Phase 3 Study of Nemtabrutinib Plus Venetoclax vs Venetoclax and Rituximab in Second Line+ Relapsed/Refractory Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma

Estado	**Tipo de Participantes**	**Rangos de Edad**
Reclutando	No aportado	Mayores de 64 , Adultos (18-64 años)
Género	**Fases**	**Participantes esperados**
Ambos	Fase III	383
Resultados	**Bajo nivel intervención**	**Enfermedad rara**
Sin resultados	No	No
Cobertura geográfica	**Ámbitos del ensayo**	**Terapia avanzada**
Sin determinar	tratamiento, seguridad, eficacia, farmacocinética, farmacodinamica	NO

Información

Identificador
2022-501560-17-01 (CTIS)

Cod. Protocolo
MK-1026-010

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

Enfermedad investigada
Relapsed/Refractory Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma

Título Científico
A Phase 3, Open-label, Randomized Study to Compare the Efficacy and Safety of Nemtabrutinib (MK-1026) Plus Venetoclax Versus Venetoclax Plus Rituximab in Participants With Relapsed/Refractory Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma Following at Least 1 Prior Therapy (BELLWAVE-010)

Justificación

No aportado

Objetivo Principal

1. Part 1: To evaluate the safety and tolerability and to confirm the dose of nemtabrutinib in combination with venetoclax
2. Part 2: To compare nemtabrutinib + venetoclax to VR with respect to PFS per 2018 iwCLL criteria, as assessed by BICR

Variables de Evaluación Primaria

Part 1: Number of Participants Experiencing Dose-Limiting Toxicities (DLTs)
Part 1: Number of Participants Experiencing Adverse Events (AEs)
Part 1: Number of Participants Discontinuing Study Treatment Due to AEs
Part 2: Progression-Free Survival (PFS) per the 2018 International Workshop on Chronic Lymphocytic Leukemia (iwCLL) Criteria as Assessed by Blinded Independent Central Review (BICR)

Momentos temporales de evaluación primaria

No aportado

Objetivo Secundario

Part 2: To compare nemtabrutinib + venetoclax to VR with respect to undetectable MRD rate in bone marrow at month 14 as assessed by central laboratory
Part 2: To compare nemtabrutinib + venetoclax to VR with respect to OS
Part 2: To compare nemtabrutinib + venetoclax to VR with respect to ORR per iwCLL criteria 2018 as assessed by BICR
Part 2: To evaluate DOR per 2018 iwCLL criteria as assessed by BICR
Part 2: To evaluate the safety and tolerability of nemtabrutinib + venetoclax

Variables de Evaluación Secundaria

Part 2: Undetectable Minimal Residual Disease (MRD) Rate in Bone Marrow as Assessed by Central Laboratory
Part 2: Overall Survival (OS)
Part 2: Objective Response Rate (ORR) per iwCLL Criteria 2018 as Assessed by BICR
Part 2: Duration of Response (DOR) per iwCLL Criteria 2018 as Assessed by BICR
Part 2: Number of Participants Experiencing AEs
Part 2: Number of Participants Discontinuing Study Treatment Due to AEs

Momentos temporales de evaluación secundaria

No aportado

Criterios de Inclusión

Confirmed diagnosis of chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) and active disease clearly documented to initiate therapy
Participants with human immunodeficiency virus (HIV) meet ALL eligibility criteria.
Participants with adequate organ function with specimens collected within 7 days before the start of study intervention.
If capable of producing sperm, participant agrees to eliminate Nemtabrutinib: 12 days, Venetoclax: 1 month (30 days), Rituximab (rituximab biosimilar: not applicable; abstains from penile-vaginal intercourse as their preferred and usual lifestyle; OR uses prescribed contraception.
Participant assigned female sex at birth is eligible to participate if not pregnant or breastfeeding and is not a person of childbearing potential (POCBP) OR is a POCBP and uses a contraceptive method that is highly effective, has a negative highly sensitive pregnancy test, and abstains from breastfeeding.
Deletion (Del) (17p) status, tumor protein 53 (TP53) mutation status, and immunoglobulin heavy chain gene (IGHV) mutation status results required before randomization for Part 2 participants only.
Relapsed or refractory to at least 1 prior available therapy.
Have at least 1 marker of disease burden.
Has an Eastern Cooperative Oncology Group (ECOG) performance status of 0 to 2 within 7 days before randomization.
Has a life expectancy of at least 3 months.
Has the ability to swallow and retain oral medication.
Participants who are hepatitis B surface antigen (HBsAg) positive are eligible if they have received hepatitis B virus (HBV) antiviral therapy for at least 4 weeks and have undetectable HBV deoxyribonucleic acid (DNA) viral load before randomization.
Participants with history of hepatitis C virus (HCV) infection are eligible if HCV ribonucleic acid (RNA) viral load is undetectable at screening.

