This study is being done to test the effectiveness and safety of an investigational drug called acalabrutinib (ACP-196) when taken with already marketed drugs called Venetoclax and Obinutzumab in comparison to chemotherapy that is already in wide use for treatment of patients who have chronic lymphocytic leukemia and who have never been treated before.

Estado	**Tipo de Participantes**	**Rangos de Edad**
Fin Reclutamiento	No aportado	Mayores de 64 , Adultos (18-64 años)
Género	**Fases**	**Participantes esperados**
Ambos	Fase III	578
Resultados	**Bajo nivel intervención**	**Enfermedad rara**
Sin resultados	No	No
Cobertura geográfica	**Ámbitos del ensayo**	**Terapia avanzada**
Sin determinar	tratamiento, seguridad, eficacia, farmacocinética	NO

Información

Identificador
2023-509349-11-00 (CTIS)

Cod. Protocolo
ACE-CL-311 (AMPLIFY)

Transicionado 2018-002443-28

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

Enfermedad investigada
Previously untreated Chronic Lymphocytic Leukemia Without del(17p) or TP53 Mutation

Título Científico

A Randomized, Multicenter, Open-Label, Phase 3 Study to Compare the Efficacy and Safety of Acalabrutinib (ACP-196) in Combination with Venetoclax with and without Obinutuzumab Compared to Investigators Choice of Chemoimmunotherapy in Subjects with Previously Untreated Chronic Lymphocytic Leukemia Without del(17p) or TP53 Mutation (AMPLIFY)

Justificación

No aportado

Objetivo Principal

To evaluate the efficacy of acalabrutinib/venetoclax (AV; Arm A) compared with chemoimmunotherapy (fludarabine/cyclophosphamide/rituximab [FCR] or bendamustine/rituximab [BR]; Arm C)

Variables de Evaluación Primaria

Progression-free survival (PFS), defined as the time from randomization to the first occurrence of disease progression or death from any cause (whichever occurs first), as determined by the Independent Review Committee (IRC) according to the International Workshop on Chronic Lymphocytic Leukemia (IWCLL) 2018 criteria.

Momentos temporales de evaluación primaria

No aportado

Objetivo Secundario

1.To evaluate the efficacy of AV (Arm A) in comparison with chemo-immunotherapy (FCR/BR [Arm C]) 2. To evaluate the efficacy of acalabrutinib/venetoclax/obinutuzumab (AVG; Arm B) versus FCR/BR (Arm C) 3. To evaluate the efficacy of AV (Arm A) versus FCR/BR (Arm C) and AVG (Arm B) versus FCR/BR (Arm C)

Variables de Evaluación Secundaria

1: Progression-free survival (PFS), defined as the time from randomization to the first occurrence of disease progression or death from any cause (whichever occurs first), as determined by the investigator assessment.
2: PFS, defined as the time from randomization to the first occurrence of disease progression or death from any cause (whichever occurs first), as determined by the IRC assessment and investigator assessment
3: Event-free survival (EFS), defined as the time from randomization to the first occurrence of disease progression, initiation of subsequent anti-chronic lymphocytic leukemia (CLL) therapy, or death from any cause per IRC assessment and the investigator assessment
- Overall response rate (ORR), defined as the proportion of subjects with a complete response (CR), complete response with incomplete marrow recovery (CRi), nodular partial response (nPR) or partial response (PR) per IRC assessment and investigator assessment
- Duration of objective response (DOR), defined as the time from the first occurrence of a documented objective

response to disease progression or death from any cause per IRC assessment and investigator assessment
- Time to next Therapy (TTNT), defined as the time from randomization to institution of non-protocol specified treatment for CLL
- Minimal residual disease (MRD) negativity rate (determined as the proportion of subjects with MRD-negativity) measured in the peripheral blood by flow cytometry (10-4) at the start of Cycle 9 (in Arm A), the start of Cycle 10 (in Arm B), and 12 weeks after the start of Cycle 6 (in Arm C)
- Overall survival (OS), defined as the time from randomization to death from any cause.

