# A Study to Compare the Efficacy and Safety of a Combined Regimen of Venetoclax and Obinutuzumab Versus Fludarabine, Cyclophosphamide, and Rituximab (FCR)/ Bendamustine and Rituximab (BR) in FIT Patients With Previously Untreated Chronic Lymphocytic Leukemia (CLL) without DEL (17P) or TP53 mutation

| | | |
|---|---|---|
| **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 | 45 |
| **Resultados** | **Bajo nivel intervención** | **Enfermedad rara** |
| Tiene resultados | No | No |
| **Cobertura geográfica** | **Ámbitos del ensayo** | **Terapia avanzada** |
| Sin determinar | seguridad, eficacia | NO |

## Información

### Identificador
2023-504036-17-00 (CTIS)

### Cod. Protocolo
CO41685

Transicionado 2019-003327-37

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

### Enfermedad investigada
Chronic Lymphocytic Leukemia (CLL)

### Título Científico
A Prospective, Open-Label, Multicenter Randomized Phase III Study to Compare the Efficacy and Safety of a

Combined Regimen of Venetoclax and Obinutuzumab Versus Fludarabine, Cyclophosphamide, and Rituximab (FCR)/ Bendamustine and Rituximab (BR) in FIT Patients with previously untreated Chronic Lymphocytic Leukemia (CLL) without DEL(17P) or TP53 Mutation

## Justificación

No aportado

## Objetivo Principal

To evaluate the efficacy of venetoclax (Venclexa® or Venclyxto®) in combination with obinutuzumab (Gazyva® or Gazyvaro®) (VEN + G) compared with fludarabine, cyclophosphamide, and rituximab (FCR)/ bendamustine and rituximab (BR) on the basis of minimal residual disease (MRD) response rate

## Variables de Evaluación Primaria

1. MRD response rate measured in PB using nextgeneration sequencing (NGS) at Month 15

## Momentos temporales de evaluación primaria

No aportado

## Objetivo Secundario

To evaluate the efficacy of VEN + G compared with FCR/BR on the basis of progression-free survival, MRD response rate in peripheral blood (PB) and bone marrow (BM), overall response rate, duration of objective response, best response achieved, event-free survival, overall survival, tumor lysis syndrome risk reduction rate and reduction in mandatory hospitalizations
To evaluate safety of VEN + G compared with FCR/BR on the basis of nature, frequency, and severity of adverse events, changes in vital signs, physical findings, clinical laboratory test results, premature withdrawals
To compare disease and treatment-related symptoms and to evaluate changes in physical functioning, role functioning, and global health status/quality of life following treatment with the combination of VEN + G compared with FCR/BR in patients with previously untreated CLL without del(17p) or TP53 mutation

## Variables de Evaluación Secundaria

1. Progression-free survival
2. MRD response rate, in PB at end of treatment response visit
3. MRD response rate in BM at end of treatment response visit
4. ORR which includes complete remission (CR), complete remission with incomplete blood count recovery (Cri), and partial response (PR) at the Month 15 assessment
5. Complete response rate at the Month 15 assessment
6. MRD response rate in PB in patients with a complete remission /complete remission with incomplete blood count

recovery (CR/Cri) at Month 15
7. MRD response rate in BM in patients with a CR/CRi at end of treatment visit
8. Best response up to and including the Month 15 assessment
9. Duration of objective response
10. Event-free survival
11. Overall survival
12. Tumor lysis syndrome risk reduction rate in Arm A
13. Reduction in mandatory hospitalizations during venetoclax ramp-up in Arm A
14. Changes in vital signs, physical findings, and clinical laboratory test results during and following study treatment
15. Premature withdrawals
16. Change in disease and treatment-related symptoms following treatment with the combination of VEN + G compared with FCR/BR in patients with previously untreated CLL without del (17p) or TP53 mutation as measured by MDASI-CLL
17. Change in physical functioning, role functioning and health-related quality of life following treatment with the combination of VEN + G compared with FCR/BR in patients with previously with previously untreated CLL without del(17p) or TP53 mutation as measured by EORTC QLQ-C30
18. Nature, frequency, and severity of adverse events and serious adverse event

