Study to evaluate Pegcetacoplan in patients with TA-TMA after hematopoietic stem cell transplantation

Estado	**Tipo de Participantes**	**Rangos de Edad**
EC Finalizado	No aportado	Mayores de 64 , Adultos (18-64 años)
Género	**Fases**	**Participantes esperados**
Ambos	Fase II	12
Resultados	**Bajo nivel intervención**	**Enfermedad rara**
Tiene resultados	No	Si
Cobertura geográfica	**Ámbitos del ensayo**	**Terapia avanzada**
Unicéntrico nacional, Multicéntrico internacional	seguridad, eficacia, farmacocinética, farmacodinamica	NO

Información

Identificador

2023-510443-37-00 (CTIS)

Cod. Protocolo

Sobi.PEGCET-201

Transicionado 2021-003157-27

Área terapéutica

Enfermedades [C] - Hematología [C15]|

Enfermedad investigada

Transplant-associated Thrombotic Microangiopathy (TA TMA)

Título Científico

An Open-label, Single-arm, Multicenter Pilot Study to Evaluate the Pharmacokinetics, Pharmacodynamics, Efficacy and Safety of Pegcetacoplan in Patients with Transplant-associated Thrombotic Microangiopathy (TA-TMA) After Hematopoietic Stem Cell Transplantation (HSCT)

Justificación

No aportado

Objetivo Principal

To evaluate the pharmacokinetics (PK), safety and tolerability of pegcetacoplan in patients with TA-TMA.

Variables de Evaluación Primaria

Pegcetacoplan PK parameters: AUC0-tau, Cmax, Tmax and Ctrough.

Momentos temporales de evaluación primaria

No aportado

Objetivo Secundario

To evaluate the PD of pegcetacoplan in patients with TA-TMA.
To evaluate the efficacy of pegcetacoplan in patients with TA-TMA

Variables de Evaluación Secundaria

PD endpoints: o Absolute levels, change from baseline, and % change from baseline to Week 24 in biomarkers of complement activation: sC5b-9, C3a, C3, Bb, C4a, functional assays for classical and alternative complement pathways. Clinical response at Week 24, defined as improvement in laboratory markers and in clinical status (renal, pulmonary, GI, Neurological responses, freedom from transfusion, cardiovascular and serositis responses). Patients meeting intercurrent events, including use of prohibited medication or study withdrawal before Week 24, will be considered as failures/nonresponders. TMA response at Week 24, defined as improvement in laboratory markers as follows: o LDH < 1.5 x ULN and o Platelet count 50 000/mm3 without transfusion support during the prior 7 days and o 50 % reduction from baseline in rUPCR. Overall survival at Day 100 from date of TA-TMA diagnosis. Overall survival at Week 24 from treatment start. Time to clinical response. Time to TMA response. Duration of clinical response. Duration of TMA response TA-TMA relapse at Week 24. Clinical response at Week 12. TMA response at Week 12.

Momentos temporales de evaluación secundaria

No aportado

Criterios de Inclusión

Male and female patients aged 18 years at the time of informed consent form (ICF) signature. Received allogeneic HSCT from a related or unrelated, human leukocyte antigen-matched or mismatched donor. Patients having received any of the following stem cell sources are eligible: granulocyte colony stimulating factor mobilized peripheral blood stem cells, bone marrow, umbilical cord blood. Diagnosis of TA-TMA established as per the laboratory markers below, indicating TMA: a. De novo or progressing thrombocytopenia (platelet count < 50 x 109 /L or > 50 % decrease in platelet count from the highest value achieved after transplantation). AND b. Elevated LDH (> 1.5 x ULN). AND at least 2 additional laboratory/clinical criteria among the following: c. Presence of schistocytes on the peripheral blood smear (2 per hpf) or histologic evidence of microangiopathy in any biopsied organ. OR d. De novo anemia (hemoglobin < LLN or anemia requiring PRBC transfusion support as per local institutional standard). OR e. Proteinuria (random urinalysis protein concentration 30 mg/dL). OR f. Elevated plasma concentration of sC5b-9 above ULN. OR g. Arterial hypertension, defined by systolic blood pressure (BP) 140 mmHg and/or diastolic BP 90 mmHg. Have a diagnosis of TA-TMA that persists despite initial management of any triggering condition. Have rUPCR 1 mg/mg Women of childbearing potential, defined as any women who have experienced menarche and who are NOT permanently sterile or postmenopausal, must have a negative serum pregnancy test at screening and agree to use protocol-defined methods of contraception for the duration of the study and 8 weeks after their last IMP dose. Note: Postmenopausal is defined as having had 12 consecutive months with no menses without an alternative medical cause. Men must agree to the following for the duration of the study and 8 weeks after their last dose of IMP: a. Avoid fathering a child. b. Use protocol-defined methods of contraception. c. Refrain from donating sperm. Patient and/or legally authorized representative must be capable of giving signed informed consent, which includes compliance with the requirements and restrictions listed in the ICF.

