Study of efficacy and safety of asciminib in addition to imatinib in CML-CP patients without a deep level or response on imatinib

Estado	**Tipo de Participantes**	**Rangos de Edad**
EC Finalizado	No aportado	Mayores de 64 , Adultos (18-64 años)
Género	**Fases**	**Participantes esperados**
Ambos	Fase II	91
Resultados	**Bajo nivel intervención**	**Enfermedad rara**
Tiene resultados	No	No
Cobertura geográfica	**Ámbitos del ensayo**	**Terapia avanzada**
Multicéntrico internacional	seguridad, eficacia, farmacocinética	NO

Información

Identificador
2024-515040-23-00 (CTIS)

Cod. Protocolo
CABL001E2201

Transicionado 2018-001594-24

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

Enfermedad investigada
Chronic Myelogenous Leukemia in chronic phase (CML-CP), previously treated with imatinib and have not achieved deep molecular response

Título Científico
A phase 2, multi-center, open-label, randomized study of oral asciminib added to imatinib versus continued imatinib versus switch to nilotinib in patients with CML-CP who have been previously treated with imatinib and have not achieved deep molecular response

Justificación

No aportado

Objetivo Principal

The primary objective of this study is to assess whether asciminib 40 mg once daily (QD) + imatinib 400 mg QD or asciminib 60 mg QD + imatinib 400 mg QD is more effective than continued imatinib by testing the MR4.5 rate at 48 weeks.

Variables de Evaluación Primaria

Molecular Response (MR)4.5 rate at 48 weeks

Momentos temporales de evaluación primaria

No aportado

Objetivo Secundario

To estimate efficacy of switch to nilotinib assessed by the MR4.5 rate at 48 weeks.
To estimate difference in efficacy between asciminib 60 mg + imatinib and switch to nilotinib considering the difference in MR4.5 rate at 48 weeks.
To estimate difference in efficacy between asciminib 40 mg + imatinib and switch to nilotinib considering the difference in MR4.5 rate at 48 weeks.
To assess additional parameters of the efficacy of asciminib 60 mg or 40 mg added to imatinib versus continued imatinib or switch to nilotinib i.e. the rate of MR4.5 at 96 weeks, rate of MR4.5 by 48 and 96 weeks, sustained MR4.5 at 96 weeks and time to MR4.5.
To characterize the safety and tolerability profile of asciminib 60 mg or 40 mg + imatinib versus continued imatinib or switch to nilotinib by comparing the incidence and severity of adverse events (AEs), changes in laboratory values, clinically notable ECG abnormalities and vital signs.
To assess the pharmacokinetic profile of asciminib 60 mg or 40 mg and imatinib when administered in combination.

Variables de Evaluación Secundaria

Molecular Response (MR)4.5 rate at 48 weeks Difference in rate of MR4.5 at 48 weeks
Rate of MR4.5 at 96 weeks Rate of MR4.5 by 48 and 96 weeks Sustained MR4.5 at 96 weeks Time to MR4.5
Incidence and severity of adverse events, changes in laboratory values, clinically notable ECG abnormalities and vital signs
Plasma concentrations of asciminib and imatinib when administered in combination. PK parameters include but are not limited to Cmax, Tmax, Cmin, AUClast and AUCtau

Momentos temporales de evaluación secundaria

No aportado

Criterios de Inclusión

Signed informed consent must be obtained prior to participation in the study. Male or female patients 18 years of age with a confirmed diagnosis of CMLCP. Minimum of one year (12 calendar months) treatment with imatinib first line for CML-CP (patients have to be on imatinib 300 mg QD or higher). BCR-ABL1 levels > 0.01% IS and 1% IS at the time of study entry as confirmed with a central assessment at screening; patients must not have achieved deep molecular response (MR4 IS) at any time during prior imatinib treatment. Patient must meet the following laboratory values before randomization: Absolute Neutrophil Count 1.5 x 109 L Platelets 75 x 109/L Hemoglobin 9 g/dL Serum creatinine (sCr) < 1.5 mg/dL Total bilirubin (TBL) 1.5 x upper limit of normal (ULN) except for patients with Gilberts syndrome who may only be included with total bilirubin 3.0 x ULN Aspartate aminotransaminase (AST) 3.0 x ULN Alanine aminotransaminase (ALT) 3.0 x ULN Alkaline phosphatase (ALP) 2.5 x ULN Serum lipase 1.5 x ULN. For serum lipase > ULN - 1.5 x ULN, value must be considered not clinically significant and not associated with risk factors for acute pancreatitis Patients must have the following laboratory values (lower limit of normal (LLN)) or corrected to within normal limits with supplements prior to randomization: Potassium (potassium increase of up to 6.0 mmol/L is acceptable if associated with creatinine clearance* within normal limits) Total calcium (corrected for serum albumin); (calcium increase of up to 12.5 mg/dl or 3.1 mmol/L is acceptable if associated with creatinine clearance* within normal limits) Magnesium (magnesium increase up to 3.0 mg/dL or 1.23 mmol/L if associated with creatinine clearance* within normal limits. *Creatinine clearance as calculated using Cockcroft-Gault formula