## Momentos temporales de evaluación secundaria

No aportado

## Criterios de Inclusión

Aged 18 years or older Have previously untreated documented CLL according to the International Workshop on Chronic Lymphocytic Leukemia (iwCLL) criteria Cumulative illness rating scale score <=6 and creatinine clearance >=70 mL/min as calculated by the Standard Cockcroft and Gault Formula Hematology values within the following limits, unless cytopenia is caused by the underlying disease (i.e., no evidence of additional BM dysfunction; e.g., myelodysplastic syndrome, hypoplastic BM): o Absolute neutrophil count >=1.0 × 109/L, unless there is BM involvement o Platelet count >=75 × 109/L and more than 7 days since last transfusion, or >=30 × 109/L if there is BM involvement Adequate liver function as indicated by a total bilirubin, aspartate aminotransferase, and Alanine transaminase <=2 times the institutional upper limit of normal value, unless directly attributable to the patients CLL Life expectancy >6 months

## Criterios de Exclusión

Transformation of CLL to aggressive non-Hodgkins lymphoma
Patients with small lymphocyclic lymphoma (SLL) only (a diagnosis of CLL/SLL is permitted)
Known central nervous system involvement
Patients with a history of confirmed progressive multifocal leukoencephalopathy
Detected del (17p) or TP53 mutation (valid test within 6-months from screening is required for randomization)
An individual organ/system impairment score of 4 as assessed by the cumulative illness rating scale (CIRS) definition limiting the ability to receive the treatment regimen of this trial with the exception of eyes, ears, nose, throat organ system

# Calendario

(Última actualización: 06/10/2025)

| Autorización | Inicio de Ensayo | Inclusión Primer Paciente | Interrumpido | Reiniciado |
|---|---|---|---|---|
| 25/02/2020 | 07/05/2020 | 15/06/2020 | No aportado | No aportado |

| Fin de reclutamiento | Fin prematuro (España) | Fin prematuro (Global) | Fin del ensayo en España | Fin del ensayo global |
|---|---|---|---|---|
| 31/12/2022 | No aportado | No aportado | 18/03/2025 | 20/03/2025 |

# Promotor

## F. Hoffmann-La Roche AG Switzerland

**Grenzacherstrasse 124**

**Contact Person**

Trial Information System - TISL

**41616881111**

**global.eudract@roche.com**

**Monetary support: N/A**

**Tipo de promotor: Comercial**

# Ceim

**CEIm Provincial de Sevilla**

**Avenida Doctor Fedriani 3 41009 Sevilla**

**administracion.eecc.hvm.sspa@juntadeandalucia.es**

**955043127**

# Centros

Cerrado (10/06/2025)

**COMPLEJO HOSPITALARIO DE NAVARRA**

Pamplona/Iruña

NAVARRA

Servicio de Hematología

Cerrado (04/06/2025)

**HOSPITAL GENERAL UNIVERSITARIO J.M. MORALES MESEGUER**

Murcia

MURCIA

Servicio de Hematología

Cerrado (18/02/2022)

**HOSPITAL UNIVERSITARI VALL D'HEBRON**

Barcelona

BARCELONA

Cerrado (09/03/2023)

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

San Cristóbal de La Laguna

STA. CRUZ DE TENERIFE

Cerrado (01/07/2025)

**Hospital Universitario De Toledo**

Toledo

TOLEDO

Servicio de Hematología

Cerrado (03/07/2025)

**HOSPITAL UNIVERSITARIO LA PAZ**

Madrid

MADRID

Servicio de Hematología

Cerrado (26/06/2025)

**HOSPITAL UNIVERSITARIO VIRGEN DEL ROCÍO**

Sevilla

SEVILLA

Servicio de Hematología

Cerrado (12/09/2025)

**Institut Catala D´oncologia**

Badalona

BARCELONA

Servicio de Hematología

# Medicamentos

### Bendamustin cell pharm® 2,5 mg/ml Pulver für ein Konzentrat zur Herstellung einer Infusionslösung
SOLUTION FOR INFUSION
IV INFUSION

Código ATC: L01AA09 - BENDAMUSTINA
Principios Activos: N/A

Experimental

### Venclexta, Venclyxto
FILM-COATED TABLET
ORAL

-

Principios Activos: N/A

Experimental

### Venclexta, Venclyxto
FILM-COATED TABLET
ORAL

-

Principios Activos: N/A

Experimental

### Fludarabin Sandoz 25 mg/ml injekný alebo infúzny koncentrát
SOLUTION FOR INJECTION/INFUSION
IV INFUSION

Código ATC: L01BB05 - FLUDARABINA
Principios Activos: N/A

Experimental

### Venclexta, Venclyxto
FILM-COATED TABLET
ORAL

-

Principios Activos: N/A

Experimental

### Neoflubin 25 mg/ml Konzentrat zur Herstellung einer Injektions- oder Infusionslösung
SOLUTION FOR INJECTION/INFUSION
IV INFUSION

