# A Study to Compare the Efficacy and Safety of a Combined Regimen of Obinutuzumab and Venetoclax (GDC-0199/ABT-199) Versus Obinutuzumab and Chlorambucil in Previously Untreated Patients with CLL and Coexisting Medical Conditions

| | | |
|---|---|---|
| **Estado** | **Tipo de Participantes** | **Rangos de Edad** |
| EC Finalizado | No aportado | Mayores de 64 , Adultos (18-64 años) |
| **Género** | **Fases** | **Participantes esperados** |
| Ambos | Fase III | 178 |
| **Resultados** | **Bajo nivel intervención** | **Enfermedad rara** |
| Tiene resultados | No | Si |
| **Cobertura geográfica** | **Ámbitos del ensayo** | **Terapia avanzada** |
| Multicéntrico internacional | seguridad, eficacia | NO |

## Información

### Identificador
2023-504034-22-00 (CTIS)

### Cod. Protocolo
BO25323

Transicionado 2014-001810-24

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

### Enfermedad investigada
Chronic Lymphocytic Leukemia (CLL)

### Título Científico
A Prospective, Open-Label, Multicenter Randomized Phase III Trial to Compare the Efficacy and Safety of a Combined Regimen of Obinutuzumab and Venetoclax (GDC-0199/ABT-199) Versus Obinutuzumab and

Chlorambucil in Previously Untreated Patients with CLL and Coexisting Medical Conditions

## Justificación

No aportado

## Objetivo Principal

To determine efficacy by investigator-assessed progression-free survival (PFS) of a combined regimen of obinutuzumab + venetoclax compared with obinutuzumab + chlorambucil (GClb) in previously untreated patients with CLL who have coexisting medical conditions

## Variables de Evaluación Primaria

Progression-free survival (PFS), defined as the time from randomization to the first occurrence of progression, relapse or death from any cause as assessed by the investigator using IWCLL criteria

## Momentos temporales de evaluación primaria

No aportado

## Objetivo Secundario

To determine efficacy as assessed by additional outcome measures, including PFS assessed by Independent Review Committee [IRC], overall response, complete response, and Minimal residual disease (MRD) response rate as measured by allele-specific oligonucleotide polymerase chain reaction [ASO-PCR]
To evaluate the safety of the combination of obinutuzumab and venetoclax, compared with GClb, in patients with previously untreated CLL and coexisting medical conditions, focusing on the nature, frequency, and severity of Grade 3 and 4 adverse events and of serious adverse events
To characterize the pharmacokinetics of venetoclax and of obinutuzumab [including population pharmacokinetics (PK) [pop-PK] techniques]. Standard non-compartmental analysis (NCA)/descriptive tables, listings, and graphs (TLGs) and pop-PK approaches will be considered
To compare disease and treatment-related symptoms following treatment with the combination of obinutuzumab + venetoclax compared with GClb in patients with previously untreated CLL and coexisting medical conditions as measured by M.D. Anderson Symptom Inventory (MDASI-CLL)
To evaluate changes in role functioning and global health status/quality of life (QoL) following treatment with the combination of obinutuzumab + venetoclax compared with GClb in patients with previously untreated CLL and coexisting medical conditions between arms as measured by European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC QLQ-C30)
To compare the health utility effects of treatment with combination of obinutuzumab and venetoclax compared with GClb in patients with previously untreated CLL and coexisting medical conditions measured by the EuroQol 5 Dimension questionnaire (EQ-5D-3L)