Criterios de Exclusión

Treatment failure according to ELN 2013 criteria during imatinib treatment.
Known second chronic phase of CML after previous progression to accelerated phase/blast crisis (AP/BC).
Previous treatment with any TKIs other than imatinib
History or current diagnosis of ECG abnormalities indicating significant risk or safety for subjects participating in the study such as: History of myocardial infarction (MI), angina pectoris, coronary artery bypass graft (CABG) within 6 months prior to randomization Concomitant clinically significant arrhythmias, e.g. sustained ventricular tachycardia, and clinically significant second or third degree atrioventricular (AV) block without a pacemaker Resting QTcF 450 msec (male) or 460 msec (female) prior to randomization Long QT syndrome, family history of idiopathic sudden death or congenital long QT syndrome, or any of the following Risk factors for Torsades de Pointes including uncorrected hypokalemia or hypomagnesemia, history of cardiac failure, or history of clinically significant/symptomatic bradycardia Concomitant medications with a "known" risk of Torsades de Pointes per qtdrugs.org that cannot be discontinued or replaced by safe alternative medication inability to determine the QTcF interval
Severe and/or uncontrolled concurrent medical disease that in the opinion of the investigator could cause unacceptable safety risks or compromise compliance with the protocol (e.g. uncontrolled diabetes, active or uncontrolled infection, uncontrolled clinically significant hyperlipidemia and high serum amylase).
History of acute pancreatitis within 1 year prior to randomization or past medical history of chronic pancreatitis or history of acute or chronic liver disease.
History of other active malignancy within 3 years prior to randomization with the exception of basal cell skin cancer, indolent prostate cancer and carcinoma in situ treated curatively.

Calendario

(Última actualización: 09/04/2025)

Autorización	Inicio de Ensayo	Inclusión Primer Paciente	Interrumpido	Reiniciado
21/09/2018	16/10/2018	09/01/2019	No aportado	No aportado

Fin de reclutamiento	Fin prematuro (España)	Fin prematuro (Global)	Fin del ensayo en España	Fin del ensayo global
07/02/2024	No aportado	No aportado	26/02/2025	27/02/2025

Promotor

Novartis Pharma AG Switzerland

Lichtstrasse 35

Contact Person

Novartis Pharma Arzneimittel GmbH

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legal.representative@novartis.com

Monetary support: N/A

Tipo de promotor: Comercial

Ceim

CEIm Provincial de Sevilla

Avenida Doctor Fedriani 3 41009 Sevilla

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955043127

Centros

Cerrado (26/02/2025)

HOSPITAL RAMÓN Y CAJAL

Madrid

MADRID

Cerrado (26/02/2025)

HOSPITAL UNIVERSITARI I POLITÈCNIC LA FE

Valencia

VALENCIA

Cerrado (20/08/2020)

HOSPITAL UNIVERSITARIO DE GRAN CANARIA DR. NEGRÍN

Palmas de Gran Canaria, Las

LAS PALMAS

Cerrado (26/02/2025)

HOSPITAL VIRGEN MACARENA

Sevilla

SEVILLA

Cerrado (26/02/2025)

Institut Catala D'oncologia

Badalona

BARCELONA

Medicamentos

Scemblix 20 mg film-coated tablets
FILM-COATED TABLET
ORAL USE

Código ATC: L01EA06 - ASCIMINIB
Principios Activos: N/A

Huérfano — Experimental

Scemblix 40 mg film-coated tablets
FILM-COATED TABLET
ORAL USE

Código ATC: L01EA06 - ASCIMINIB
Principios Activos: N/A

Huérfano — Experimental

NILOTINIB
CAPSULE, HARD
ORAL USE

-
Principios Activos: N/A

Huérfano — Experimental

NILOTINIB
CAPSULE, HARD
ORAL USE

-
Principios Activos: N/A

Huérfano — Experimental

IMATINIB
FILM-COATED TABLET
ORAL USE

-
Principios Activos: N/A

Experimental

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IMATINIB
FILM-COATED TABLET
ORAL USE

-

Principios Activos: N/A

Experimental

Tiene resultados

Study of efficacy and safety of asciminib in addition to imatinib in CML-CP patients without a deep level or response on imatinib

State	Type of participants	Age Ranges
Finished CT	Not provided	Older than 64 , Adults (18-64 years)
Gender	**Phases**	**Expected Participants**
Both	Phase II	91
Results	**Low level of intervention**	**Rare disease**
Has results	No	No
Geographic coverage	**Areas of the study**	**Advanced therapy**
International multicenter	safety, effectiveness, pharmacokinetics	NO

Information

Identifier

2024-515040-23-00 (CTIS)

