A Study to Evaluate How Safe Pozelimab + Cemdisiran Combination Therapy is and How Well it Works in Adult Patients with Paroxysmal Nocturnal Hemoglobinuria (PNH) Who Have Not Recently Received or Have Not Received Complement Inhibitor Treatment

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	173
Resultados	**Bajo nivel intervención**	**Enfermedad rara**
Sin resultados	No	Si
Cobertura geográfica	**Ámbitos del ensayo**	**Terapia avanzada**
Sin determinar	seguridad, eficacia	NO

Información

Identificador
2023-509657-31-00 (CTIS)

Cod. Protocolo
R3918-PNH-2021

Transicionado 2020-004486-40

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

Enfermedad investigada
Paroxysmal nocturnal haemoglobinuria (PNH)

Título Científico
A Randomized, Open-Label, C5 Inhibitor-Controlled Study to Evaluate the Efficacy and Safety of Pozelimab and Cemdisiran Combination Therapy in Patients with Paroxysmal Nocturnal Hemoglobinuria who are Complement

Inhibitor Treatment-Naive or Have Not Recently Received Complement Inhibitor Therapy

Justificación

No aportado

Objetivo Principal

Cohort A: To describe the effect of pozelimab + cemdisiran combination treatment compared to ravulizumab treatment on hemolysis, as assessed by lactate dehydrogenase (LDH), over a 26-week treatment period in patients with active PNH who are complement inhibitor treatment-naive or have not recently received complement inhibitor therapy.
Cohort B: To evaluate the effect of pozelimab + cemdisiran combination treatment compared to eculizumab treatment on hemolysis, as assessed by suppression of LDH, and transfusion avoidance over a 26- week treatment period in patients with active PNH who are complement inhibitor treatment-naive or have not recently received complement inhibitor therapy.

Variables de Evaluación Primaria

Cohort A: Percent change in lactate dehydrogenase (LDH)
Cohort B: Adequate control of hemolysis (defined as LDH 1.5 × ULN) at each visit
Cohort B: Transfusion avoidance (not requiring a red blood cell (RBC) transfusion per the protocol)

Momentos temporales de evaluación primaria

No aportado

Objetivo Secundario

Cohort A: Describe the effect of pozelimab + cemdisiran combination treatment versus ravulizumab on the following: -Measures of hemolysis -Transfusion parameters -Hemoglobin levels -Fatigue as assessed by clinical outcome assessments (COAs) -Health-related quality of life (HRQoL) as assessed by COAs -Safety and tolerability -Complement activation
Cohort A: To assess the concentrations of total pozelimab and total ravulizumab in serum and cemdisiran and total C5 protein in plasma
Cohort A: To assess the immunogenicity of pozelimab and cemdisiran
Cohort B: Evaluate the effect of pozelimab + cemdisiran combination treatment versus eculizumab on the following: -Measures of hemolysis -Transfusion parameters -Hemoglobin levels-Fatigue as assessed by COAs -HRQoL as assessed by COAs -Safety and tolerability -Complement activation
Cohort B: To assess the concentrations of total pozelimab and total eculizumab in serum and cemdisiran and total C5 protein in plasma
Cohort B: To assess the immunogenicity of pozelimab and cemdisiran