## Variables de Evaluación Secundaria

1. PFS based on IRC-assessments, defined as the time from randomization to the first occurrence of progression or relapse or death from any cause
2. Objective response rate ([ORR] defined as rate of a clinical response of complete response [CR], CR with incomplete bone marrow recovery [CRi] or partial response [PR]) as determined by the investigator, according to the IWCLL criteria
3. Complete response rate (defined as rate of a clinical response of CR or CRi) at the completion of treatment assessment, as determined by the investigator according to the IWCLL guidelines)
4. Minimal residual disease (MRD) response rate (determined as the proportion of patients with MRD-negativity) measured in the peripheral blood at the completion of treatment assessment and also MRD response rate as measured in the bone marrow at the completion of treatment, both measured by ASO-PCR
5. Overall survival (OS), defined as the time between the date of randomization and the date of death due to any cause. Patients who were not reported as having died at the time of the analysis will be censored at the date when they were last known to be alive
6. MRD response rates in the peripheral blood at completion of combination treatment assessment (Cycle 9, Day 1 or 3 months after last IV infusion) and also MRD response rate as measured in the bone marrow, both measured by ASO-PCR
7. Overall response rate (ORR) at completion of combination treatment response assessment (Cycle 7, Day 1 or 28 days after last IV infusion)
8. Duration of response, defined as the time from the first occurrence of a documented Overall survival (OS) (CR, CRi or PR) to the time of progressive disease (PD) as determined by the investigator, or death from any cause
9. Best response achieved (CR, CRi, PR, stable disease, or PD) up to and including the assessment at completion of treatment assessment (within 3 months of last day of treatment)
10. Event-free survival (EFS), defined as the time between date of randomization and the date of disease progression/relapse as assessed by the investigator, death, or start of a new anti-leukemic therapy. Patients without an EFS event will be will be censored on the date of the last disease assessment.
11. Time to new anti-leukemic treatment, defined as the time between the date of randomization and the date of first intake of new anti leukemic therapy. Patients who have not taken new anti-leukemic therapy will be censored at their last assessment prior to the analysis or date of death
12. Incidence of adverse events assessed according to the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) version 4.0
13. Incidence of severe adverse events
14. Incidence of adverse events of special interest
15. To characterize the pharmacokinetics of venetoclax and of obinutuzumab (including population PK [pop-PK] techniques)

## Momentos temporales de evaluación secundaria

No aportado

## Criterios de Inclusión

Documented previously untreated CLL according to the International Workshop on Chronic Lymphocytic Leukemia (IWCLL) criteria CLL requiring treatment according to IWCLL criteria Total Cumulative Illness Rating Scale (CIRS) score > 6 or creatinine clearance (CrCl) < 70 mL/min Adequate marrow function independent of growth factor or transfusion support within 2 weeks of screening as per protocol, unless cytopenia is due to marrow involvement of CLL Adequate liver function Life expectancy > 6 months

## Criterios de Exclusión

Transformation of CLL to aggressive Non-Hodgkin's lymphoma (Richters transformation or pro-lymphocytic leukemia)
Patients with a history of confirmed progressive multifocal leukoencephalopathy (PML)
An individual organ/ system impairment score of 4 as assessed by the CIRS definition limiting the ability to receive the treatment regimen of this trial with the exception of eyes, ears, nose, throat organ system
Patients with uncontrolled autoimmune hemolytic anemia or immune thrombocytopenia
Hypersensitivity to chlorambucil, obinutuzumab, or Venetoclax or to any of the excipients
Patients with active infections requiring intravenous (IV) treatment (grade 3 or 4) within the last two months prior to enrollment

# Calendario

(Última actualización: 15/09/2025)

| Autorización | Inicio de Ensayo | Inclusión Primer Paciente | Interrumpido | Reiniciado |
|---|---|---|---|---|
| 30/01/2015 | 12/03/2015 | 12/05/2015 | No aportado | No aportado |

| Fin de reclutamiento | Fin prematuro (España) | Fin prematuro (Global) | Fin del ensayo en España | Fin del ensayo global |
|---|---|---|---|---|
| 04/08/2016 | No aportado | No aportado | No aportado | 29/08/2025 |

# Promotor

### F. Hoffmann-La Roche AG Switzerland

**Grenzacherstrasse 124**

**Contact Person**

Head of CTRM Clinical Trial Regulatory Management, Product Development Regulatory

