranges**
Recruiting	Not provided	Older than 64 , Adults (18-64 years)
Gender	**Phases**	**Expected Participants**
Both	Phase I , Phase II	218
Results	**Low level of intervention**	**Rare disease**
No results	No	Yes
Geographic coverage	**Areas of the study**	**Advanced therapy**
International multicenter	safety, effectiveness, pharmacokinetics, pharmacodynamics, dose	NO

Information

Identifier
2023-503244-14-00 (CTIS)

Protocol Code
HM-FLTI-101

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

Investigated Disease
Relapsed or Refractory Acute Myeloid Leukemia (AML)<br/

Scientific Title
A Phase 1/2, Open-label, Multicenter, Dose Escalation and Expansion Study of the Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of HM43239 in Patients with Relapsed or Refractory Acute Myeloid Leukemia (AML)

Rationale

Phase 1/2, open-label, multicenter, dose- escalation and expansion study<br/

Main Objective

- To determine the recommended phase 2 dose based on safety, efficacy, pharmacokinetics (PK), and pharmacodynamics (PD) consideration.
- To evaluate the safety, tolerability, and PK parameters of HM43239 when administered in patients with relapsed or treatment-refractory (R/R) AML.
- To evaluate the safety, tolerability, and PK parameters of HM43239 in combination with venetoclax when administered in patients with R/R AML.

Primary Endpoints

PART A (Dose Escalation) and Part B (Dose Exploration): - Safety and tolerability (determined by monitoring the frequency, duration, and severity of AEs to establish the RP2D) - Pharmacokinetic profile of HM43239 and, if required, its metabolite(s) will be determined in terms of the following variables but not limited to: Cmax, Tmax, AUC0-¿ at C1D1 of Part A, AUCtau, t1/2, CL/F, and Vd/F. PART C (Dose Expansion): - Safety and tolerability of HM43239 in combination with venetoclax<br/

Temporary moments of secondary assessment

Not provided

Secondary Objective

To investigate anti-leukemic activity of various doses of HM43239 in patients with relapsed or treatment-refractory AML. To investigate anti-leukemic activity of HM43239 in combination with venetoclax in patients with relapsed or treatment-refractory AML.<br/

Secondary Endpoints

Efficacy of HM43239 in AML as a single agent or in combination with venetoclax o CR rate o CRc rate (CR + CRh + CRp + CRi) - Best response rate (CRc + PR) - Duration of response - Overall survival (OS) - Event free survival (EFS) - Cumulative incidence of relapse (CIR)<br/

Temporary moments of secondary assessment

Not provided

Inclusion criteria

Patient is ¿ 18 years of age (or country's legal age of majority if the legal age is > 18 years) at the time of obtaining informed consent. Patient is defined as having morphologically documented primary or secondary AML by the World Health Organization criteria (2016) and fulfills one of the following: a) Refractory to at least 1 cycle of prior therapy. b) Relapsed after achieving remission with the most recent prior therapy. Patient has an Eastern Cooperative Oncology Group (ECOG) performance status ¿ 2. Patient¿s interval from prior treatment to time of study drug administration is at least 2 weeks for cytotoxic agents (except hydroxyurea given for controlling blast cells), at least 4 weeks for biologic cellular immunotherapies, or at least 5 half-lives for prior experimental agents or immunosuppressive therapy post hematopoietic stem cell transplantation (HSCT). (Upon discussion with the Medical Monitor, shorter than stated washout period may be considered provided that the patient has recovered from any clinically relevant safety issue and recovered to Grade ¿ 1 toxicity from prior therapies). Patient must meet the following criteria as indicated on the clinical laboratory tests: a) Serum aspartate aminotransferase and alanine aminotransferase ¿ 2.5× institutional upper limit of normal (ULN). b) Total serum bilirubin ¿ 1.5× institutional ULN. c) Serum creatinine ¿ 1.5× institutional ULN or an estimated glomerular filtration rate of > 45 mL/min as calculated by the Modification of Diet in Renal Disease equation.<br/

Exclusion criteria

Patient was diagnosed as acute promyelocytic leukemia. Patient has known BCR-ABL-positive leukemia. Patient has an active malignancy requiring therapy other than AML or myelodysplastic syndrome. Patient has persistent non-hematological toxicities of ¿ Grade 2 (Common Terminology Criteria for Adverse Events v4.03), with symptoms and objective findings, from prior AML treatment (including chemotherapy, kinase inhibitors, immunotherapy, experimental agents, radiation, or surgery). Patient has had HSCT and meets any of the following: a) Has undergone HSCT within the 2-month period prior to the first study dose b) Has clinically significant graft-versus-host-disease requiring treatment c) Has ¿ Grade 2 persistent non-hematological toxicity related to the transplant d) Has a donor lymphocytes infusion (DLI) ¿ 30 days prior to the first study dose or during the first 2 cycles of treatment in the study. Patient has meningeal or central nervous system (CNS) involvement with leukemia or other CNS disease related to underlying and secondary effects of malignancy. Patient has any condition which, in the investigator's opinion, makes the patient unsuitable for study participation. Patient has a history of Grade 3 or 4 non-hematologic toxicity related to a tyrosine kinase inhibitor.<br/

Calendar

(Last Update: 09/10/2023)

Authorization	Start of Trial	First patient inclusion	Halted	Restarted
16/06/2023	11/08/2023	28/08/2023	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

Aptose Biosciences Inc. United States

12770 High Bluff Drive Suite 120

Contact Person

Zoey Liu-Imanuel

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zimanuel@aptose.com

Monetary support: N/A

Sponsor type: Commercial

Sites

Active (28/06/2023)

Fir Huvh Fundacio Institut De Recerca Hospital Universitari Vall De Hebron

Barcelona

BARCELONA

Hematology

Active (15/06/2023)

Hospital Clinic De Barcelona

Barcelona

BARCELONA

Hematology

Active (28/06/2023)

Hospital Clinico Universitario De Valencia

Valencia

VALENCIA

Hematology

Active (11/07/2023)

Hospital De La Santa Creu I Sant Pau

Barcelona

BARCELONA

Hematology

Active (29/06/2023)

Hospital General Universitario De Alicante

Alicante

ALICANTE

Hematology

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

Hospital General Universitario Gregorio Maranon

Madrid

MADRID

Hematology

Active (06/10/2023)

Hospital Universitario Central De Asturias

Oviedo

ASTURIAS

Hematology

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

Hospital Universitario De Salamanca

Salamanca

SALAMANCA

Hematology

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

Hospital Universitario Fundacion Jimenez Diaz

Madrid

MADRID

Hematology

Active (26/06/2023)

Hospital Universitario Quironsalud Madrid

Pozuelo De Alarcon

MADRID

Hematology

Active (17/07/2023)

Hospital Universitario Y Politecnico La Fe

Valencia

VALENCIA

Hematology

Medication

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

Tuspetinib
FILM COATED TABLET
ORAL

-
Active Principles: N/A

Experimental

Tuspetinib
FILM COATED TABLET
ORAL

-
Active Principles: N/A

Experimental

No results