Acalabrutinib Monotherapy vs Investigators Choice of Treatment in Patients with Chronic Lymphocytic Leukaemia and Moderate to Severe Cardiac Impairment

Estado	**Tipo de Participantes**	**Rangos de Edad**
Reclutando	No aportado	Mayores de 64 , Adultos (18-64 años)
Género	**Fases**	**Participantes esperados**
Ambos	Fase IV	33
Resultados	**Bajo nivel intervención**	**Enfermedad rara**
Sin resultados	No	No
Cobertura geográfica	**Ámbitos del ensayo**	**Terapia avanzada**
Sin determinar	seguridad, eficacia	NO

Información

Identificador
2023-510147-37-00 (CTIS)

Cod. Protocolo
D8223C00016

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

Enfermedad investigada
Chronic Lymphocytic Leukaemia and Moderate to Severe Cardiac Impairment

Título Científico
A Multicentre, Open-Label, Randomized, Phase IV Study to Investigate Acalabrutinib Monotherapy Compared to Investigators Choice of Treatment in Adults (> 18 Years) with Chronic Lymphocytic Leukemia and Moderate to Severe Cardiac Impairment

Justificación

No aportado

Objetivo Principal

To evaluate the safety and tolerability of acalabrutinib monotherapy vs investigators choice of treatment in patients with treatment naïve or
relapsed/refractory chronic lymphocytic leukaemia and moderate to severe cardiac impairment.

Variables de Evaluación Primaria

Frequency and time to discontinuation of any study treatment due to worsening in cardiovascular. function or cardiovascular Adverse events (AEs).
Incidence of Grade 4 and 5 cardiovascular events of interest.
Incidence and relationship to study treatment of: - Grade 3 AEs. - Serious adverse events (SAEs). - Non-cardiovascular AE that lead to discontinuation of any study treatment. - Events of clinical interest (ECI)as defined in the Statistical Analysis Plan (SAP).

Momentos temporales de evaluación primaria

No aportado

Objetivo Secundario

To evaluate the extent and duration of tumour response and survival after acalabrutinib vs investigators choice of treatment in patients with treatment naïve or relapsed/refractory chronic lymphocytic leukaemia and moderate to severe cardiac impairment.

Variables de Evaluación Secundaria

Overall survival (OS), defined as the time from randomisation to death from any cause.
Per iwCLL 2018 criteria (Hallek et al, 2018): Event-free survival (EFS), defined as the time from randomisation to disease progression, initiation of subsequent anti-CLL therapy, or death from any cause, whichever occurs first.
Overall response rate (ORR), defined as the proportion of patients with a complete response (CR), complete response with incomplete bone marrow recovery (CRi), nodular partial response (nPR) or partial response (PR).
Duration of response (DOR), defined as the time from the first documented response (PR or better) to disease progression or death (by any cause in the absence of disease progression).
Progressionfree survival (PFS), defined as the time from randomisation to disease progression or death (by any cause in the absence of disease progression).

Momentos temporales de evaluación secundaria

No aportado

Criterios de Inclusión

Men and women 18 years of age, at the time of signing the informed consent. Eastern Cooperative Oncology Group (ECOG) performance status of 0 to 3. Meet at least one of the following cardiovascular inclusion criteria: (a) Left ventricular ejection fraction (LVEF) < 50% as assessed by local ECHO at screening. (b) History of heart failure or meeting Universal Definition of Heart Failure at screening (Appendix M), regardless of current LVEF. (c) History of ischaemic heart disease (IHD) including acute coronary syndrome, myocardial infarction, or coronary revascularization (percutaneous coronary intervention/stent or coronary artery bypass surgery). (d) Diagnosis of cardiomyopathy. (e) Ongoing clinically significant (symptomatic or requiring intervention) cardiac arrhythmia, including atrial fibrillation or other arrhythmias. (f) History of moderate or severe cardiac valvular diseases as documented per cardiac imaging. Diagnosis of CLL per (Hallek et al, 2018). Treatment naïve (TN) or relapsed/refractory (R/R) patients who have received no more than 2 prior lines of systemic anti-CLL treatment. Active disease per iwCLL 2018 (Hallek et al, 2018) criteria that requires treatment. Meet the following laboratory parameters: - Absolute neutrophil count (ANC) 500 cells/L (0.50 × 109/L). - Platelet count 30,000 cells/L (30 × 109/L). - Serum aspartate aminotransferase (AST) and alanine aminotransferase (ALT) 3.0 × upper limit of normal (ULN). - Total bilirubin 1.5 × ULN, unless directly attributable to Gilberts syndrome. - Estimated creatinine clearance (ie, estimated glomerular filtration rate [eGFR] using Cockcroft-Gault) 40 mL/min, or serum creatinine 2 x ULN. Women and men who are sexually active and can bear children must agree to use highly effective forms of contraception. Contraceptives used by men or women should follow the respective Prescribing Information requirements and be consistent with local regulations. Patients must be willing and able to adhere to the study visit schedule, understand, and comply with other protocol requirements, and provide written informed consent and authorisation to use protected health information (in accordance with national and local patient privacy regulations). Note: vulnerable patients, as defined in the International Council for Harmonisation (ICH) Good Clinical Practice (GCP), are not allowed on this protocol (eg, prisoners or institutionalised patients).