Variables de Evaluación Secundaria

Maintenance of adequate control of hemolysis (defined as LDH 1.5 × ULN) (Cohort A and B)
Breakthrough hemolysis (defined as LDH 2 × ULN per the protocol) (Cohort A and B)
Adequate control of hemolysis (defined as LDH 1.5 × ULN) (Cohort A)
Hemoglobin stabilization (defined as patients who do not receive an RBC transfusion and have no decrease in hemoglobin level per the protocol) (Cohort A and B)
Normalization of LDH (defined as LDH 1.0 × ULN per the protocol) (Cohort A and B)
Transfusion Avoidance (defined as Not requiring an RBC transfusion as per protocol algorithm based on post-baseline hemoglobin values) (Cohort A)
Change in fatigue as measured by the Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT)-Fatigue Scale (Cohort A and B)
Change in physical function (PF) scores on the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC-QLQ-C30) (Cohort A and B)
Change in global health status (GHS)/QoL scale score on the EORTC-QLC- C30 (Cohort A and B)
Percent change in LDH (Cohort B)
Rate of RBC transfused per protocol algorithm (Cohort A and B)
Number of units of RBC transfused per protocol algorithm (Cohort A and B)
Time to first LDH 1.5 × ULN (Cohort A and B)
Time to first LDH 1.0 × ULN (Cohort A and B)
Percentage of days with LDH 1.5 × ULN (Cohort A and B)
Change in hemoglobin levels (Cohort A and B)
Incidence and severity of treatment emergent serious adverse events (SAEs) (Cohort A and B)
Incidence and severity of treatment-emergent adverse events (TEAEs) of special interest (Cohort A and B)
Incidence and severity of TEAEs leading to treatment discontinuation (Cohort A and B)
Change in total CH50 (Cohort A and B)
Percent change in total CH50 (Cohort A and B)
Concentration of total C5 in plasma (Cohort A and B)
Concentrations of total pozelimab in serum (Cohort A and B)
Concentrations of cemdisiran in plasma (Cohort A and B)
Concentrations of total ravulizumab (Cohort A) and total eculizumab (Cohort B) in serum
Incidence of treatment emergent anti-drug antibodies (ADAs) to pozelimab (Cohort A and B)
Incidence of treatment emergent ADAs to cemdisiran (Cohort A and B)

Momentos temporales de evaluación secundaria

No aportado

Criterios de Inclusión

Diagnosis of PNH confirmed by high-sensitivity flow cytometry testing with PNH granulocytes or monocytes as described in the protocol
Active disease, as defined by the presence of 1 or more PNH-related signs or symptoms as described in the protocol
LDH level 2 × ULN at the screening visit
Willing and able to comply with clinic/remote visits and study-related procedures, including completion of the full series of meningococcal vaccinations required per protocol Note: Other protocol-defined Inclusion Criteria apply

Criterios de Exclusión

Prior treatment with eculizumab within 3 months prior to screening, ravulizumab within 6 months prior to screening, or other complement inhibitors within 5 half-lives of the respective agent prior to screening Receipt of an organ transplant, history of bone marrow transplantation or other hematologic transplant Body weight <40 kilograms at screening visit Planned use of any complement inhibitor therapy other than study drugs during the treatment period Not meeting meningococcal vaccination requirements and, at a minimum documentation of quadrivalent meningococcal vaccination within 5 years prior to the screening visit and serotype B vaccine within 3 years prior to the screening visit as described in the protocol. Any contraindication for receiving Neisseria meningitidis vaccinations (serotypes ACWY and B) Unable to take antibiotics for meningococcal prophylaxis (if required by local ravulizumab [Cohort A] or eculizumab [Cohort B] prescribing information, where available, or national guidelines/local practice, or if necessary when administration of the first dose of the quadrivalent meningococcal vaccine [serotype ACWY] or the second dose of the serotype B meningococcal vaccine [when available] is less than 2 weeks prior to study treatment initiation) as described in the protocol. Any active, ongoing infection or a recent infection requiring ongoing systemic treatment with antibiotics, antivirals, or antifungals within 2 weeks of screening or during the screening period Documented history of active, uncontrolled, ongoing systemic autoimmune diseases Note: Other protocol-defined Exclusion Criteria apply

Calendario

(Última actualización: 10/08/2026)

Autorización	Inicio de Ensayo	Inclusión Primer Paciente	Interrumpido	Reiniciado
09/05/2022	15/09/2022	23/09/2022	No aportado	No aportado

Fin de reclutamiento	Fin prematuro (España)	Fin prematuro (Global)	Fin del ensayo en España	Fin del ensayo global
20/02/2026	No aportado	No aportado	18/06/2026	No aportado

Promotor

Regeneron Pharmaceuticals Inc. United States

777 Old Saw Mill River Road

Contact Person

Clinical Trial Information

+18447346643

clinicaltrials@regeneron.com

Monetary support: N/A

Tipo de promotor: Comercial

Ceim

CEIm Hospital Clinic de Barcelona

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Centros

Activo (15/09/2022)

