Safety and Efficacy of Quizartinib in Children and Young Adults With Acute Myeloid Leukemia (AML), a Cancer of the Blood

Estado	**Tipo de Participantes**	**Rangos de Edad**
Fin Reclutamiento	Sujetos incapaces de otorgar consentimiento	Menores de 18 , Adultos (18-64 años)
Género	**Fases**	**Participantes esperados**
Ambos	Fase I , Fase II	2
Resultados	**Bajo nivel intervención**	**Enfermedad rara**
Sin resultados	No	Si
Cobertura geográfica	**Ámbitos del ensayo**	**Terapia avanzada**
Sin determinar	seguridad, eficacia, farmacocinética, farmacodinamica, dosis	NO

Información

Identificador
2023-510009-16-00 (CTIS)

Cod. Protocolo
AC220-A-U202

Transicionado 2016-002919-18

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

Enfermedad investigada
Acute Myeloid Leukemia

Título Científico
PHASE 1/2, MULTICENTER, DOSE-ESCALATING STUDY TO EVALUATE THE SAFETY, PHARMACOKINETICS, PHARMACODYNAMICS, AND EFFICACY OF QUIZARTINIB ADMINISTERED IN COMBINATION WITH RE-INDUCTION CHEMOTHERAPY, AND AS A SINGLE-AGENT CONTINUATION THERAPY, IN PEDIATRIC

RELAPSED/REFRACTORY AML SUBJECTS AGED 1 MONTH TO <18 YEARS (AND YOUNG ADULTS AGED UP TO 21 YEARS) WITH FLT3-ITD MUTATIONS

Justificación

No aportado

Objetivo Principal

Phase 1 only: - To determine the recommended Phase 2 dose (RP2D) of quizartinib, in combination with chemotherapy, for subjects in the older (1 year to 21 years) and younger (1 month to <12 months) age groups. - To determine the composite complete remission (CRc) rate (ie, complete remission [CR] + CR with incomplete recovery [CRi]) after completion of up to 2 Re-Induction Cycles. - To determine the safety and cumulative toxicity of quizartinib administered in combination with re-induction chemotherapy for up to 2 cycles, with optional consolidation therapy, and as a single-agent continuation therapy over 12 cycles. - To determine estimates of individual pharmacokinetic (PK) parameters of quizartinib and AC886 (metabolite of quizartinib).

Variables de Evaluación Primaria

Efficacy (ie, the primary outcome measure): CRc rate after completion of up to 2 Re-Induction Cycles.(based on investigators assessment).
Safety: The safety profile of quizartinib administered in combination with reinduction chemotherapy for up to 2 cycles, with optional consolidation chemotherapy, and as a single-agent continuation therapy over 12 cycles. And phase 1 only: Number of DLTs in dose cohorts in Re-Induction Cycle 1
Estimates of AUC, apparent clearance (CL/F), and apparent volume of distribution (Vz/F) for quizartinib and AC886 by the use of PopPK modeling or other applicable methods

Momentos temporales de evaluación primaria

No aportado

Objetivo Secundario

To determine: CR and CRi rate after completion of up to 2 Re-Induction Cycles and Durations of CRi, CRc, and CR.
To assess time to relapse, rate of relapse after 1, 2 and 3 years, and cumulative incidence of relapse at the EoT.
To determine the rates of CR, CRi, and CRc after completion of Re-Induction Cycle 1.
To assess OS and EFS at 1, 2, and 3 years.
To assess number of subjects proceeding to high-dose conditioning therapy/ HSCT.
To assess activity of quizartinib on FLT3-ITD autophosphorylation activity by an ex-vivo PIA during Re-Induction, Continuation, and at time of relapse.
To assess FLT-ITD/FLT3-wild-type (WT) allelic ratio at Screening, during Re- Induction, and at time of relapse.
To evaluate somatic mutations present in blasts at Screening and at time of refractory disease or relapse.
To assess rate of CRc (CR, CRi) without FLT3-ITD minimal residual disease (MRD) using next-generation sequencing.
To assess acceptability including palatability of quizartinib formulations.