Criterios de Exclusión

Positive direct Coombs test. Previously or currently treated with a complement inhibitor (approved or investigational). Pregnancy or breastfeeding Positive human immunodeficiency virus antibody at screening or documented in pre-HSCT medical record. Hepatitis C virus detectable by polymerase chain reaction at screening or documented in pre-HSCT medical record. Chronic inactive hepatitis B virus with viral loads > 1000IU/mL (> 5000copies/mL) at screening or documented in pre-HSCT medical record. Eligible patients who are chronic active carriers (1000IU/mL) must receive prophylactic antiviral treatment (e.g., entecavir, tenofovir, lamivudine) according to local country guidelines Known or suspected hereditary fructose intolerance. Hypersensitivity to pegcetacoplan or any of its excipients. Inability to cooperate with study procedures or any condition that, in the opinion of the investigator, could increase the patients risk by participating in the study or confound the outcome of the study. Known familial or acquired ADAMTS13 deficiency. Known Shiga toxin-related hemolytic uremic syndrome. Known bone marrow or graft failure. Diagnosis of disseminated intravascular coagulation. Diagnosis of veno-occlusive disease (VOD). Active GI bleeding (hematemesis or hematochezia) at baseline Body weight < 30 kg and > 100 kg. Uncontrolled systemic bacterial or fungal infection, presence or suspicion of sepsis.

Calendario

(Última actualización: 09/04/2025)

Autorización	Inicio de Ensayo	Inclusión Primer Paciente	Interrumpido	Reiniciado
13/12/2021	23/02/2022	15/03/2022	No aportado	No aportado

Fin de reclutamiento	Fin prematuro (España)	Fin prematuro (Global)	Fin del ensayo en España	Fin del ensayo global
19/07/2024	No aportado	No aportado	19/07/2024	09/12/2024

Promotor

Swedish Orphan Biovitrum AB (publ) Sweden

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Contact Person

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Monetary support: N/A

Tipo de promotor: Comercial

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Centros

Cerrado (19/07/2024)

HOSPITAL UNIVERSITARIO PUERTA DE HIERRO MAJADAHONDA

Majadahonda

MADRID

Servicio de Hematologia

Medicamentos

PEGCETACOPLAN
SOLUTION FOR INFUSION
INTRAVENOUS

-

Principios Activos: N/A

Experimental

PEGCETACOPLAN
SOLUTION FOR INFUSION
SUBCUTANEOUS

-

Principios Activos: N/A

Experimental

Tiene resultados

Study to evaluate Pegcetacoplan in patients with TA-TMA after hematopoietic stem cell transplantation

State	Type of participants	Age Ranges
Finished CT	Not provided	Older than 64 , Adults (18-64 years)
Gender	**Phases**	**Expected Participants**
Both	Phase II	12
Results	**Low level of intervention**	**Rare disease**
Has results	No	Yes
Geographic coverage	**Areas of the study**	**Advanced therapy**
National One-center , International multicenter	safety, effectiveness, pharmacokinetics, pharmacodynamics	NO

Information

Identifier
2023-510443-37-00 (CTIS)

Protocol Code
Sobi.PEGCET-201

Transitioned 2021-003157-27

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

Investigated Disease
Transplant-associated Thrombotic Microangiopathy (TA TMA)

Scientific Title
An Open-label, Single-arm, Multicenter Pilot Study to Evaluate the Pharmacokinetics, Pharmacodynamics, Efficacy and Safety of Pegcetacoplan in Patients with Transplant-associated Thrombotic Microangiopathy (TA-TMA) After Hematopoietic Stem Cell Transplantation (HSCT)

Rationale

Not provided

Main Objective

To evaluate the pharmacokinetics (PK), safety and tolerability of pegcetacoplan in patients with TA-TMA.

Primary Endpoints

Pegcetacoplan PK parameters: AUC0-tau, Cmax, Tmax and Ctrough.

Temporary moments of secondary assessment

Not provided

Secondary Objective

To evaluate the PD of pegcetacoplan in patients with TA-TMA.
To evaluate the efficacy of pegcetacoplan in patients with TA-TMA

Secondary Endpoints

PD endpoints: o Absolute levels, change from baseline, and % change from baseline to Week 24 in biomarkers of complement activation: sC5b-9, C3a, C3, Bb, C4a, functional assays for classical and alternative complement pathways. Clinical response at Week 24, defined as improvement in laboratory markers and in clinical status (renal, pulmonary, GI, Neurological responses, freedom from transfusion, cardiovascular and serositis responses). Patients meeting intercurrent events, including use of prohibited medication or study withdrawal before Week 24, will be considered as failures/nonresponders. TMA response at Week 24, defined as improvement in laboratory markers as follows: o LDH < 1.5 x ULN and o Platelet count 50 000/mm3 without transfusion support during the prior 7 days and o 50 % reduction from baseline in rUPCR. Overall survival at Day 100 from date of TA-TMA diagnosis. Overall survival at Week 24 from treatment start. Time to clinical response. Time to TMA response. Duration of clinical response. Duration of TMA response TA-TMA relapse at Week 24. Clinical response at Week 12. TMA response at Week 12.