Criterios de Exclusión

Known active central nervous system (CNS) leukaemia, leptomeningeal disease or spinal cord compression. In case of R/R patients with prior history of CNS localisation of leukaemia who received treatment are eligible provided that there is no evidence of CNS involvement at study entry as documented by CSF cytology and/or brain MRI. Breastfeeding or pregnant. Concurrent participation in another therapeutic clinical trial. Ongoing Richters transformation. Uncontrolled cardiac/cardiovascular disease including the following: (a) Baseline cardiac troponin (cTnI or cTnT or hs-cTn) levels greater than the upper limit of normal (per the local laboratories reference range) that is due to an acute coronary event and cannot be fully explained by non-ischaemic conditions. (b) Uncontrolled cardiac tachyarrhythmias (sinus, atrial or ventricular) that require new/additional therapy within the last month. (c) Clinically significant QT prolongation defined as QT interval corrected by Fridericias formula (QTcF) values; QTcF > 500 ms. (d) Any of the following within the last 3 months: i. Unstable IHD: percutaneous coronary intervention, coronary artery bypass surgery, or an episode of acute coronary syndrome including acute myocardial infarction and unstable angina pectoris. ii. Major cardiac surgery/procedures or valvular surgery. iii. Hospitalization due to heart failure. Uncontrolled hypertension (> 140/90 mmHg) despite optimal management. Current life-threatening illness, medical conditions, organ system dysfunction or lifestyle habits which, in the investigators opinion, could compromise the patients safety or ability to adhere to the study protocol. Prior exposure to a BTKi. Major surgery within 30 days before first dose of study treatment. Uncontrolled haemolytic anaemia. Received any investigational drug within 30 days or 5-half-lives (whichever is shorter) before first dose of study treatment. Unable to swallow tablets or malabsorption syndrome, or disease significantly affecting gastrointestinal function, or resection of the stomach or small bowel or gastric bypass, symptomatic inflammatory bowel disease, or partial or complete bowel obstruction. Received a live virus vaccination within 28 days of first dose of study treatment. History of or ongoing confirmed progressive multifocal leukoencephalopathy (PML). History of prior malignancy except for the following: - Prior history of malignancy with no evidence of active disease present for more than 3 years before screening or felt to be

at low risk for recurrence by the treating physician. - Adequately treated lentigo maligna melanoma without current evidence of disease or adequately resected non-melanomatous skin cancer (ie, basal cell carcinoma or squamous cell carcinoma of the skin). - Curatively treated in situ carcinoma of the cervix or carcinoma in situ of the prostate at any time prior to study without current evidence of disease. Hypersensitivity to the study treatments active substance or to any of the excipients listed in the Prescribing Information. Any contraindication to the study treatments in Arm B as per the local Prescribing Information. Active uncontrolled systemic infection (bacterial, fungal, viral, or other) or clinically significant localised infection. Known history of infection with human immunodeficiency virus (HIV). Serologic status reflecting active HepB or HepC infection.Patients who are hepatitis B core antibody (anti-HBc) positive and who are hepatitis B surface antigen (HBsAg) negative will need to have a negative DNA polymerase chain reaction (PCR) result before randomisation and must be willing to undergo DNA PCR testing during the study. Those who are HBsAg-positive or hepatitis B PCR positive will be excluded. Patients who are hepatitis C antibody positive will need to have a negative RNA PCR result before randomisation. Those who are hepatitis C PCR positive will be excluded. History of stroke or intracranial haemorrhage within 6 months prior to randomisation. History of bleeding diathesis (eg, haemophilia, von Willebrand disease). Requires or receiving anticoagulation with warfarin or equivalent vitamin K antagonists (eg, phenprocoumon) within 7 days of first dose of study treatment. Direct anti-X (DOACs) or low molecular weight heparins (LMWH, eg, enoxaparin) on stable dosing schedule is allowed. Requires treatment with a strong cytochrome P450 3A (CYP3A) inhibitor/inducer. The use of strong CYP3A inhibitors within 1 week or strong CYP3A inducers within 3 weeks of the first dose of study treatment is prohibited.