Criterios de Exclusión

Has active hepatitis B virus/ hepatitis C virus (HBV/HCV) infection.
Has received prior systemic anticancer therapy within 5 half-lives or 4 weeks (if prior therapy was a monoclonal antibody) before randomization.
Has received prior B-cell lymphoma 2 inhibitor(s) (BCL2i) within 12 months before randomization or has received prior radiotherapy within 2 weeks of start of study intervention, or radiation related toxicities, requiring corticosteroids.
Is currently being treated with p-glycoprotein (P-gp) substrates with a narrow therapeutic index, cytochrome P450 3A (CYP3A) strong inducers or inhibitors, or CYP3A moderate inducers
Has received a live or live attenuated vaccine within 30 days before the first dose of study intervention.
Has received an investigational agent or has used an investigational device within 4 weeks before study intervention administration.
Has known psychiatric or substance use disorder that would interfere with the participants ability to cooperate with the requirements of the study.
Participants who have not adequately recovered from major surgery or have ongoing surgical complications.
Has gastrointestinal (GI) dysfunction that may affect drug absorption.
Has known additional malignancy that is progressing or has required active treatment within the past 2 years.
Has diagnosis of Richter Transformation or active central nervous system (CNS) involvement by CLL/SLL.
Has active infection requiring systemic therapy, such as intravenous (IV) antibiotics, during screening.
HIV-infected participants with a history of Kaposis sarcoma and/or Multicentric Castlemans Disease and/or acquired

immune deficiency syndrome (AIDS)-defining opportunistic infection in the past 12 months before screening.
Clinically significant cardiovascular disease.
Has known allergy/sensitivity to nemtabrutinib or contraindication to venetoclax/rituximab (or rituximab biosimilar), or any of the excipients.
Has history of severe bleeding disorders (eg, hemophilia).

Calendario

(Última actualización: 25/03/2026)

Autorización	Inicio de Ensayo	Inclusión Primer Paciente	Interrumpido	Reiniciado
29/11/2023	18/12/2023	29/02/2024	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

Merck Sharp & Dohme LLC United States
126 East Lincoln Avenue

Contact Person
Ima Paydar¿
+16102169935
ima.paydar@merck.com

Monetary support: N/A
Tipo de promotor: Comercial

Ceim

CEIm Hospital Clínico San Carlos

C/ Doctor Martín Lagos, s/n - Ciudad Universitaria 28040 Madrid

ceic.hcsc@salud.madrid.org

917044160

Centros

Activo (18/12/2023)

Hospital Clinico Universitario De Valencia

Valencia

VALENCIA

Hematology

Activo (18/01/2024)

Hospital Universitario Quironsalud Madrid

Pozuelo De Alarcon

MADRID

Hematology

Activo (31/01/2024)

Institut Catala D'oncologia

L'hospitalet De Llobregat

BARCELONA

Hematology

Medicamentos

RITUXIMAB
SOLUTION FOR INFUSION
INTRAVENOUS INFUSION

-

Principios Activos: N/A

Experimental

RITUXIMAB
SOLUTION FOR INFUSION
INTRAVENOUS INFUSION

-

Principios Activos: N/A

Experimental

Truxima 500 mg concentrate for solution for infusion
SOLUTION FOR INFUSION
OTHER USE

Código ATC: L01FA01 - RITUXIMAB
Principios Activos: N/A

Experimental

Nemtabrutinib
TABLET
ORAL

-

Principios Activos: N/A

Experimental

Ruxience 100 mg concentrate for solution for infusion
SOLUTION FOR INFUSION
OTHER USE

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

Experimental

Truxima 100 mg concentrate for solution for infusion
SOLUTION FOR INFUSION
OTHER USE

Código ATC: L01FA01 - RITUXIMAB
Principios Activos: N/A

Experimental

-
-
ORAL

Código ATC: L01XX52 - VENETOCLAX
Principios Activos: N/A

Experimental

Ruxience 500 mg concentrate for solution for infusion
SOLUTION FOR INFUSION
OTHER USE