Código ATC: L01BB05 - FLUDARABINA
Principios Activos: N/A

Experimental

### Endoxan
SOLUTION FOR INJECTION
IV INFUSION

Código ATC: L01AA01 - CICLOFOSFAMIDA
Principios Activos: N/A

Experimental

### Fludarabin Ebewe 25 mg/ml injektio-/infuusiokonsentraatti, liuosta varten
SOLUTION FOR INJECTION/INFUSION
IV INFUSION

Código ATC: L01BB05 - FLUDARABINA
Principios Activos: N/A

Experimental

**Fludarabine Ebewe 25 mg/ml, süste-/infusioonilahuse kontsentraat**
SOLUTION FOR INJECTION/INFUSION
IV INFUSION

Código ATC: L01BB05 - FLUDARABINA
Principios Activos: N/A

Experimental

**Levact 2,5 mg/ml poudre pour solution à diluer pour perfusion**
SOLUTION FOR INFUSION
IV INFUSION

Código ATC: L01AA09 - BENDAMUSTINA
Principios Activos: N/A

Experimental

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

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

Huérfano
Experimental

**MabThera 500 mg concentrate for solution for infusion**
SOLUTION FOR INFUSION
IV INFUSION

Código ATC: L01XC02 - RITUXIMAB
Principios Activos: N/A

Experimental

**Levact 2,5 mg/ml Pulver für ein Konzentrat zur Herstellung einer Infusionslösung**
SOLUTION FOR INFUSION
IV INFUSION

Código ATC: L01AA09 - BENDAMUSTINA
Principios Activos: N/A

Experimental

**Fludarabinphosphat "Ebewe", koncentrat til injektions-/infusionsvæske, opløsning**
SOLUTION FOR INJECTION/INFUSION
IV INFUSION

Código ATC: L01BB05 - FLUDARABINA
Principios Activos: N/A

Experimental

## Tiene resultados

# A Study to Compare the Efficacy and Safety of a Combined Regimen of Venetoclax and Obinutuzumab Versus Fludarabine, Cyclophosphamide, and Rituximab (FCR)/ Bendamustine and Rituximab (BR) in FIT Patients With Previously Untreated Chronic Lymphocytic Leukemia (CLL) without DEL (17P) or TP53 mutation

| | | |
|---|---|---|
| **State** | **Type of participants** | **Age Ranges** |
| Finished CT | Not provided | Older than 64 , Adults (18-64 years) |
| **Gender** | **Phases** | **Expected Participants** |
| Both | Phase III | 45 |
| **Results** | **Low level of intervention** | **Rare disease** |
| Has results | No | No |
| **Geographic coverage** | **Areas of the study** | **Advanced therapy** |
| Undetermined | safety, effectiveness | NO |

## Information

### Identifier
2023-504036-17-00 (CTIS)

### Protocol Code
CO41685

Transitioned 2019-003327-37

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

### Investigated Disease
Chronic Lymphocytic Leukemia (CLL)

### Scientific Title
A Prospective, Open-Label, Multicenter Randomized Phase III Study to Compare the Efficacy and Safety of a

Combined Regimen of Venetoclax and Obinutuzumab Versus Fludarabine, Cyclophosphamide, and Rituximab (FCR)/ Bendamustine and Rituximab (BR) in FIT Patients with previously untreated Chronic Lymphocytic Leukemia (CLL) without DEL(17P) or TP53 Mutation

## Rationale

Not provided

## Main Objective

To evaluate the efficacy of venetoclax (Venclexa® or Venclyxto®) in combination with obinutuzumab (Gazyva® or Gazyvaro®) (VEN + G) compared with fludarabine, cyclophosphamide, and rituximab (FCR)/ bendamustine and rituximab (BR) on the basis of minimal residual disease (MRD) response rate