Momentos temporales de evaluación secundaria

No aportado

Criterios de Inclusión

1. Men and women 18 years of age. 2. Eastern Cooperative Oncology Group (ECOG) performance status of 02. 3. Diagnosis of CLL that meets published diagnostic criteria (Hallek et al. 2018): Monoclonal B-cells (either kappa or lambda light chain restricted) that are clonally co-expressing B-cell marker (CD19, CD20, and CD23) and CD5. Prolymphocytes may comprise <55% of blood lymphocytes. Presence of 5x109 B lymphocytes/L (5000/µL) in the peripheral blood (at any point since the initial diagnosis). 4. Active disease per IWCLL 2018 criteria that requires treatment (see Section 4.5.6). 5. Meet the following laboratory parameters: a) Adequate bone marrow function independent of growth factor or transfusion support within 1 week of Screening, as follows: i.ANC 750 cells/L (0.75x109/L); ANC 500 cells/L (0.50x109/L) in subjects with documented bone marrow involvement of CLL ii.Platelet count 50,000 cells/L (50x109/L); platelet count 30,000 cells/L (30x109/L) in subjects with documented bone marrow involvement of CLL b)Serum aspartate aminotransferase (AST) and alanine aminotransferase (ALT) 2.5xULN. c)Total bilirubin 2xULN, unless directly attributable to Gilberts syndrome d)Estimated creatinine clearance of 50 mL/min, calculated using the formula of Cockcroft and Gault (if male, [140Age] x Mass (kg) / [72 x creatinine mg/dL]; multiply by 0.85 if female); estimated creatinine clearance of 70 mL/min for subjects selected by investigator to receive FCR in Arm C

Criterios de Exclusión

1. Any prior CLL-specific therapies (except corticosteroid treatment administered due to necessary immediate intervention; within the last 10 days before start of study treatment, only dose equivalents up to 20 mg prednisone daily are permitted). 2. Detected del(17p) or TP53 mutation. 3. Transformation of CLL to aggressive non-Hodgkin lymphoma (NHL) (e.g., Richters transformation, PLL, or diffuse large B cell lymphoma [DLBCL]), or central nervous system (CNS) involvement by leukemia. 4. Any comorbidity or organ system impairment rated with a single CIRS score of 4 (excluding the eyes/ears/nose/throat/larynx organ system), or a total CIRS score of >6. 5. Uncontrolled autoimmune hemolytic anemia or idiopathic thrombocytopenic purpura. 6. History of confirmed progressive multifocal leukoencephalopathy (PML). 7. Received any investigational drug within 30 days before first dose of study drug. 8. Major surgical procedure within 30 days before the first dose of study drug. Note: If a subject had major surgery, they must have recovered adequately from any toxicity and/or complications from the intervention before the first dose of study drug. 9. History of prior malignancy that could affect compliance with the protocol, or interpretation of results, except for the following: Curatively treated basal cell carcinoma or squamous cell carcinoma of the skin or carcinoma in situ of the cervix or carcinoma in situ of the prostate at any time prior to study. Other cancers not specified above which have been curatively treated by surgery and/or radiation therapy from which subject is disease-free for 3 years without further treatment.

Calendario

(Última actualización: 19/06/2026)

Autorización	Inicio de Ensayo	Inclusión Primer Paciente	Interrumpido	Reiniciado
08/05/2019	22/03/2019	25/03/2019	15/10/2019	01/12/2019

Fin de reclutamiento	Fin prematuro (España)	Fin prematuro (Global)	Fin del ensayo en España	Fin del ensayo global
06/04/2021	No aportado	No aportado	No aportado	No aportado

Promotor

Acerta Pharma B.V. Netherlands

Kloosterstraat 9

Contact Person

AstraZeneca Clinical Study Information Center

0018772409479

information.center@astrazeneca.com

Monetary support: N/A

Tipo de promotor: Comercial

Ceim

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C/ Joaquin Rodrigo, 2 Majadahonda 28222 Madrid

secreceic.hpth@salud.madrid.org

911917479-911917662

Centros

No iniciado (17/03/2020)

HOSPITAL DE LA SANTA CREU I SANT PAU

Barcelona

BARCELONA

Servicio de Hematología

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

Hospital General Universitario Gregorio Maranon

Madrid

MADRID

Hematology

Activo (28/10/2019)

HOSPITAL GENERAL UNIVERSITARIO GREGORIO MARAÑÓN

Madrid

MADRID

Servicio de Hematología

Cerrado (03/12/2020)

