A study of Gilteritinib combined with chemotherapy to treat Children, Adolescents and Young Adults with Relapsed or Refractory Acute Myeloid Leukemia (AML) with a FLT3 gene mutation

Estado	**Tipo de Participantes**	**Rangos de Edad**
EC Finalizado	Sujetos incapaces de otorgar consentimiento	Menores de 18 , Adultos (18-64 años)
Género	**Fases**	**Participantes esperados**
Ambos	Fase I , Fase II	97
Resultados	**Bajo nivel intervención**	**Enfermedad rara**
Tiene resultados	No	Si
Cobertura geográfica	**Ámbitos del ensayo**	**Terapia avanzada**
Multicéntrico internacional	diagnóstico, tratamiento, seguridad, eficacia, farmacocinética, farmacodinamica, dosis, farmacogenómica	NO

Información

Identificador
2024-512469-15-00 (CTIS)

Cod. Protocolo
2215-CL-0603

Transicionado 2018-002301-61

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

Enfermedad investigada
FMS-like Tyrosine Kinase 3 (FLT3)/Internal Tandem Duplication (ITD) Positive Relapsed or Refractory Acute Myeloid Leukemia (AML)

Título Científico
A Phase 1/2, Multicenter, Open-Label, Single Arm, Dose Escalation and Expansion Study of Gilteritinib (ASP2215)

Combined with Chemotherapy in Children, Adolescents and Young Adults with FMS-like Tyrosine Kinase 3 (FLT3)/Internal Tandem Duplication (ITD) Positive Relapsed or Refractory Acute Myeloid Leukemia (AML)

Justificación

No aportado

Objetivo Principal

Phase 1 (Dose Escalation Phase):
To determine the maximum tolerated dose (MTD) and/or optimally safe and biologically active recommended phase 2 dose (RP2D) of gilteritinib given in sequential combination with FLAG in children, adolescents and young adults with relapsed/refractory (R/R) FMS-like tyrosine
kinase 3 (FLT3) (internal tandem duplication (ITD) and/or tyrosine kinase domain (TKD) acute myeloid leukemia (AML).
Phase 2 (Dose Expansion Phase):
To determine complete remission (CR) rates and composite complete remission (CRc) rates after 2 cycles of gilteritinib in sequential combination with FLAG in children, adolescents and young adults with FLT3 (ITD) AML who are refractory to or at the first hematologic relapse after first-line remission induction AML therapy (up to 2 induction cycles).

Variables de Evaluación Primaria

Phase 1: Determination of MTD and/or RP2D Phase 2: o CRc rates (overall best response) after 2 cycles of therapy. o CR rates after 2 cycles of therapy; CR rate will be further described by the duration of CR (only for USA).

Momentos temporales de evaluación primaria

No aportado

Objetivo Secundario

To assess the safety, tolerability and toxicities of gilteritinib when given in sequential combination with FLAG in children, adolescents, and young adults with R/R FLT3/ITD AML
To evaluate FLT3 inhibition due to gilteritinib treatment
To characterize gilteritinib pharmacokinetics
To perform serial measurements of minimal residual disease (MRD) and examine the relationship with study endpoints
To obtain preliminary estimates of 1-year event-free survival (EFS) and overall survival (OS) rate
To assess the acceptability and palatability of the formulation.

Variables de Evaluación Secundaria

Inhibition of phosphorylated FLT3 (pFLT3) measured by PIA assay
Gilteritinib plasma concentration
Pharmacokinetic parameters (e.g., oral clearance [CL/F], apparent volume of distribution [Vd/F], maximum concentration [Cmax], time of maximum concentration [tmax], area under the concentration-time curve [AUC]) of gilteritinib
Safety, tolerability and toxicity assessments of gilteritinib when given in combination with FLAG
EFS rate
OS rate
MRD assessment
Acceptability and palatability assessment of the formulation

Momentos temporales de evaluación secundaria

No aportado

Criterios de Inclusión

2. Phase 1: Subject is positive for FLT3 (ITD and/or TKD) mutation in bone marrow or blood as determined by the local institution. Phase 2: Subject is positive for the FLT3 (ITD) mutation in bone marrow or blood as determined by the local institution. 3. Subject is aged 6 months and < 21 years of age* at the time of signing informed consent and/or assent, as applicable. * For phase 2: Enrollment of subjects from 6 months to less than 1 year (Group 3) and 1 year to less than 2 years (Group 2) will be dependent on the establishment of RP2D in the respective for age groups during phase 1. 4. Subject has a diagnosis of AML according to The FrenchAmericanBritish (FAB) classification with 5% blasts in the bone marrow, with or without extramedullary disease (except subjects with active central nervous system (CNS) Leukemia). a) In the phase 1 portion of the study, subject must be in first or greater relapse or refractory to induction therapy with no more than 1 attempt at remission induction (up to 2 induction cycles). b) For the phase 2 portion of the study, subject must be refractory to or at the first hematologic relapse after first-line remission induction AML therapy (up to 2 induction cycles)