## Primary Endpoints

1. MRD response rate measured in PB using nextgeneration sequencing (NGS) at Month 15

## Temporary moments of secondary assessment

Not provided

## Secondary Objective

To evaluate the efficacy of VEN + G compared with FCR/BR on the basis of progression-free survival, MRD response rate in peripheral blood (PB) and bone marrow (BM), overall response rate, duration of objective response, best response achieved, event-free survival, overall survival, tumor lysis syndrome risk reduction rate and reduction in mandatory hospitalizations
To evaluate safety of VEN + G compared with FCR/BR on the basis of nature, frequency, and severity of adverse events, changes in vital signs, physical findings, clinical laboratory test results, premature withdrawals
To compare disease and treatment-related symptoms and to evaluate changes in physical functioning, role functioning, and global health status/quality of life following treatment with the combination of VEN + G compared with FCR/BR in patients with previously untreated CLL without del(17p) or TP53 mutation

## Secondary Endpoints

1. Progression-free survival
2. MRD response rate, in PB at end of treatment response visit
3. MRD response rate in BM at end of treatment response visit
4. ORR which includes complete remission (CR), complete remission with incomplete blood count recovery (Cri), and partial response (PR) at the Month 15 assessment
5. Complete response rate at the Month 15 assessment
6. MRD response rate in PB in patients with a complete remission /complete remission with incomplete blood count

recovery (CR/Cri) at Month 15
7. MRD response rate in BM in patients with a CR/CRi at end of treatment visit
8. Best response up to and including the Month 15 assessment
9. Duration of objective response
10. Event-free survival
11. Overall survival
12. Tumor lysis syndrome risk reduction rate in Arm A
13. Reduction in mandatory hospitalizations during venetoclax ramp-up in Arm A
14. Changes in vital signs, physical findings, and clinical laboratory test results during and following study treatment
15. Premature withdrawals
16. Change in disease and treatment-related symptoms following treatment with the combination of VEN + G compared with FCR/BR in patients with previously untreated CLL without del (17p) or TP53 mutation as measured by MDASI-CLL
17. Change in physical functioning, role functioning and health-related quality of life following treatment with the combination of VEN + G compared with FCR/BR in patients with previously with previously untreated CLL without del(17p) or TP53 mutation as measured by EORTC QLQ-C30
18. Nature, frequency, and severity of adverse events and serious adverse event

## Temporary moments of secondary assessment

Not provided

## Inclusion criteria

Aged 18 years or older Have previously untreated documented CLL according to the International Workshop on Chronic Lymphocytic Leukemia (iwCLL) criteria Cumulative illness rating scale score <=6 and creatinine clearance >=70 mL/min as calculated by the Standard Cockcroft and Gault Formula Hematology values within the following limits, unless cytopenia is caused by the underlying disease (i.e., no evidence of additional BM dysfunction; e.g., myelodysplastic syndrome, hypoplastic BM): o Absolute neutrophil count >=1.0 × 109/L, unless there is BM involvement o Platelet count >=75 × 109/L and more than 7 days since last transfusion, or >=30 × 109/L if there is BM involvement Adequate liver function as indicated by a total bilirubin, aspartate aminotransferase, and Alanine transaminase <=2 times the institutional upper limit of normal value, unless directly attributable to the patients CLL Life expectancy >6 months

## Exclusion criteria

Transformation of CLL to aggressive non-Hodgkins lymphoma
Patients with small lymphocyclic lymphoma (SLL) only (a diagnosis of CLL/SLL is permitted)
Known central nervous system involvement
Patients with a history of confirmed progressive multifocal leukoencephalopathy
Detected del (17p) or TP53 mutation (valid test within 6-months from screening is required for randomization)
An individual organ/system impairment score of 4 as assessed by the cumulative illness rating scale (CIRS) definition limiting the ability to receive the treatment regimen of this trial with the exception of eyes, ears, nose, throat organ system

# Calendar

(Last Update: 06/10/2025)

| Authorization | Start of Trial | First patient inclusion | Halted | Restarted |
|---|---|---|---|---|
| 25/02/2020 | 07/05/2020 | 15/06/2020 | Not aported | Not aported |

| End of recruitment | Premature end (Spain) | Premature End (Global) | Trial end (Spain) | Trial end (Global) |
|---|---|---|---|---|
| 31/12/2022 | Not aported | Not aported | 18/03/2025 | 20/03/2025 |