HOSPITAL CLINIC DE BARCELONA

Barcelona

BARCELONA

Servicio de Hematología

Activo (24/10/2024)

Hospital G. Universitario J.M. Morales Meseguer

Murcia

MURCIA

Servicio Hematología

Activo (23/11/2022)

HOSPITAL UNIVERSITARIO BASURTO

Bilbao

VIZCAYA/BIZKAIA

Servicio de Hematología

Cerrado (03/08/2026)

Hospital Universitario de Salamanca (Complejo Asistencial Universitario De

Salamanca

SALAMANCA

Servicio de Hematologia

Medicamentos

Cemdisiran
SOLUTION FOR INJECTION
SUBCUTANEOUS INJECTION

-

Principios Activos: N/A

Huérfano Experimental

Ultomiris 300 mg/3 mL concentrate for solution for infusion
SOLUTION FOR INFUSION
INTRAVENOUS USE

Código ATC: L04AA43 - RAVULIZUMAB

Principios Activos: N/A

Experimental

Pozelimab
SOLUTION FOR INJECTION
INTRAVENOUS/SUBCUTANEOUS/INTRAMUSCULAR

-

Principios Activos: N/A

Experimental

Soliris 300 mg concentrate for solution for infusion
SOLUTION FOR INFUSION
SOLUTION FOR INFUSION

Código ATC: L04AA25 - ECULIZUMAB

Principios Activos: N/A

Experimental

Sin resultados

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State	**Type of participants**	**Age Ranges**
Finished CT	Not provided	Older than 64 , Adults (18-64 years)
Gender	**Phases**	**Expected Participants**
Both	Phase III	173
Results	**Low level of intervention**	**Rare disease**
No results	No	Yes
Geographic coverage	**Areas of the study**	**Advanced therapy**
Undetermined	safety, effectiveness	NO

Information

Identifier
2023-509657-31-00 (CTIS)

Protocol Code
R3918-PNH-2021

Transitioned 2020-004486-40

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

Investigated Disease
Paroxysmal nocturnal haemoglobinuria (PNH)

Scientific Title
A Randomized, Open-Label, C5 Inhibitor-Controlled Study to Evaluate the Efficacy and Safety of Pozelimab and Cemdisiran Combination Therapy in Patients with Paroxysmal Nocturnal Hemoglobinuria who are Complement

Inhibitor Treatment-Naive or Have Not Recently Received Complement Inhibitor Therapy

Rationale

Not provided

Main Objective

Cohort A: To describe the effect of pozelimab + cemdisiran combination treatment compared to ravulizumab treatment on hemolysis, as assessed by lactate dehydrogenase (LDH), over a 26-week treatment period in patients with active PNH who are complement inhibitor treatment-naive or have not recently received complement inhibitor therapy.
Cohort B: To evaluate the effect of pozelimab + cemdisiran combination treatment compared to eculizumab treatment on hemolysis, as assessed by suppression of LDH, and transfusion avoidance over a 26- week treatment period in patients with active PNH who are complement inhibitor treatment-naive or have not recently received complement inhibitor therapy.

Primary Endpoints

Cohort A: Percent change in lactate dehydrogenase (LDH)
Cohort B: Adequate control of hemolysis (defined as LDH 1.5 × ULN) at each visit
Cohort B: Transfusion avoidance (not requiring a red blood cell (RBC) transfusion per the protocol)

Temporary moments of secondary assessment

Not provided

Secondary Objective

Cohort A: Describe the effect of pozelimab + cemdisiran combination treatment versus ravulizumab on the following: -Measures of hemolysis -Transfusion parameters -Hemoglobin levels -Fatigue as assessed by clinical outcome assessments (COAs) -Health-related quality of life (HRQoL) as assessed by COAs -Safety and tolerability -Complement activation
Cohort A: To assess the concentrations of total pozelimab and total ravulizumab in serum and cemdisiran and total C5 protein in plasma
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Cohort B: To assess the concentrations of total pozelimab and total eculizumab in serum and cemdisiran and total C5 protein in plasma
Cohort B: To assess the immunogenicity of pozelimab and cemdisiran