**41616881111**

**global.eudract@roche.com**

**Monetary support: N/A**

**Tipo de promotor: Comercial**

# Ceim

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**934894010**

# Centros

Activo (13/06/2016)

**COMPLEJO HOSPITALARIO DE NAVARRA**

PAMPLONA/IRUÑA

NAVARRA

Activo (13/06/2016)

**HOSPITAL ARNAU DE VILANOVA**

VALENCIA

VALENCIA

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

**Hospital Clinic De Barcelona**

Barcelona

BARCELONA

Hematology

Activo (13/06/2016)

**HOSPITAL CLÍNIC I PROVINCIAL DE BARCELONA**

BARCELONA

BARCELONA

Activo (13/06/2016)

**HOSPITAL CLÍNICO UNIVERSITARIO DE VALENCIA**

VALENCIA

VALENCIA

Activo (13/06/2016)

**HOSPITAL DEL MAR**

BARCELONA

BARCELONA

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

**Hospital Del Mar**

Barcelona

BARCELONA

Hematology

Cerrado (12/02/2020)

**HOSPITAL RAMÓN Y CAJAL**

MADRID

MADRID

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

**Hospital Universitari Vall D Hebron**

Barcelona

BARCELONA

Hematology

Activo (13/06/2016)

**HOSPITAL UNIVERSITARI VALL D'HEBRON**

BARCELONA

BARCELONA

Activo (13/06/2016)

**HOSPITAL UNIVERSITARIO DE CANARIAS (H.U.C)**

SAN CRISTÓBAL DE LA LAGUNA

Activo (13/06/2016)

**HOSPITAL UNIVERSITARIO DE LA PRINCESA**

MADRID

MADRID

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

**Hospital Universitario De La Princesa**

Madrid

MADRID

Hematology

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

**Hospital Universitario De Navarra**

Pamplona

NAVARRA

Hematology

Activo (13/06/2016)

**HOSPITAL UNIVERSITARIO DE SALAMANCA**

SALAMANCA

SALAMANCA

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

**Hospital Universitario De Salamanca**

Salamanca

SALAMANCA

Hematology

Activo (13/06/2016)

**HOSPITAL UNIVERSITARIO LA PAZ**

MADRID

MADRID

Cerrado (09/09/2016)

**HOSPITAL UNIVERSITARIO PUERTA DE HIERRO MAJADAHONDA**

MAJADAHONDA

MADRID

Activo (13/06/2016)

**HOSPITAL UNIVERSITARIO 12 DE OCTUBRE**

MADRID

MADRID

Cerrado (12/07/2017)

**HOSPITAL VIRGEN DE LA SALUD**

TOLEDO

TOLEDO

Activo (13/06/2016)

**HOSPITAL VIRGEN DEL ROCÍO**

SEVILLA

SEVILLA

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

**University Hospital Of Canary Islands**

San Cristobal De La Laguna

STA. CRUZ DE TENERIFE

Hematology

# Medicamentos

### Chlorambucil 2 mg tablets
FILM-COATED TABLET
ORAL

Código ATC: L01AA02 - CLORAMBUCILO
Principios Activos: N/A

Experimental

### Venclexta, Venclyxto
FILM-COATED TABLET
ORAL

-
Principios Activos: N/A

Huérfano Experimental

### Venclexta, Venclyxto
FILM-COATED TABLET
ORAL

-
Principios Activos: N/A

Huérfano Experimental

### Gazyvaro 1,000 mg concentrate for solution for infusion.
SOLUTION FOR INFUSION
INTRAVENOUS INFUSION

Código ATC: L01XC15 - OBINUTUZUMAB
Principios Activos: N/A

Huérfano Experimental

### Venclexta, Venclyxto
FILM-COATED TABLET
ORAL

-
Principios Activos: N/A

Huérfano Experimental

### Fasturtec 1.5 mg/ml powder and solvent for concentrate for solution for infusion.
SOLUTION FOR INFUSION
INTRAVENOUS INFUSION