# Sponsor

## F. Hoffmann-La Roche AG Switzerland

**Grenzacherstrasse 124**

**Contact Person**

Trial Information System - TISL

**41616881111**

**global.eudract@roche.com**

**Monetary support: N/A**

**Sponsor type: Commercial**

# Ceim

## CEIm Provincial de Sevilla

**Avenida Doctor Fedriani 3 41009 Sevilla**

**administracion.eecc.hvm.sspa@juntadeandalucia.es**

**955043127**

# Sites

Closed (10/06/2025)

**COMPLEJO HOSPITALARIO DE NAVARRA**

Pamplona/Iruña

NAVARRA

Servicio de Hematología

Closed (04/06/2025)

**HOSPITAL GENERAL UNIVERSITARIO J.M. MORALES MESEGUER**

Murcia

MURCIA

Servicio de Hematología

Closed (18/02/2022)

**HOSPITAL UNIVERSITARI VALL D'HEBRON**

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San Cristóbal de La Laguna

STA. CRUZ DE TENERIFE

Closed (01/07/2025)

**Hospital Universitario De Toledo**

Toledo

TOLEDO

Servicio de Hematología

Closed (03/07/2025)

**HOSPITAL UNIVERSITARIO LA PAZ**

Madrid

MADRID

Servicio de Hematología

Closed (26/06/2025)

**HOSPITAL UNIVERSITARIO VIRGEN DEL ROCÍO**

Sevilla

SEVILLA

Servicio de Hematología

Closed (12/09/2025)

**Institut Catala D´oncologia**

Badalona

BARCELONA

Servicio de Hematología

# Medication

### Bendamustin cell pharm® 2,5 mg/ml Pulver für ein Konzentrat zur Herstellung einer Infusionslösung

SOLUTION FOR INFUSION

IV INFUSION

ATC code: L01AA09 - BENDAMUSTINA

Active Principles: N/A

Experimental

### Venclexta, Venclyxto

FILM-COATED TABLET

ORAL

-

Active Principles: N/A

Experimental

### Venclexta, Venclyxto

FILM-COATED TABLET

ORAL

-

Active Principles: N/A

Experimental

### Fludarabin Sandoz 25 mg/ml injekný alebo infúzny koncentrát

SOLUTION FOR INJECTION/INFUSION

IV INFUSION

ATC code: L01BB05 - FLUDARABINA

Active Principles: N/A

Experimental

### Venclexta, Venclyxto

FILM-COATED TABLET

ORAL

-

Active Principles: N/A

Experimental

### Neoflubin 25 mg/ml Konzentrat zur Herstellung einer Injektions- oder Infusionslösung

SOLUTION FOR INJECTION/INFUSION

IV INFUSION

ATC code: L01BB05 - FLUDARABINA

Active Principles: N/A

Experimental

### Endoxan

SOLUTION FOR INJECTION

IV INFUSION

ATC code: L01AA01 - CICLOFOSFAMIDA

Active Principles: N/A

Experimental

### Fludarabin Ebewe 25 mg/ml injektio-/infuusiokonsentraatti, liuosta varten

SOLUTION FOR INJECTION/INFUSION

IV INFUSION

ATC code: L01BB05 - FLUDARABINA

Active Principles: N/A

Experimental

**Fludarabine Ebewe 25 mg/ml, süste-/infusioonilahuse kontsentraat**
SOLUTION FOR INJECTION/INFUSION
IV INFUSION

ATC code: L01BB05 - FLUDARABINA
Active Principles: N/A

Experimental

**Levact 2,5 mg/ml poudre pour solution à diluer pour perfusion**
SOLUTION FOR INFUSION
IV INFUSION

ATC code: L01AA09 - BENDAMUSTINA
Active Principles: N/A

Experimental

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

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

Orphan
Experimental

**MabThera 500 mg concentrate for solution for infusion**
SOLUTION FOR INFUSION
IV INFUSION

ATC code: L01XC02 - RITUXIMAB
Active Principles: N/A

Experimental

**Levact 2,5 mg/ml Pulver für ein Konzentrat zur Herstellung einer Infusionslösung**
SOLUTION FOR INFUSION
IV INFUSION

ATC code: L01AA09 - BENDAMUSTINA
Active Principles: N/A

Experimental

**Fludarabinphosphat "Ebewe", koncentrat til injektions-/infusionsvæske, opløsning**
SOLUTION FOR INJECTION/INFUSION
IV INFUSION

ATC code: L01BB05 - FLUDARABINA
Active Principles: N/A

Experimental

## Has results