Criterios de Exclusión

1. Subject has active central nervous system (CNS) leukemia. 3. Subject has uncontrolled or significant cardiovascular disease, including: Diagnosed or suspected congenital long QT syndrome or any history of clinically significant ventricular arrhythmias (such as ventricular tachycardia, ventricular fibrillation, or torsades de pointes); any history of arrhythmia will be discussed with the sponsors medical monitor prior to subjects entry into the study Prolonged Fridericia-corrected QT interval (QTcF) interval on pre-entry electrocardiogram (ECG) (450 ms) Any history of second- or third-degree heart block (may be eligible if the subject currently has a pacemaker) Heart rate < 50 beats/minute on pre-entry ECG Uncontrolled hypertension Complete left bundle branch block 6. Subject has active clinically significant graft-versus-host disease (GVHD) or is on treatment with immunosuppressive drugs for treatment of active GVHD, with the exception of subjects being weaned from systemic corticosteroids where the subject is receiving 0.5 mg/kg of prednisone (or equivalent) daily dose for prior GVHD. Subject has received calcineurin inhibitors within 4 weeks prior to screening, unless used as GVHD prophylaxis 7. Subject has active malignant tumors other than AML. 9. Subject has hypokalemia and/or hypomagnesemia at Screening (defined as values below institutional lower limit of normal [LLN]). Repletion of potassium and magnesium levels during the screening period is allowed. 10. Subject requires treatment with concomitant drugs that are strong inducers of cytochrome P450 (CYP)3A/P-glycoprotein (P-gp).

Calendario

(Última actualización: 02/10/2025)

Autorización	Inicio de Ensayo	Inclusión Primer Paciente	Interrumpido	Reiniciado
10/12/2019	19/01/2022	07/04/2022	No aportado	No aportado

Fin de reclutamiento	Fin prematuro (España)	Fin prematuro (Global)	Fin del ensayo en España	Fin del ensayo global
17/03/2025	No aportado	No aportado	No aportado	18/03/2025

Promotor

Astellas Pharma Global Development Inc. United States

2375 Waterview Drive

Contact Person

Clinical Trial Unit Head

+31715454006

ctu@astellas.com

Monetary support: N/A

Tipo de promotor: Comercial

Ceim

CEIm Fundacio Sant Joan de Deu

Santa Rosa, 39-57, 3a planta 08950 Esplugues de Llobregat

frecerca.ceic@sjd.es

Centros

Cerrado (22/05/2025)

HOSPITAL DE SANT JOAN DE DÉU.

Esplugues de Llobregat

BARCELONA

Servicio de Hematologia

Cerrado (16/04/2025)

HOSPITAL UNIVERSITARI VALL D'HEBRON

Barcelona

BARCELONA

Servicio Oncología y Hematología Pediátrica

Cerrado (30/05/2025)

HOSPITAL UNIVERSITARIO VIRGEN DEL ROCÍO

Sevilla

SEVILLA

Servicio de Hematología y Hemoterapia

Medicamentos

ARA-cell® 40 mg Injektion 20 mg/ml Injektionslösung / Konzentrat zur Herstellung einer Infusionslösung

SOLUTION FOR INJECTION / CONCENTRATE FOR SOLUTION FOR INFUSION

INTRATHECAL

Código ATC: L01BC01 - CITARABINA

Principios Activos: N/A

Experimental

Gilteritinib

FILM-COATED TABLET

ORAL

Código ATC: L01EX13 - GILTERITINIB

Principios Activos: N/A

Huérfano

Experimental

Citarabina Hikma 1 g/10mL Soluzione Iniettabile

SOLUTION FOR INJECTION

INTRAVENOUS

Código ATC: L01BC01 - CITARABINA

Principios Activos: N/A

Experimental

Gilteritinib

FILM-COATED TABLET

ORAL

Código ATC: L01EX13 - GILTERITINIB

Principios Activos: N/A

Huérfano

Experimental

Zarzio 30 MU/0.5 ml solution for injection or infusion in pre-filled syringe

SOLUTION FOR INJECTION/INFUSION

SUBCUTANEOUS

Código ATC: L03AA02 - FILGRASTIM

Principios Activos: N/A

Experimental

Bendarabin 50 mg Pulver zur Herstellung einer Injektions- oder Infusionslösung

SOLUTION FOR INJECTION/INFUSION

INTRAVENOUS

Código ATC: L01BB05 - FLUDARABINA

Principios Activos: N/A

Experimental

Tiene resultados

A study of Gilteritinib combined with chemotherapy to treat Children, Adolescents and Young Adults with Relapsed or Refractory Acute Myeloid Leukemia (AML) with a FLT3 gene mutation