Código ATC: V03AF07 - RASBURICASA
Principios Activos: N/A

Experimental

# Tiene resultados

# A Study to Compare the Efficacy and Safety of a Combined Regimen of Obinutuzumab and Venetoclax (GDC-0199/ABT-199) Versus Obinutuzumab and Chlorambucil in Previously Untreated Patients with CLL and Coexisting Medical Conditions

| State | Type of participants | Age Ranges |
|---|---|---|
| Finished CT | Not provided | Older than 64 , Adults (18-64 years) |
| **Gender** | **Phases** | **Expected Participants** |
| Both | Phase III | 178 |
| **Results** | **Low level of intervention** | **Rare disease** |
| Has results | No | Yes |
| **Geographic coverage** | **Areas of the study** | **Advanced therapy** |
| International multicenter | safety, effectiveness | NO |

## Information

### Identifier
2023-504034-22-00 (CTIS)

### Protocol Code
BO25323

Transitioned 2014-001810-24

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

### Investigated Disease
Chronic Lymphocytic Leukemia (CLL)

### Scientific Title
A Prospective, Open-Label, Multicenter Randomized Phase III Trial to Compare the Efficacy and Safety of a Combined Regimen of Obinutuzumab and Venetoclax (GDC-0199/ABT-199) Versus Obinutuzumab and

Chlorambucil in Previously Untreated Patients with CLL and Coexisting Medical Conditions

## Rationale

Not provided

## Main Objective

To determine efficacy by investigator-assessed progression-free survival (PFS) of a combined regimen of obinutuzumab + venetoclax compared with obinutuzumab + chlorambucil (GClb) in previously untreated patients with CLL who have coexisting medical conditions

## Primary Endpoints

Progression-free survival (PFS), defined as the time from randomization to the first occurrence of progression, relapse or death from any cause as assessed by the investigator using IWCLL criteria

## Temporary moments of secondary assessment

Not provided

## Secondary Objective

To determine efficacy as assessed by additional outcome measures, including PFS assessed by Independent Review Committee [IRC], overall response, complete response, and Minimal residual disease (MRD) response rate as measured by allele-specific oligonucleotide polymerase chain reaction [ASO-PCR]
To evaluate the safety of the combination of obinutuzumab and venetoclax, compared with GClb, in patients with previously untreated CLL and coexisting medical conditions, focusing on the nature, frequency, and severity of Grade 3 and 4 adverse events and of serious adverse events
To characterize the pharmacokinetics of venetoclax and of obinutuzumab [including population pharmacokinetics (PK) [pop-PK] techniques]. Standard non-compartmental analysis (NCA)/descriptive tables, listings, and graphs (TLGs) and pop-PK approaches will be considered
To compare disease and treatment-related symptoms following treatment with the combination of obinutuzumab + venetoclax compared with GClb in patients with previously untreated CLL and coexisting medical conditions as measured by M.D. Anderson Symptom Inventory (MDASI-CLL)
To evaluate changes in role functioning and global health status/quality of life (QoL) following treatment with the combination of obinutuzumab + venetoclax compared with GClb in patients with previously untreated CLL and coexisting medical conditions between arms as measured by European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC QLQ-C30)
To compare the health utility effects of treatment with combination of obinutuzumab and venetoclax compared with GClb in patients with previously untreated CLL and coexisting medical conditions measured by the EuroQol 5 Dimension questionnaire (EQ-5D-3L)