Variables de Evaluación Secundaria

Efficacy (ie, the secondary outcome measures): CR rate, which is defined as the percent of subjects achieving a CR after completion of up to 2 Re-Induction cycles
CRi rate, which is defined as the percent of subjects achieving CRi after completion of up to 2 Re-Induction Cycles.
Duration of CR defined as the time from the first documented CR until documented relapse
Duration of CRi, defined as the time from the first documented CRi until documented relapse
Duration of CRc, defined as the time from the first documented CR or CRi until documented relapse
CR rate after completion of Re-Induction Cycle 1 which is defined as the percent of subjects achieving CR after completion of Re-Induction Cycle 1
CRi rate after completion of Re-Induction Cycle 1, which is defined as the percent of subjects achieving a CRi after completion of Re-Induction Cycle 1
CRc rate after completion of Re-Induction Cycle 1, which is defined as the percent of subjects achieving CR+ CRi after completion of Re- Induction Cycle 1
Time to relapse, defined as the time from the first documented response (CR, CRi) until documented relapse
Rate of relapse after 1, 2 and 3 years
Cumulative incidence of relapse at the end of the study, defined as the percentage of subjects who achieved CRc at the end of Re-Induction and relapse at these defined time points
OS, defined as the time from the start of Re-Induction therapy until death from any cause
EFS defined as the time from the start of Re-Induction therapy until the earliest date of the following: - Refractory disease (or treatmetn failure) at the end of Re-Induction. - Relapse after CR or CRi. - Death from any cause at any time during the study.
Pharmacodynamic: Inhibition of FLT3-ITD autophosphorylation activity in an ex-vivo PIA during Re-Induction, Continuation, and at the time of relapse
FLT3-ITD to FLT3-WT allelic ratio at Screening, during Re- Induction, and at the time of relapse
Mutations present in blasts (eg, in the kinase and juxtamembrane domains of FLT3 and other mutations known to be associated with AML) at Screening and at the time of refractory disease or relapse
Biomarker: Rate of CRc (CR, CRi) without MRD using next generation sequencing
Others: Acceptability including palatability of quizartinib formulations

Momentos temporales de evaluación secundaria

No aportado

Criterios de Inclusión

Has diagnosis of AML according to the World Health Organization (WHO) 2008 classification with 5% blasts in bone marrow, with or without extramedullary disease
Male participants must be surgically sterile or willing to use highly effective birth control during the treatment period, and for 6 months following the last dose of quizartinib, etoposide, fludarabine, methotrexate, or cytarabine, whichever is later.
Participant/legal representative is capable of understanding the investigational nature of the study, potential risks, and benefits, and the patient (and/or legal representative) signs a written assent/informed consent
Female subjects must not donate or retrieve for their own use ova from the time of Screening and throughout the treatment period, and for at least 7 months following the last dose
Male subjects must not freeze or donate sperm starting at Screening and throughout the treatment period, and at least 4 months following the last dose.
In first relapse or refractory to first-line high-dose chemotherapy with no more than 1 attempt (1 to 2 cycles of induction chemotherapy) at remission induction - prior HSCT is permitted
Has presence of the FLT3-ITD activating mutation in bone marrow or peripheral blood as defined in the protocol
Is between 1 month and 21 years of age at the time the Informed Consent/Assent form is signed

Has protocol-defined adequate performance status score
Has fully recovered from the acute clinically significant toxicity effects of previous anti-cancer therapy prior to Re-Induction Cycle 1, Day 1, defined as toxicities (other than alopecia) not yet resolved by the National Cancer Institute - Common Terminology Criteria for Adverse Events Version 5.0 (NCI-CTCAE v5.0) to Grade 1 or baseline.
Has protocol-defined adequate renal, hepatic and cardiac functions
If of reproductive potential, is permanently sterile or agrees to use highly effective birth control upon enrollment, during the period of therapy, and for 6 months following the last dose of quizartinib, etoposide, fludarabine, methotrexate, or cytarabine, whichever is later
If female of child-bearing potential, tests negative for pregnancy and agrees not to breast feed

Criterios de Exclusión

Has been diagnosed with isolated central nervous system relapse, acute promyelocytic leukemia (APL), juvenile myelomonocytic leukemia, French-American-British classification M3 or WHO classification of APL with translocation, or with myeloid proliferations related to Down syndrome
Is otherwise considered inappropriate for the study by the Investigator
Has uncontrolled or pre-defined significant cardiovascular disease as detailed in the protocol
Has systemic fungal, bacterial, viral or other infection that is exhibiting ongoing signs/symptoms related to the infection without improvement despite appropriate antibiotics or other treatment. The patient must be off vasopressors and have negative blood cultures for at least 48 hours prior to the start of systematic protocol therapy
Has known active clinically relevant liver disease (e.g., active hepatitis B or active hepatitis C)
Has known history of human immunodeficiency virus (HIV)
Has history of hypersensitivity to any of the study medications or their excipients
Is receiving or is anticipated to receive concomitant chemotherapy, radiation, or immunotherapy other than as specified in the protocol
Has any significant concurrent disease, illness, psychiatric disorder or social issue that would compromise subject safety or compliance, interfere with consent/assent, study participation, follow up, or interpretation of study results
Is currently participating in another investigative interventional procedure (observational or long-term interventional follow-up is allowed)

Calendario

(Última actualización: 06/11/2025)

Autorización	Inicio de Ensayo	Inclusión Primer Paciente	Interrumpido	Reiniciado
10/07/2018	04/12/2018	04/12/2018	No aportado	No aportado

Fin de reclutamiento	Fin prematuro (España)	Fin prematuro (Global)	Fin del ensayo en España	Fin del ensayo global
21/08/2025	No aportado	No aportado	No aportado	No aportado

Promotor

Daiichi Sankyo Inc. United States

211 Mount Airy Road

Contact Person

Clinical Trial Office

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TBEU-clinicaltrials_eu@daiichisankyo.com