State	**Type of participants**	**Age Ranges**
Finished CT	Incapable subjects of giving consent	Less than 18 , Adults (18-64 years)
Gender	**Phases**	**Expected Participants**
Both	Phase I , Phase II	97
Results	**Low level of intervention**	**Rare disease**
Has results	No	Yes
Geographic coverage	**Areas of the study**	**Advanced therapy**
International multicenter	diagnosis, treatment, safety, effectiveness, pharmacokinetics, pharmacodynamics, dose, pharmacogenomics	NO

Information

Identifier
2024-512469-15-00 (CTIS)

Protocol Code
2215-CL-0603

Transitioned 2018-002301-61

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

Investigated Disease
FMS-like Tyrosine Kinase 3 (FLT3)/Internal Tandem Duplication (ITD)
Positive Relapsed or Refractory Acute Myeloid Leukemia (AML)

Scientific Title
A Phase 1/2, Multicenter, Open-Label, Single Arm, Dose Escalation and Expansion Study of Gilteritinib (ASP2215)

Combined with Chemotherapy in Children, Adolescents and Young Adults with FMS-like Tyrosine Kinase 3 (FLT3)/Internal Tandem Duplication (ITD) Positive Relapsed or Refractory Acute Myeloid Leukemia (AML)

Rationale

Not provided

Main Objective

Phase 1 (Dose Escalation Phase):
To determine the maximum tolerated dose (MTD) and/or optimally safe and biologically active recommended phase 2 dose (RP2D) of gilteritinib given in sequential combination with FLAG in children, adolescents and young adults with relapsed/refractory (R/R) FMS-like tyrosine
kinase 3 (FLT3) (internal tandem duplication (ITD) and/or tyrosine kinase domain (TKD) acute myeloid leukemia (AML).
Phase 2 (Dose Expansion Phase):
To determine complete remission (CR) rates and composite complete remission (CRc) rates after 2 cycles of gilteritinib in sequential combination with FLAG in children, adolescents and young adults with FLT3 (ITD) AML who are refractory to or at the first hematologic relapse after first-line remission induction AML therapy (up to 2 induction cycles).

Primary Endpoints

Phase 1: Determination of MTD and/or RP2D Phase 2: o CRc rates (overall best response) after 2 cycles of therapy. o CR rates after 2 cycles of therapy; CR rate will be further described by the duration of CR (only for USA).

Temporary moments of secondary assessment

Not provided

Secondary Objective

To assess the safety, tolerability and toxicities of gilteritinib when given in sequential combination with FLAG in children, adolescents, and young adults with R/R FLT3/ITD AML
To evaluate FLT3 inhibition due to gilteritinib treatment
To characterize gilteritinib pharmacokinetics
To perform serial measurements of minimal residual disease (MRD) and examine the relationship with study endpoints
To obtain preliminary estimates of 1-year event-free survival (EFS) and overall survival (OS) rate
To assess the acceptability and palatability of the formulation.

Secondary Endpoints

Inhibition of phosphorylated FLT3 (pFLT3) measured by PIA assay
Gilteritinib plasma concentration
Pharmacokinetic parameters (e.g., oral clearance [CL/F], apparent volume of distribution [Vd/F], maximum concentration [Cmax], time of maximum concentration [tmax], area under the concentration-time curve [AUC]) of gilteritinib
Safety, tolerability and toxicity assessments of gilteritinib when given in combination with FLAG
EFS rate
OS rate
MRD assessment
Acceptability and palatability assessment of the formulation

Temporary moments of secondary assessment

Not provided

Inclusion criteria

2. Phase 1: Subject is positive for FLT3 (ITD and/or TKD) mutation in bone marrow or blood as determined by the local institution. Phase 2: Subject is positive for the FLT3 (ITD) mutation in bone marrow or blood as determined by the local institution. 3. Subject is aged 6 months and < 21 years of age* at the time of signing informed consent and/or assent, as applicable. * For phase 2: Enrollment of subjects from 6 months to less than 1 year (Group 3) and 1 year to less than 2 years (Group 2) will be dependent on the establishment of RP2D in the respective for age groups during phase 1. 4. Subject has a diagnosis of AML according to The FrenchAmericanBritish (FAB) classification with 5% blasts in the bone marrow, with or without extramedullary disease (except subjects with active central nervous system (CNS) Leukemia). a) In the phase 1 portion of the study, subject must be in first or greater relapse or refractory to induction therapy with no more than 1 attempt at remission induction (up to 2 induction cycles). b) For the phase 2 portion of the study, subject must be refractory to or at the first hematologic relapse after first-line remission induction AML therapy (up to 2 induction cycles)