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

Experimental

Nemtabrutinib
FILM-COATED TABLET
ORAL

-
Principios Activos: N/A

Experimental

Nemtabrutinib
TABLET
ORAL

-
Principios Activos: N/A

Experimental

Nemtabrutinib
FILM-COATED TABLET
ORAL

-
Principios Activos: N/A

Experimental

Sin resultados

Phase 3 Study of Nemtabrutinib Plus Venetoclax vs Venetoclax and Rituximab in Second Line+ Relapsed/Refractory Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma

State	Type of participants	Age Ranges
Recruiting	Not provided	Older than 64 , Adults (18-64 years)
Gender	**Phases**	**Expected Participants**
Both	Phase III	383
Results	**Low level of intervention**	**Rare disease**
No results	No	No
Geographic coverage	**Areas of the study**	**Advanced therapy**
Undetermined	treatment, safety, effectiveness, pharmacokinetics, pharmacodynamics	NO

Information

Identifier
2022-501560-17-01 (CTIS)

Protocol Code
MK-1026-010

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

Investigated Disease
Relapsed/Refractory Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma

Scientific Title
A Phase 3, Open-label, Randomized Study to Compare the Efficacy and Safety of Nemtabrutinib (MK-1026) Plus Venetoclax Versus Venetoclax Plus Rituximab in Participants With Relapsed/Refractory Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma Following at Least 1 Prior Therapy (BELLWAVE-010)

Rationale

Not provided

Main Objective

1. Part 1: To evaluate the safety and tolerability and to confirm the dose of nemtabrutinib in combination with venetoclax
2. Part 2: To compare nemtabrutinib + venetoclax to VR with respect to PFS per 2018 iwCLL criteria, as assessed by BICR

Primary Endpoints

Part 1: Number of Participants Experiencing Dose-Limiting Toxicities (DLTs)
Part 1: Number of Participants Experiencing Adverse Events (AEs)
Part 1: Number of Participants Discontinuing Study Treatment Due to AEs
Part 2: Progression-Free Survival (PFS) per the 2018 International Workshop on Chronic Lymphocytic Leukemia (iwCLL) Criteria as Assessed by Blinded Independent Central Review (BICR)

Temporary moments of secondary assessment

Not provided

Secondary Objective

Part 2: To compare nemtabrutinib + venetoclax to VR with respect to undetectable MRD rate in bone marrow at month 14 as assessed by central laboratory
Part 2: To compare nemtabrutinib + venetoclax to VR with respect to OS
Part 2: To compare nemtabrutinib + venetoclax to VR with respect to ORR per iwCLL criteria 2018 as assessed by BICR
Part 2: To evaluate DOR per 2018 iwCLL criteria as assessed by BICR
Part 2: To evaluate the safety and tolerability of nemtabrutinib + venetoclax

Secondary Endpoints

Part 2: Undetectable Minimal Residual Disease (MRD) Rate in Bone Marrow as Assessed by Central Laboratory
Part 2: Overall Survival (OS)
Part 2: Objective Response Rate (ORR) per iwCLL Criteria 2018 as Assessed by BICR
Part 2: Duration of Response (DOR) per iwCLL Criteria 2018 as Assessed by BICR
Part 2: Number of Participants Experiencing AEs
Part 2: Number of Participants Discontinuing Study Treatment Due to AEs

Temporary moments of secondary assessment

Not provided

Inclusion criteria

Confirmed diagnosis of chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) and active disease clearly documented to initiate therapy
Participants with human immunodeficiency virus (HIV) meet ALL eligibility criteria.
Participants with adequate organ function with specimens collected within 7 days before the start of study intervention.
If capable of producing sperm, participant agrees to eliminate Nemtabrutinib: 12 days, Venetoclax: 1 month (30 days), Rituximab (rituximab biosimilar: not applicable; abstains from penile-vaginal intercourse as their preferred and usual lifestyle; OR uses prescribed contraception.
Participant assigned female sex at birth is eligible to participate if not pregnant or breastfeeding and is not a person of childbearing potential (POCBP) OR is a POCBP and uses a contraceptive method that is highly effective, has a negative highly sensitive pregnancy test, and abstains from breastfeeding.
Deletion (Del) (17p) status, tumor protein 53 (TP53) mutation status, and immunoglobulin heavy chain gene (IGHV) mutation status results required before randomization for Part 2 participants only.
Relapsed or refractory to at least 1 prior available therapy.
Have at least 1 marker of disease burden.
Has an Eastern Cooperative Oncology Group (ECOG) performance status of 0 to 2 within 7 days before randomization.
Has a life expectancy of at least 3 months.
Has the ability to swallow and retain oral medication.
Participants who are hepatitis B surface antigen (HBsAg) positive are eligible if they have received hepatitis B virus (HBV) antiviral therapy for at least 4 weeks and have undetectable HBV deoxyribonucleic acid (DNA) viral load before randomization.
Participants with history of hepatitis C virus (HCV) infection are eligible if HCV ribonucleic acid (RNA) viral load is undetectable at screening.