Monetary support: N/A

Tipo de promotor: Comercial

Ceim

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Centros

Activo (17/09/2018)

COMPLEJO UNIVERSITARIO LA PAZ

Madrid

MADRID

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

Hospital Infantil Universitario Nino Jesus

Madrid

MADRID

Oncology

Activo (14/09/2018)

HOSPITAL INFANTIL UNIVERSITARIO NIÑO JESUS

Madrid

MADRID

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

Hospital Universitario La Paz

Madrid

MADRID

Oncology

Medicamentos

Quizartinib

ORAL SOLUTION

ORAL

-

Principios Activos: N/A

Experimental

Sin resultados

Safety and Efficacy of Quizartinib in Children and Young Adults With Acute Myeloid Leukemia (AML), a Cancer of the Blood

State	Type of participants	Age Ranges
End of recruitment	Incapable subjects of giving consent	Less than 18 , Adults (18-64 years)
Gender	**Phases**	**Expected Participants**
Both	Phase I , Phase II	2
Results	**Low level of intervention**	**Rare disease**
No results	No	Yes
Geographic coverage	**Areas of the study**	**Advanced therapy**
Undetermined	safety, effectiveness, pharmacokinetics, pharmacodynamics, dose	NO

Information

Identifier
2023-510009-16-00 (CTIS)

Protocol Code
AC220-A-U202

Transitioned 2016-002919-18

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

Investigated Disease
Acute Myeloid Leukemia

Scientific Title
PHASE 1/2, MULTICENTER, DOSE-ESCALATING STUDY TO EVALUATE THE SAFETY, PHARMACOKINETICS, PHARMACODYNAMICS, AND EFFICACY OF QUIZARTINIB ADMINISTERED IN COMBINATION WITH RE-INDUCTION CHEMOTHERAPY, AND AS A SINGLE-AGENT CONTINUATION THERAPY, IN PEDIATRIC

RELAPSED/REFRACTORY AML SUBJECTS AGED 1 MONTH TO <18 YEARS (AND YOUNG ADULTS AGED UP TO 21 YEARS) WITH FLT3-ITD MUTATIONS

Rationale

Not provided

Main Objective

Phase 1 only: - To determine the recommended Phase 2 dose (RP2D) of quizartinib, in combination with chemotherapy, for subjects in the older (1 year to 21 years) and younger (1 month to <12 months) age groups. - To determine the composite complete remission (CRc) rate (ie, complete remission [CR] + CR with incomplete recovery [CRi]) after completion of up to 2 Re-Induction Cycles. - To determine the safety and cumulative toxicity of quizartinib administered in combination with re-induction chemotherapy for up to 2 cycles, with optional consolidation therapy, and as a single-agent continuation therapy over 12 cycles. - To determine estimates of individual pharmacokinetic (PK) parameters of quizartinib and AC886 (metabolite of quizartinib).

Primary Endpoints

Efficacy (ie, the primary outcome measure): CRc rate after completion of up to 2 Re-Induction Cycles.(based on investigators assessment).
Safety: The safety profile of quizartinib administered in combination with reinduction chemotherapy for up to 2 cycles, with optional consolidation chemotherapy, and as a single-agent continuation therapy over 12 cycles. And phase 1 only: Number of DLTs in dose cohorts in Re-Induction Cycle 1
Estimates of AUC, apparent clearance (CL/F), and apparent volume of distribution (Vz/F) for quizartinib and AC886 by the use of PopPK modeling or other applicable methods

Temporary moments of secondary assessment

Not provided

Secondary Objective

To determine: CR and CRi rate after completion of up to 2 Re-Induction Cycles and Durations of CRi, CRc, and CR.
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To assess acceptability including palatability of quizartinib formulations.

Secondary Endpoints

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Is currently participating in another investigative interventional procedure (observational or long-term interventional follow-up is allowed)

Calendar

(Last Update: 06/11/2025)

Authorization	Start of Trial	First patient inclusion	Halted	Restarted
10/07/2018	04/12/2018	04/12/2018	Not aported	Not aported

End of recruitment	Premature end (Spain)	Premature End (Global)	Trial end (Spain)	Trial end (Global)
21/08/2025	Not aported	Not aported	Not aported	Not aported

Sponsor

Daiichi Sankyo Inc. United States

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Contact Person

Clinical Trial Office

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Monetary support: N/A

Sponsor type: Commercial

Ceim

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Sites

Active (17/09/2018)

COMPLEJO UNIVERSITARIO LA PAZ

Madrid

MADRID

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

Hospital Infantil Universitario Nino Jesus

Madrid

MADRID

Oncology

Active (14/09/2018)

HOSPITAL INFANTIL UNIVERSITARIO NIÑO JESUS

Madrid

MADRID

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

Hospital Universitario La Paz

Madrid

MADRID

Oncology

Medication

Quizartinib

ORAL SOLUTION

ORAL

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Active Principles: N/A

Experimental

No results