Exclusion criteria

1. Subject has active central nervous system (CNS) leukemia. 3. Subject has uncontrolled or significant cardiovascular disease, including: Diagnosed or suspected congenital long QT syndrome or any history of clinically significant ventricular arrhythmias (such as ventricular tachycardia, ventricular fibrillation, or torsades de pointes); any history of arrhythmia will be discussed with the sponsors medical monitor prior to subjects entry into the study Prolonged Fridericia-corrected QT interval (QTcF) interval on pre-entry electrocardiogram (ECG) (450 ms) Any history of second- or third-degree heart block (may be eligible if the subject currently has a pacemaker) Heart rate < 50 beats/minute on pre-entry ECG Uncontrolled hypertension Complete left bundle branch block 6. Subject has active clinically significant graft-versus-host disease (GVHD) or is on treatment with immunosuppressive drugs for treatment of active GVHD, with the exception of subjects being weaned from systemic corticosteroids where the subject is receiving 0.5 mg/kg of prednisone (or equivalent) daily dose for prior GVHD. Subject has received calcineurin inhibitors within 4 weeks prior to screening, unless used as GVHD prophylaxis 7. Subject has active malignant tumors other than AML. 9. Subject has hypokalemia and/or hypomagnesemia at Screening (defined as values below institutional lower limit of normal [LLN]). Repletion of potassium and magnesium levels during the screening period is allowed. 10. Subject requires treatment with concomitant drugs that are strong inducers of cytochrome P450 (CYP)3A/P-glycoprotein (P-gp).

Calendar

(Last Update: 02/10/2025)

Authorization	Start of Trial	First patient inclusion	Halted	Restarted
10/12/2019	19/01/2022	07/04/2022	Not aported	Not aported

End of recruitment	Premature end (Spain)	Premature End (Global)	Trial end (Spain)	Trial end (Global)
17/03/2025	Not aported	Not aported	Not aported	18/03/2025

Sponsor

Astellas Pharma Global Development Inc. United States

2375 Waterview Drive

Contact Person

Clinical Trial Unit Head

+31715454006

ctu@astellas.com

Monetary support: N/A

Sponsor type: Commercial

Ceim

CEIm Fundacio Sant Joan de Deu

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Sites

Closed (22/05/2025)

HOSPITAL DE SANT JOAN DE DÉU.

Esplugues de Llobregat

BARCELONA

Servicio de Hematologia

Closed (16/04/2025)

HOSPITAL UNIVERSITARI VALL D'HEBRON

Barcelona

BARCELONA

Servicio Oncología y Hematología Pediátrica

Closed (30/05/2025)

HOSPITAL UNIVERSITARIO VIRGEN DEL ROCÍO

Sevilla

SEVILLA

Servicio de Hematología y Hemoterapia

Medication

ARA-cell® 40 mg Injektion 20 mg/ml Injektionslösung / Konzentrat zur Herstellung einer Infusionslösung

SOLUTION FOR INJECTION / CONCENTRATE FOR SOLUTION FOR INFUSION

INTRATHECAL

ATC code: L01BC01 - CITARABINA

Active Principles: N/A

Experimental

Gilteritinib

FILM-COATED TABLET

ORAL

ATC code: L01EX13 - GILTERITINIB

Active Principles: N/A

Orphan

Experimental

Citarabina Hikma 1 g/10mL Soluzione Iniettabile

SOLUTION FOR INJECTION

INTRAVENOUS

ATC code: L01BC01 - CITARABINA

Active Principles: N/A

Experimental

Gilteritinib

FILM-COATED TABLET

ORAL

ATC code: L01EX13 - GILTERITINIB

Active Principles: N/A

Orphan

Experimental

Zarzio 30 MU/0.5 ml solution for injection or infusion in pre-filled syringe

SOLUTION FOR INJECTION/INFUSION

SUBCUTANEOUS

ATC code: L03AA02 - FILGRASTIM

Active Principles: N/A

Experimental

Bendarabin 50 mg Pulver zur Herstellung einer Injektions- oder Infusionslösung

SOLUTION FOR INJECTION/INFUSION

INTRAVENOUS

ATC code: L01BB05 - FLUDARABINA

Active Principles: N/A

Experimental

Has results