Temporary moments of secondary assessment

Not provided

Inclusion criteria

Male and female patients aged 18 years at the time of informed consent form (ICF) signature. Received allogeneic HSCT from a related or unrelated, human leukocyte antigen-matched or mismatched donor. Patients having received any of the following stem cell sources are eligible: granulocyte colony stimulating factor mobilized peripheral blood stem cells, bone marrow, umbilical cord blood. Diagnosis of TA-TMA established as per the laboratory markers below, indicating TMA: a. De novo or progressing thrombocytopenia (platelet count < 50 x 109 /L or > 50 % decrease in platelet count from the highest value achieved after transplantation). AND b. Elevated LDH (> 1.5 x ULN). AND at least 2 additional laboratory/clinical criteria among the following: c. Presence of schistocytes on the peripheral blood smear (2 per hpf) or histologic evidence of microangiopathy in any biopsied organ. OR d. De novo anemia (hemoglobin < LLN or anemia requiring PRBC transfusion support as per local institutional standard). OR e. Proteinuria (random urinalysis protein concentration 30 mg/dL). OR f. Elevated plasma concentration of sC5b-9 above ULN. OR g. Arterial hypertension, defined by systolic blood pressure (BP) 140 mmHg and/or diastolic BP 90 mmHg. Have a diagnosis of TA-TMA that persists despite initial management of any triggering condition. Have rUPCR 1 mg/mg Women of childbearing potential, defined as any women who have experienced menarche and who are NOT permanently sterile or postmenopausal, must have a negative serum pregnancy test at screening and agree to use protocol-defined methods of contraception for the duration of the study and 8 weeks after their last IMP dose. Note: Postmenopausal is defined as having had 12 consecutive months with no menses without an alternative medical cause. Men must agree to the following for the duration of the study and 8 weeks after their last dose of IMP: a. Avoid fathering a child. b. Use protocol-defined methods of contraception. c. Refrain from donating sperm. Patient and/or legally authorized representative must be capable of giving signed informed consent, which includes compliance with the requirements and restrictions listed in the ICF.

Exclusion criteria

Positive direct Coombs test. Previously or currently treated with a complement inhibitor (approved or investigational). Pregnancy or breastfeeding Positive human immunodeficiency virus antibody at screening or documented in pre-HSCT medical record. Hepatitis C virus detectable by polymerase chain reaction at screening or documented in pre-HSCT medical record. Chronic inactive hepatitis B virus with viral loads > 1000IU/mL (> 5000copies/mL) at screening or documented in pre-HSCT medical record. Eligible patients who are chronic active carriers (1000IU/mL) must receive prophylactic antiviral treatment (e.g., entecavir, tenofovir, lamivudine) according to local country guidelines Known or suspected hereditary fructose intolerance. Hypersensitivity to pegcetacoplan or any of its excipients. Inability to cooperate with study procedures or any condition that, in the opinion of the investigator, could increase the patients risk by participating in the study or confound the outcome of the study. Known familial or acquired ADAMTS13 deficiency. Known Shiga toxin-related hemolytic uremic syndrome. Known bone marrow or graft failure. Diagnosis of disseminated intravascular coagulation. Diagnosis of veno-occlusive disease (VOD). Active GI bleeding (hematemesis or hematochezia) at baseline Body weight < 30 kg and > 100 kg. Uncontrolled systemic bacterial or fungal infection, presence or suspicion of sepsis.

Calendar

(Last Update: 09/04/2025)

Authorization	Start of Trial	First patient inclusion	Halted	Restarted
13/12/2021	23/02/2022	15/03/2022	Not aported	Not aported

End of recruitment	Premature end (Spain)	Premature End (Global)	Trial end (Spain)	Trial end (Global)
19/07/2024	Not aported	Not aported	19/07/2024	09/12/2024

Sponsor

Swedish Orphan Biovitrum AB (publ) Sweden

-

Contact Person

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Monetary support: N/A

Sponsor type: Commercial

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Sites

Closed (19/07/2024)

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Majadahonda

MADRID

Servicio de Hematologia

Medication

PEGCETACOPLAN
SOLUTION FOR INFUSION
INTRAVENOUS

-

Active Principles: N/A

Experimental

PEGCETACOPLAN
SOLUTION FOR INFUSION
SUBCUTANEOUS

-

Active Principles: N/A

Experimental

Has results