Exclusion criteria

Has active hepatitis B virus/ hepatitis C virus (HBV/HCV) infection.
Has received prior systemic anticancer therapy within 5 half-lives or 4 weeks (if prior therapy was a monoclonal antibody) before randomization.
Has received prior B-cell lymphoma 2 inhibitor(s) (BCL2i) within 12 months before randomization or has received prior radiotherapy within 2 weeks of start of study intervention, or radiation related toxicities, requiring corticosteroids.
Is currently being treated with p-glycoprotein (P-gp) substrates with a narrow therapeutic index, cytochrome P450 3A (CYP3A) strong inducers or inhibitors, or CYP3A moderate inducers
Has received a live or live attenuated vaccine within 30 days before the first dose of study intervention.
Has received an investigational agent or has used an investigational device within 4 weeks before study intervention administration.
Has known psychiatric or substance use disorder that would interfere with the participants ability to cooperate with the requirements of the study.
Participants who have not adequately recovered from major surgery or have ongoing surgical complications.
Has gastrointestinal (GI) dysfunction that may affect drug absorption.
Has known additional malignancy that is progressing or has required active treatment within the past 2 years.
Has diagnosis of Richter Transformation or active central nervous system (CNS) involvement by CLL/SLL.
Has active infection requiring systemic therapy, such as intravenous (IV) antibiotics, during screening.
HIV-infected participants with a history of Kaposis sarcoma and/or Multicentric Castlemans Disease and/or acquired

immune deficiency syndrome (AIDS)-defining opportunistic infection in the past 12 months before screening.
Clinically significant cardiovascular disease.
Has known allergy/sensitivity to nemtabrutinib or contraindication to venetoclax/rituximab (or rituximab biosimilar), or any of the excipients.
Has history of severe bleeding disorders (eg, hemophilia).

Calendar

(Last Update: 25/03/2026)

Authorization	Start of Trial	First patient inclusion	Halted	Restarted
29/11/2023	18/12/2023	29/02/2024	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

Merck Sharp & Dohme LLC United States
126 East Lincoln Avenue

Contact Person
Ima Paydar¿
+16102169935
ima.paydar@merck.com

Monetary support: N/A
Sponsor type: Commercial

Ceim

CEIm Hospital Clínico San Carlos

C/ Doctor Martín Lagos, s/n - Ciudad Universitaria 28040 Madrid

ceic.hcsc@salud.madrid.org

917044160

Sites

Active (18/12/2023)

Hospital Clinico Universitario De Valencia

Valencia

VALENCIA

Hematology

Active (18/01/2024)

Hospital Universitario Quironsalud Madrid

Pozuelo De Alarcon

MADRID

Hematology

Active (31/01/2024)

Institut Catala D'oncologia

L'hospitalet De Llobregat

BARCELONA

Hematology

Medication

RITUXIMAB
SOLUTION FOR INFUSION
INTRAVENOUS INFUSION

-
Active Principles: N/A

Experimental

RITUXIMAB
SOLUTION FOR INFUSION
INTRAVENOUS INFUSION

-
Active Principles: N/A

Experimental

Truxima 500 mg concentrate for solution for infusion
SOLUTION FOR INFUSION
OTHER USE

ATC code: L01FA01 - RITUXIMAB
Active Principles: N/A

Experimental

Nemtabrutinib
TABLET
ORAL

-
Active Principles: N/A

Experimental

Ruxience 100 mg concentrate for solution for infusion
SOLUTION FOR INFUSION
OTHER USE

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

Experimental

Truxima 100 mg concentrate for solution for infusion
SOLUTION FOR INFUSION
OTHER USE

ATC code: L01FA01 - RITUXIMAB
Active Principles: N/A

Experimental

-
-
ORAL

ATC code: L01XX52 - VENETOCLAX
Active Principles: N/A

Experimental

Ruxience 500 mg concentrate for solution for infusion
SOLUTION FOR INFUSION
OTHER USE

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

Experimental

Nemtabrutinib
FILM-COATED TABLET
ORAL

-

Active Principles: N/A

Experimental

Nemtabrutinib
TABLET
ORAL

-

Active Principles: N/A

Experimental

Nemtabrutinib
FILM-COATED TABLET
ORAL

-

Active Principles: N/A

Experimental

No results