## Secondary Endpoints

1. PFS based on IRC-assessments, defined as the time from randomization to the first occurrence of progression or relapse or death from any cause
2. Objective response rate ([ORR] defined as rate of a clinical response of complete response [CR], CR with incomplete bone marrow recovery [CRi] or partial response [PR]) as determined by the investigator, according to the IWCLL criteria
3. Complete response rate (defined as rate of a clinical response of CR or CRi) at the completion of treatment assessment, as determined by the investigator according to the IWCLL guidelines)
4. Minimal residual disease (MRD) response rate (determined as the proportion of patients with MRD-negativity) measured in the peripheral blood at the completion of treatment assessment and also MRD response rate as measured in the bone marrow at the completion of treatment, both measured by ASO-PCR
5. Overall survival (OS), defined as the time between the date of randomization and the date of death due to any cause. Patients who were not reported as having died at the time of the analysis will be censored at the date when they were last known to be alive
6. MRD response rates in the peripheral blood at completion of combination treatment assessment (Cycle 9, Day 1 or 3 months after last IV infusion) and also MRD response rate as measured in the bone marrow, both measured by ASO-PCR
7. Overall response rate (ORR) at completion of combination treatment response assessment (Cycle 7, Day 1 or 28 days after last IV infusion)
8. Duration of response, defined as the time from the first occurrence of a documented Overall survival (OS) (CR, CRi or PR) to the time of progressive disease (PD) as determined by the investigator, or death from any cause
9. Best response achieved (CR, CRi, PR, stable disease, or PD) up to and including the assessment at completion of treatment assessment (within 3 months of last day of treatment)
10. Event-free survival (EFS), defined as the time between date of randomization and the date of disease progression/relapse as assessed by the investigator, death, or start of a new anti-leukemic therapy. Patients without an EFS event will be will be censored on the date of the last disease assessment.
11. Time to new anti-leukemic treatment, defined as the time between the date of randomization and the date of first intake of new anti leukemic therapy. Patients who have not taken new anti-leukemic therapy will be censored at their last assessment prior to the analysis or date of death
12. Incidence of adverse events assessed according to the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) version 4.0
13. Incidence of severe adverse events
14. Incidence of adverse events of special interest
15. To characterize the pharmacokinetics of venetoclax and of obinutuzumab (including population PK [pop-PK] techniques)

## Temporary moments of secondary assessment

Not provided

## Inclusion criteria

Documented previously untreated CLL according to the International Workshop on Chronic Lymphocytic Leukemia (IWCLL) criteria CLL requiring treatment according to IWCLL criteria Total Cumulative Illness Rating Scale (CIRS) score > 6 or creatinine clearance (CrCl) < 70 mL/min Adequate marrow function independent of growth factor or transfusion support within 2 weeks of screening as per protocol, unless cytopenia is due to marrow involvement of CLL Adequate liver function Life expectancy > 6 months

## Exclusion criteria

Transformation of CLL to aggressive Non-Hodgkin's lymphoma (Richters transformation or pro-lymphocytic leukemia)
Patients with a history of confirmed progressive multifocal leukoencephalopathy (PML)
An individual organ/ system impairment score of 4 as assessed by the CIRS definition limiting the ability to receive the treatment regimen of this trial with the exception of eyes, ears, nose, throat organ system
Patients with uncontrolled autoimmune hemolytic anemia or immune thrombocytopenia
Hypersensitivity to chlorambucil, obinutuzumab, or Venetoclax or to any of the excipients
Patients with active infections requiring intravenous (IV) treatment (grade 3 or 4) within the last two months prior to enrollment

# Calendar

(Last Update: 15/09/2025)

| Authorization | Start of Trial | First patient inclusion | Halted | Restarted |
|---|---|---|---|---|
| 30/01/2015 | 12/03/2015 | 12/05/2015 | Not aported | Not aported |

| End of recruitment | Premature end (Spain) | Premature End (Global) | Trial end (Spain) | Trial end (Global) |
|---|---|---|---|---|
| 04/08/2016 | Not aported | Not aported | Not aported | 29/08/2025 |