HOSPITAL UNIVERSITARI I POLITÈCNIC LA FE

Valencia

VALENCIA

Servicio de Hematología

Activo (19/09/2019)

HOSPITAL UNIVERSITARI VALL D'HEBRON

Barcelona

BARCELONA

Servicio de Hematología

Activo (13/01/2020)

HOSPITAL UNIVERSITARIO DE SALAMANCA

Salamanca

SALAMANCA

Servicio de Hematología

Activo (05/07/2019)

HOSPITAL UNIVERSITARIO INFANTA LEONOR

Madrid

MADRID

Servicio de Hematología y Hemoterapia

Activo (30/09/2019)

HOSPITAL UNIVERSITARIO MARQUÉS DE VALDECILLA

Santander

CANTABRIA

Servicio de Hematología

Activo (22/07/2019)

HOSPITAL UNIVERSITARIO PUERTA DE HIERRO MAJADAHONDA

Majadahonda

MADRID

Servicio de Hematología/ Hemoterapia

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

Institut Catala D´oncologia

Badalona

BARCELONA

Hematology

Medicamentos

BENDAMUSTINE

POWDER FOR CONCENTRATE FOR SOLUTION FOR INFUSION

INTRAVENOUS USE

-

Principios Activos: N/A

Experimental

VENETOCLAX

FILM-COATED TABLET

ORAL

-

Principios Activos: N/A

Experimental

FLUDARABINE

CONCENTRATE FOR SOLUTION FOR INFUSION

INTRAVENOUS USE

-

Principios Activos: N/A

Experimental

VENETOCLAX

FILM-COATED TABLET

ORAL

-

Principios Activos: N/A

Experimental

OBINUTUZUMAB

SOLUTION FOR INFUSION

INTRAVENOUS USE

-

Principios Activos: N/A

Huérfano

Experimental

RITUXIMAB

CONCENTRATE FOR SOLUTION FOR INFUSION

INTRAVENOUS USE

-

Principios Activos: N/A

Experimental

CYCLOPHOSPHAMIDE

POWDER FOR SOLUTION FOR INJECTION/INFUSION

INTRAVENOUS USE

-

Principios Activos: N/A

Experimental

VENETOCLAX

FILM-COATED TABLET

ORAL

-

Principios Activos: N/A

Experimental

ACALABRUTINIB
CAPSULE, HARD
ORAL

-

Principios Activos: N/A

Huérfano **Experimental**

Sin resultados

This study is being done to test the effectiveness and safety of an investigational drug called acalabrutinib (ACP-196) when taken with already marketed drugs called Venetoclax and Obinutzumab in comparison to chemotherapy that is already in wide use for treatment of patients who have chronic lymphocytic leukemia and who have never been treated before.

State	**Type of participants**	**Age Ranges**
End of recruitment	Not provided	Older than 64 , Adults (18-64 years)
Gender	**Phases**	**Expected Participants**
Both	Phase III	578
Results	**Low level of intervention**	**Rare disease**
No results	No	No
Geographic coverage	**Areas of the study**	**Advanced therapy**
Undetermined	treatment, safety, effectiveness, pharmacokinetics	NO

Information

Identifier
2023-509349-11-00 (CTIS)

Protocol Code
ACE-CL-311 (AMPLIFY)

Transitioned 2018-002443-28

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

Investigated Disease
Previously untreated Chronic Lymphocytic Leukemia Without del(17p) or TP53 Mutation

Scientific Title

A Randomized, Multicenter, Open-Label, Phase 3 Study to Compare the Efficacy and Safety of Acalabrutinib (ACP-196) in Combination with Venetoclax with and without Obinutuzumab Compared to Investigators Choice of Chemoimmunotherapy in Subjects with Previously Untreated Chronic Lymphocytic Leukemia Without del(17p) or TP53 Mutation (AMPLIFY)

Rationale

Not provided

Main Objective

To evaluate the efficacy of acalabrutinib/venetoclax (AV; Arm A) compared with chemoimmunotherapy (fludarabine/cyclophosphamide/rituximab [FCR] or bendamustine/rituximab [BR]; Arm C)

Primary Endpoints

Progression-free survival (PFS), defined as the time from randomization to the first occurrence of disease progression or death from any cause (whichever occurs first), as determined by the Independent Review Committee (IRC) according to the International Workshop on Chronic Lymphocytic Leukemia (IWCLL) 2018 criteria.