Calendario

(Última actualización: 17/07/2026)

Autorización	Inicio de Ensayo	Inclusión Primer Paciente	Interrumpido	Reiniciado
22/07/2024	18/12/2024	15/04/2025	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

AstraZeneca AB Sweden

-

Contact Person

Clinical Study Information Center

18772409479

information.center@astrazeneca.com

Monetary support: N/A

Tipo de promotor: Comercial

Ceim

CEIm Hospital Universitario La Paz

Paseo de la Castellana, 261 28046 Madrid

ceic.hulp@salud.madrid.org

917277413

Centros

Activo (30/07/2024)

Hospital Del Mar

Barcelona

BARCELONA

Hematology

Activo (21/02/2025)

Hospital Universitario Fundacion Jimenez Diaz

Madrid

MADRID

Hematology

Activo (09/10/2024)

Hospital Universitario Virgen De La Macarena

Sevilla

SEVILLA

Hematology

Medicamentos

Calquence 100 mg film-coated tablets
FILM-COATED TABLET
ORAL USE

Código ATC: L01EL02 - ACALABRUTINIB
Principios Activos: N/A

Experimental

Calquence 100 mg film-coated tablets
FILM-COATED TABLET
ORAL USE

Código ATC: L01EL02 - ACALABRUTINIB
Principios Activos: N/A

Experimental

Sin resultados

Acalabrutinib Monotherapy vs Investigators Choice of Treatment in Patients with Chronic Lymphocytic Leukaemia and Moderate to Severe Cardiac Impairment

State	**Type of participants**	**Age Ranges**
Recruiting	Not provided	Older than 64 , Adults (18-64 years)
Gender	**Phases**	**Expected Participants**
Both	Phase IV	33
Results	**Low level of intervention**	**Rare disease**
No results	No	No
Geographic coverage	**Areas of the study**	**Advanced therapy**
Undetermined	safety, effectiveness	NO

Information

Identifier
2023-510147-37-00 (CTIS)

Protocol Code
D8223C00016

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

Investigated Disease
Chronic Lymphocytic Leukaemia and Moderate to Severe Cardiac Impairment

Scientific Title
A Multicentre, Open-Label, Randomized, Phase IV Study to Investigate Acalabrutinib Monotherapy Compared to Investigators Choice of Treatment in Adults (> 18 Years) with Chronic Lymphocytic Leukemia and Moderate to Severe Cardiac Impairment

Rationale

Not provided

Main Objective

To evaluate the safety and tolerability of acalabrutinib monotherapy vs investigators choice of treatment in patients with treatment naïve or
relapsed/refractory chronic lymphocytic leukaemia and moderate to severe cardiac impairment.

Primary Endpoints

Frequency and time to discontinuation of any study treatment due to worsening in cardiovascular. function or cardiovascular Adverse events (AEs).
Incidence of Grade 4 and 5 cardiovascular events of interest.
Incidence and relationship to study treatment of: - Grade 3 AEs. - Serious adverse events (SAEs). - Non-cardiovascular AE that lead to discontinuation of any study treatment. - Events of clinical interest (ECI)as defined in the Statistical Analysis Plan (SAP).

Temporary moments of secondary assessment

Not provided

Secondary Objective

To evaluate the extent and duration of tumour response and survival after acalabrutinib vs investigators choice of treatment in patients with treatment naïve or relapsed/refractory chronic lymphocytic leukaemia and moderate to severe cardiac impairment.

Secondary Endpoints

Overall survival (OS), defined as the time from randomisation to death from any cause.
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Temporary moments of secondary assessment

Not provided

Inclusion criteria

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Calendar

(Last Update: 17/07/2026)

Authorization	Start of Trial	First patient inclusion	Halted	Restarted
22/07/2024	18/12/2024	15/04/2025	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

AstraZeneca AB Sweden

-

Contact Person

Clinical Study Information Center

18772409479

information.center@astrazeneca.com

Monetary support: N/A

Sponsor type: Commercial

Ceim

CEIm Hospital Universitario La Paz

Paseo de la Castellana, 261 28046 Madrid

ceic.hulp@salud.madrid.org

917277413

Sites

Active (30/07/2024)

Hospital Del Mar

Barcelona

BARCELONA

Hematology

Active (21/02/2025)

Hospital Universitario Fundacion Jimenez Diaz

Madrid

MADRID

Hematology

Active (09/10/2024)

Hospital Universitario Virgen De La Macarena

Sevilla

SEVILLA

Hematology

Medication

Calquence 100 mg film-coated tablets
FILM-COATED TABLET
ORAL USE

ATC code: L01EL02 - ACALABRUTINIB
Active Principles: N/A

Experimental

Calquence 100 mg film-coated tablets
FILM-COATED TABLET
ORAL USE

ATC code: L01EL02 - ACALABRUTINIB
Active Principles: N/A

Experimental

No results