Protocol Code

CABL001E2201

Transitioned 2018-001594-24

Therapeutic area

Diseases [C] - Cancer [C04]|

Investigated Disease

Chronic Myelogenous Leukemia in chronic phase (CML-CP), previously treated with imatinib and have not achieved deep molecular response

Scientific Title

A phase 2, multi-center, open-label, randomized study of oral asciminib added to imatinib versus continued imatinib versus switch to nilotinib in patients with CML-CP who have been previously treated with imatinib and have not achieved deep molecular response

Rationale

Not provided

Main Objective

The primary objective of this study is to assess whether asciminib 40 mg once daily (QD) + imatinib 400 mg QD or asciminib 60 mg QD + imatinib 400 mg QD is more effective than continued imatinib by testing the MR4.5 rate at 48 weeks.

Primary Endpoints

Molecular Response (MR)4.5 rate at 48 weeks

Temporary moments of secondary assessment

Not provided

Secondary Objective

To estimate efficacy of switch to nilotinib assessed by the MR4.5 rate at 48 weeks.
To estimate difference in efficacy between asciminib 60 mg + imatinib and switch to nilotinib considering the difference in MR4.5 rate at 48 weeks.
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Secondary Endpoints

Molecular Response (MR)4.5 rate at 48 weeks Difference in rate of MR4.5 at 48 weeks
Rate of MR4.5 at 96 weeks Rate of MR4.5 by 48 and 96 weeks Sustained MR4.5 at 96 weeks Time to MR4.5
Incidence and severity of adverse events, changes in laboratory values, clinically notable ECG abnormalities and vital signs
Plasma concentrations of asciminib and imatinib when administered in combination. PK parameters include but are not limited to Cmax, Tmax, Cmin, AUClast and AUCtau

Temporary moments of secondary assessment

Not provided

Inclusion criteria

Signed informed consent must be obtained prior to participation in the study. Male or female patients 18 years of age with a confirmed diagnosis of CMLCP. Minimum of one year (12 calendar months) treatment with imatinib first line for CML-CP (patients have to be on imatinib 300 mg QD or higher). BCR-ABL1 levels > 0.01% IS and 1% IS at the time of study entry as confirmed with a central assessment at screening; patients must not have achieved deep molecular response (MR4 IS) at any time during prior imatinib treatment. Patient must meet the following laboratory values before randomization: Absolute Neutrophil Count 1.5 x 109 L Platelets 75 x 109/L Hemoglobin 9 g/dL Serum creatinine (sCr) < 1.5 mg/dL Total bilirubin (TBL) 1.5 x upper limit of normal (ULN) except for patients with Gilberts syndrome who may only be included with total bilirubin 3.0 x ULN Aspartate aminotransaminase (AST) 3.0 x ULN Alanine aminotransaminase (ALT) 3.0 x ULN Alkaline phosphatase (ALP) 2.5 x ULN Serum lipase 1.5 x ULN. For serum lipase > ULN - 1.5 x ULN, value must be considered not clinically significant and not associated with risk factors for acute pancreatitis Patients must have the following laboratory values (lower limit of normal (LLN)) or corrected to within normal limits with supplements prior to randomization: Potassium (potassium increase of up to 6.0 mmol/L is acceptable if associated with creatinine clearance* within normal limits) Total calcium (corrected for serum albumin); (calcium increase of up to 12.5 mg/dl or 3.1 mmol/L is acceptable if associated with creatinine clearance* within normal limits) Magnesium (magnesium increase up to 3.0 mg/dL or 1.23 mmol/L if associated with creatinine clearance* within normal limits. *Creatinine clearance as calculated using Cockcroft-Gault formula

Exclusion criteria

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History of other active malignancy within 3 years prior to randomization with the exception of basal cell skin cancer, indolent prostate cancer and carcinoma in situ treated curatively.

Calendar

(Last Update: 09/04/2025)

Authorization	Start of Trial	First patient inclusion	Halted	Restarted
21/09/2018	16/10/2018	09/01/2019	Not aported	Not aported

End of recruitment	Premature end (Spain)	Premature End (Global)	Trial end (Spain)	Trial end (Global)
07/02/2024	Not aported	Not aported	26/02/2025	27/02/2025

Sponsor

Novartis Pharma AG Switzerland

Lichtstrasse 35

Contact Person

Novartis Pharma Arzneimittel GmbH

+499112730

legal.representative@novartis.com

Monetary support: N/A

Sponsor type: Commercial

Ceim

CEIm Provincial de Sevilla

Avenida Doctor Fedriani 3 41009 Sevilla

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955043127

Sites

Closed (26/02/2025)

HOSPITAL RAMÓN Y CAJAL

Madrid

MADRID

Closed (26/02/2025)

HOSPITAL UNIVERSITARI I POLITÈCNIC LA FE

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ORAL USE

-
Active Principles: N/A
Experimental

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ORAL USE

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Active Principles: N/A

Experimental

Has results