# Sponsor

**F. Hoffmann-La Roche AG Switzerland**

**Grenzacherstrasse 124**

**Contact Person**

Head of CTRM Clinical Trial Regulatory Management, Product Development Regulatory

**41616881111**

**global.eudract@roche.com**

**Monetary support: N/A**

**Sponsor type: Commercial**

# Ceim

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**934894010**

# Sites

Active (13/06/2016)

**COMPLEJO HOSPITALARIO DE NAVARRA**

PAMPLONA/IRUÑA

NAVARRA

Active (13/06/2016)

**HOSPITAL ARNAU DE VILANOVA**

VALENCIA

VALENCIA

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

**Hospital Clinic De Barcelona**

Barcelona

BARCELONA

Hematology

Active (13/06/2016)

**HOSPITAL CLÍNIC I PROVINCIAL DE BARCELONA**

BARCELONA

BARCELONA

Active (13/06/2016)

**HOSPITAL CLÍNICO UNIVERSITARIO DE VALENCIA**

VALENCIA

VALENCIA

Active (13/06/2016)

**HOSPITAL DEL MAR**

BARCELONA

BARCELONA

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

**Hospital Del Mar**

Barcelona

BARCELONA

Hematology

Closed (12/02/2020)

**HOSPITAL RAMÓN Y CAJAL**

MADRID

MADRID

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

**Hospital Universitari Vall D Hebron**

Barcelona

BARCELONA

Hematology

Active (13/06/2016)

**HOSPITAL UNIVERSITARI VALL D'HEBRON**

BARCELONA

BARCELONA

Active (13/06/2016)

**HOSPITAL UNIVERSITARIO DE CANARIAS (H.U.C)**

SAN CRISTÓBAL DE LA LAGUNA

Active (13/06/2016)

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MADRID

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

**Hospital Universitario De La Princesa**

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MADRID

Hematology

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

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Pamplona

NAVARRA

Hematology

Active (13/06/2016)

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SALAMANCA

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Salamanca

SALAMANCA

Hematology

Active (13/06/2016)

**HOSPITAL UNIVERSITARIO LA PAZ**

MADRID

MADRID

Closed (09/09/2016)

**HOSPITAL UNIVERSITARIO PUERTA DE HIERRO MAJADAHONDA**

MAJADAHONDA

MADRID

Active (13/06/2016)

**HOSPITAL UNIVERSITARIO 12 DE OCTUBRE**

MADRID

MADRID

Closed (12/07/2017)

**HOSPITAL VIRGEN DE LA SALUD**

TOLEDO

TOLEDO

Active (13/06/2016)

**HOSPITAL VIRGEN DEL ROCÍO**

SEVILLA

SEVILLA

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

**University Hospital Of Canary Islands**

San Cristobal De La Laguna

STA. CRUZ DE TENERIFE

Hematology

# Medication

**Chlorambucil 2 mg tablets**
FILM-COATED TABLET
ORAL

ATC code: L01AA02 - CLORAMBUCILO
Active Principles: N/A

Experimental

**Venclexta, Venclyxto**
FILM-COATED TABLET
ORAL

-
Active Principles: N/A

Orphan Experimental

**Venclexta, Venclyxto**
FILM-COATED TABLET
ORAL

-
Active Principles: N/A

Orphan Experimental

**Gazyvaro 1,000 mg concentrate for solution for infusion.**
SOLUTION FOR INFUSION
INTRAVENOUS INFUSION

ATC code: L01XC15 - OBINUTUZUMAB
Active Principles: N/A

Orphan Experimental

**Venclexta, Venclyxto**
FILM-COATED TABLET
ORAL

-
Active Principles: N/A

Orphan Experimental

**Fasturtec 1.5 mg/ml powder and solvent for concentrate for solution for infusion.**
SOLUTION FOR INFUSION
INTRAVENOUS INFUSION

ATC code: V03AF07 - RASBURICASA
Active Principles: N/A

Experimental

# Has results