Temporary moments of secondary assessment

Not provided

Secondary Objective

1.To evaluate the efficacy of AV (Arm A) in comparison with chemo-immunotherapy (FCR/BR [Arm C]) 2. To evaluate the efficacy of acalabrutinib/venetoclax/obinutuzumab (AVG; Arm B) versus FCR/BR (Arm C) 3. To evaluate the efficacy of AV (Arm A) versus FCR/BR (Arm C) and AVG (Arm B) versus FCR/BR (Arm C)

Secondary Endpoints

1: Progression-free survival (PFS), defined as the time from randomization to the first occurrence of disease progression or death from any cause (whichever occurs first), as determined by the investigator assessment.
2: PFS, defined as the time from randomization to the first occurrence of disease progression or death from any cause (whichever occurs first), as determined by the IRC assessment and investigator assessment
3: Event-free survival (EFS), defined as the time from randomization to the first occurrence of disease progression, initiation of subsequent anti-chronic lymphocytic leukemia (CLL) therapy, or death from any cause per IRC assessment and the investigator assessment
- Overall response rate (ORR), defined as the proportion of subjects with a complete response (CR), complete response with incomplete marrow recovery (CRi), nodular partial response (nPR) or partial response (PR) per IRC assessment and investigator assessment
- Duration of objective response (DOR), defined as the time from the first occurrence of a documented objective

response to disease progression or death from any cause per IRC assessment and investigator assessment
- Time to next Therapy (TTNT), defined as the time from randomization to institution of non-protocol specified treatment for CLL
- Minimal residual disease (MRD) negativity rate (determined as the proportion of subjects with MRD-negativity) measured in the peripheral blood by flow cytometry (10-4) at the start of Cycle 9 (in Arm A), the start of Cycle 10 (in Arm B), and 12 weeks after the start of Cycle 6 (in Arm C)
- Overall survival (OS), defined as the time from randomization to death from any cause.

Temporary moments of secondary assessment

Not provided

Inclusion criteria

1. Men and women 18 years of age. 2. Eastern Cooperative Oncology Group (ECOG) performance status of 02. 3. Diagnosis of CLL that meets published diagnostic criteria (Hallek et al. 2018): Monoclonal B-cells (either kappa or lambda light chain restricted) that are clonally co-expressing B-cell marker (CD19, CD20, and CD23) and CD5. Prolymphocytes may comprise <55% of blood lymphocytes. Presence of 5x109 B lymphocytes/L (5000/µL) in the peripheral blood (at any point since the initial diagnosis). 4. Active disease per IWCLL 2018 criteria that requires treatment (see Section 4.5.6). 5. Meet the following laboratory parameters: a) Adequate bone marrow function independent of growth factor or transfusion support within 1 week of Screening, as follows: i.ANC 750 cells/L (0.75x109/L); ANC 500 cells/L (0.50x109/L) in subjects with documented bone marrow involvement of CLL ii.Platelet count 50,000 cells/L (50x109/L); platelet count 30,000 cells/L (30x109/L) in subjects with documented bone marrow involvement of CLL b)Serum aspartate aminotransferase (AST) and alanine aminotransferase (ALT) 2.5xULN. c)Total bilirubin 2xULN, unless directly attributable to Gilberts syndrome d)Estimated creatinine clearance of 50 mL/min, calculated using the formula of Cockcroft and Gault (if male, [140Age] x Mass (kg) / [72 x creatinine mg/dL]; multiply by 0.85 if female); estimated creatinine clearance of 70 mL/min for subjects selected by investigator to receive FCR in Arm C