Secondary Endpoints

Maintenance of adequate control of hemolysis (defined as LDH 1.5 × ULN) (Cohort A and B)
Breakthrough hemolysis (defined as LDH 2 × ULN per the protocol) (Cohort A and B)
Adequate control of hemolysis (defined as LDH 1.5 × ULN) (Cohort A)
Hemoglobin stabilization (defined as patients who do not receive an RBC transfusion and have no decrease in hemoglobin level per the protocol) (Cohort A and B)
Normalization of LDH (defined as LDH 1.0 × ULN per the protocol) (Cohort A and B)
Transfusion Avoidance (defined as Not requiring an RBC transfusion as per protocol algorithm based on post-baseline hemoglobin values) (Cohort A)
Change in fatigue as measured by the Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT)-Fatigue Scale (Cohort A and B)
Change in physical function (PF) scores on the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC-QLQ-C30) (Cohort A and B)
Change in global health status (GHS)/QoL scale score on the EORTC-QLC- C30 (Cohort A and B)
Percent change in LDH (Cohort B)
Rate of RBC transfused per protocol algorithm (Cohort A and B)
Number of units of RBC transfused per protocol algorithm (Cohort A and B)
Time to first LDH 1.5 × ULN (Cohort A and B)
Time to first LDH 1.0 × ULN (Cohort A and B)
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Concentrations of cemdisiran in plasma (Cohort A and B)
Concentrations of total ravulizumab (Cohort A) and total eculizumab (Cohort B) in serum
Incidence of treatment emergent anti-drug antibodies (ADAs) to pozelimab (Cohort A and B)
Incidence of treatment emergent ADAs to cemdisiran (Cohort A and B)

Temporary moments of secondary assessment

Not provided

Inclusion criteria

Diagnosis of PNH confirmed by high-sensitivity flow cytometry testing with PNH granulocytes or monocytes as described in the protocol
Active disease, as defined by the presence of 1 or more PNH-related signs or symptoms as described in the protocol
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Calendar

(Last Update: 10/08/2026)

Authorization	Start of Trial	First patient inclusion	Halted	Restarted
09/05/2022	15/09/2022	23/09/2022	Not aported	Not aported

End of recruitment	Premature end (Spain)	Premature End (Global)	Trial end (Spain)	Trial end (Global)
20/02/2026	Not aported	Not aported	18/06/2026	Not aported

Sponsor

Regeneron Pharmaceuticals Inc. United States

777 Old Saw Mill River Road

Contact Person

Clinical Trial Information

+18447346643

clinicaltrials@regeneron.com

Monetary support: N/A

Sponsor type: Commercial

Ceim

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Sites

Active (15/09/2022)

HOSPITAL CLINIC DE BARCELONA

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BARCELONA

Servicio de Hematología

Active (24/10/2024)

Hospital G. Universitario J.M. Morales Meseguer

Murcia

MURCIA

Servicio Hematología

Active (23/11/2022)

HOSPITAL UNIVERSITARIO BASURTO

Bilbao

VIZCAYA/BIZKAIA

Servicio de Hematología

Closed (03/08/2026)

Hospital Universitario de Salamanca (Complejo Asistencial Universitario De

Salamanca

SALAMANCA

Servicio de Hematologia

Medication

Cemdisiran

SOLUTION FOR INJECTION

SUBCUTANEOUS INJECTION

-

Active Principles: N/A

Orphan

Experimental

Ultomiris 300 mg/3 mL concentrate for solution for infusion

SOLUTION FOR INFUSION

INTRAVENOUS USE

ATC code: L04AA43 - RAVULIZUMAB

Active Principles: N/A

Experimental

Pozelimab

SOLUTION FOR INJECTION

INTRAVENOUS/SUBCUTANEOUS/INTRAMUSCULAR

-

Active Principles: N/A

Experimental

Soliris 300 mg concentrate for solution for infusion

SOLUTION FOR INFUSION

SOLUTION FOR INFUSION

ATC code: L04AA25 - ECULIZUMAB

Active Principles: N/A

Experimental

No results