Exclusion criteria

1. Any prior CLL-specific therapies (except corticosteroid treatment administered due to necessary immediate intervention; within the last 10 days before start of study treatment, only dose equivalents up to 20 mg prednisone daily are permitted). 2. Detected del(17p) or TP53 mutation. 3. Transformation of CLL to aggressive non-Hodgkin lymphoma (NHL) (e.g., Richters transformation, PLL, or diffuse large B cell lymphoma [DLBCL]), or central nervous system (CNS) involvement by leukemia. 4. Any comorbidity or organ system impairment rated with a single CIRS score of 4 (excluding the eyes/ears/nose/throat/larynx organ system), or a total CIRS score of >6. 5. Uncontrolled autoimmune hemolytic anemia or idiopathic thrombocytopenic purpura. 6. History of confirmed progressive multifocal leukoencephalopathy (PML). 7. Received any investigational drug within 30 days before first dose of study drug. 8. Major surgical procedure within 30 days before the first dose of study drug. Note: If a subject had major surgery, they must have recovered adequately from any toxicity and/or complications from the intervention before the first dose of study drug. 9. History of prior malignancy that could affect compliance with the protocol, or interpretation of results, except for the following: Curatively treated basal cell carcinoma or squamous cell carcinoma of the skin or carcinoma in situ of the cervix or carcinoma in situ of the prostate at any time prior to study. Other cancers not specified above which have been curatively treated by surgery and/or radiation therapy from which subject is disease-free for 3 years without further treatment.

Calendar

(Last Update: 19/06/2026)

Authorization	Start of Trial	First patient inclusion	Halted	Restarted
08/05/2019	22/03/2019	25/03/2019	15/10/2019	01/12/2019

End of recruitment	Premature end (Spain)	Premature End (Global)	Trial end (Spain)	Trial end (Global)
06/04/2021	Not aported	Not aported	Not aported	Not aported

Sponsor

Acerta Pharma B.V. Netherlands

Kloosterstraat 9

Contact Person

AstraZeneca Clinical Study Information Center

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information.center@astrazeneca.com

Monetary support: N/A

Sponsor type: Commercial

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911917479-911917662

Sites

not initialized (17/03/2020)

HOSPITAL DE LA SANTA CREU I SANT PAU

Barcelona

BARCELONA

Servicio de Hematología

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

Hospital General Universitario Gregorio Maranon

Madrid

MADRID

Hematology

Active (28/10/2019)

HOSPITAL GENERAL UNIVERSITARIO GREGORIO MARAÑÓN

Madrid

MADRID

Servicio de Hematología

Closed (03/12/2020)

HOSPITAL UNIVERSITARI I POLITÈCNIC LA FE

Valencia

VALENCIA

Servicio de Hematología

Active (19/09/2019)

HOSPITAL UNIVERSITARI VALL D'HEBRON

Barcelona

BARCELONA

Servicio de Hematología

Active (13/01/2020)

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Salamanca

SALAMANCA

Servicio de Hematología

Active (05/07/2019)

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Active (30/09/2019)

HOSPITAL UNIVERSITARIO MARQUÉS DE VALDECILLA

Santander

CANTABRIA

Servicio de Hematología

Active (22/07/2019)

HOSPITAL UNIVERSITARIO PUERTA DE HIERRO MAJADAHONDA

Majadahonda

MADRID

Servicio de Hematología/ Hemoterapia

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

Institut Catala D´oncologia

Badalona

BARCELONA

Hematology

Medication

BENDAMUSTINE
POWDER FOR CONCENTRATE FOR SOLUTION FOR INFUSION
INTRAVENOUS USE

-

Active Principles: N/A

Experimental

VENETOCLAX
FILM-COATED TABLET
ORAL

-

Active Principles: N/A

Experimental

FLUDARABINE
CONCENTRATE FOR SOLUTION FOR INFUSION
INTRAVENOUS USE

-

Active Principles: N/A

Experimental

VENETOCLAX
FILM-COATED TABLET
ORAL

-

Active Principles: N/A

Experimental

OBINUTUZUMAB
SOLUTION FOR INFUSION
INTRAVENOUS USE

-

Active Principles: N/A

Orphan

Experimental

RITUXIMAB
CONCENTRATE FOR SOLUTION FOR INFUSION
INTRAVENOUS USE

-

Active Principles: N/A

Experimental

CYCLOPHOSPHAMIDE
POWDER FOR SOLUTION FOR INJECTION/INFUSION
INTRAVENOUS USE

-

Active Principles: N/A

Experimental

VENETOCLAX
FILM-COATED TABLET
ORAL

-

Active Principles: N/A

Experimental

ACALABRUTINIB
CAPSULE, HARD
ORAL

-

Active Principles: N/A

Orphan **Experimental**

No results