A Phase 1 Study of JNJ-88549968, a T-cell Redirecting Antibody, for CALR-mutated Myeloproliferative Neoplasms

Estado	Tipo de Participantes	Rangos de Edad
Reclutando	No aportado	Mayores de 64 , Adultos (18-64 años)
Género	**Fases**	**Participantes esperados**
Ambos	Fase I	170
Resultados	**Bajo nivel intervención**	**Enfermedad rara**
Sin resultados	No	No
Cobertura geográfica	**Ámbitos del ensayo**	**Terapia avanzada**
Sin determinar	diagnóstico, tratamiento, seguridad, eficacia, farmacocinética, farmacodinamica, dosis	NO

Información

Identificador
2023-505584-36-00 (CTIS)

Cod. Protocolo
88549968MPN1001

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

Enfermedad investigada
CALR-mutated Myeloproliferative Neoplasms

Título Científico
A First-in-Human Study of the Safety, Pharmacokinetics, and Pharmacodynamics of JNJ-88549968, a T-cell Redirecting Bispecific Antibody for CALR-mutated Myeloproliferative Neoplasms

Justificación

No aportado

Objetivo Principal

Part 1 (Dose Escalation)
To characterize safety and to determine the putative RP2D(s) and optimal dosing schedule(s) of JNJ-88549968 in monotherapy (ET and MF) and in combination with ruxolitinib or momelotinib (MF only)
Part 2 (Cohort Expansion)
To further characterize the safety of JNJ-88549968 at the putative RP2D(s) in monotherapy (ET and MF) and in combination with ruxolitinib or momelotinib (MF only)

Variables de Evaluación Primaria

For Part 1 (Dose Escalation) Frequency and severity of AEs (including DLTs)
For Part 2 (Cohort Expansion) Frequency and severity of AEs

Momentos temporales de evaluación primaria

No aportado

Objetivo Secundario

No aportado

Variables de Evaluación Secundaria

No aportado

Momentos temporales de evaluación secundaria

No aportado

Criterios de Inclusión

18 years of age 2.1. Criterion modified per EEA-4: 2.2 Have a diagnosis of either ET or MF as defined by the 2022 WHO criteria (WHO Classification of Tumours Editorial Board 2022) that meets the stated risk criteria: Essential Thrombocythemia High-risk of thrombosis or hemorrhage, defined as any 1 of the following: - Age >60 years - Platelet count >1500 x 10^9 /L at any point during the participants disease - Previous documented thrombosis

(including transient ischemic attack [TIA]), erythromelalgia, or migraine (severe, recurrent, requiring medications, and felt to be secondary to the MPN) either after diagnosis or within 10 years before diagnosis and considered to be disease-related. -Previous hemorrhage or coagulopathy related to ET -Diabetes mellitus or hypertension requiring pharmacological therapy >6 months. AND Intolerant or resistant or refractory to HU (unless contraindicated), defined as any 1 of the following according to NCCN Guidelines Version 1.2023: - Platelet count >600 x 10^9 /L after 3 months of at least 2 g/day or MTD of HU (2.5 g/day in participants with a body weight >80 kg) - Platelet count >400 x 10^9 /L and WBC 400 x 10^9 /L and hemoglobulin <10 g/dL at any dose of HU (for a period of at least 3 months) - Presence of leg ulcers or other unacceptable mucocutaneous manifestations at any dose of HU - HU-related fever. Myelofibrosis (primary or post-ET) Primary Myelofibrosis: DIPSS -Intermediate 1-2 or High-Risk with a blast percentage not consistently exceeding 20% in blood or bone marrow. Post-ET MYSEC-PM Intermediate 1-2 or High-Risk with a blast percentage not consistently exceeding 20% in blood or bone marrow AND Ineligible for Hematopoietic Stem Cell Transplantation (HSCT) AND EITHER Ineligible or intolerant or resistant / refractory to JAKi therapy Positive for CALR mutation Criterion modified per Amendment EEA-4: 4.1. Have received prior therapy(ies): ET: have received at least 2 (unless unavailable or contraindicated) lines of prior cytoreductive therapy Have discontinued concurrent use of the following therapies: ET: Interferon- (pegylated or standard preparation), anagrelide, busulfan. Exception: HU is permitted. MF: JAKi, immunomodulatory drug therapy (such as thalidomide), danazol, or other therapy intended to lead to disease modification Have an ECOG performance status grade of 0 or 1 Required clinical hematology laboratory values predose: o Hemoglobin 8.0 g/dL o Neutrophils 0.75 x 10^9/L without the assistance of granulocyte growth factors within 4 weeks of the first dose of study drug o Platelets 50 x 10^9/L without the assistance of thrombopoietic factors or transfusions Criterion modified per Amendment EEA-3: 8.1 Participants should have the following clinical chemistry laboratory values predose: a. ALT: 3 x ULN b. AST: 3 x ULN c. Direct bilirubin: 1.5 x ULN d. Renal function: Estimated or measured glomerular filtration rate 40 mL/min per CKD-EPI (Creatinine) or BIS1 formula (See Appendix 9.) Known HIV-positive participants are eligible if they meet all of the following at screening: o No detectable viral load o CD4+ count >300 cells/mm^3 o No AIDS-defining opportunistic infection within 6 months o Receiving HAART.

Criterios de Exclusión

Chemo, targeted therapy, immunotherapy or cytoreductive therapy at 5 half-lives prior planned first study treatment Any prior treatment with CALRmut-targeted therapy. Concurrent or recently diagnosed or treated malignancies present at the time of screening Prior solid organ transplant HSCT restriction: HSCT6mo, GVHD that requires chronic immunosuppressant therapy Active autoimmune disease that requires systemic immunosuppressive medication Uncontrolled CV disease within 6 months of first dose Clinically significant pulmonary compromise Reported temperature > 38ºC within 48 hours of first dose Evidence of active viral (including chronic EBV), bacterial, or uncontrolled systemic fungal infection requiring systemic treatment within 14 days before the first dose of study treatment. History of pneumonitis or interstitial lung disease. Active or uncontrolled infection within 14 days of first dose Those without evidence of stable anticoagulant therapy, defined as 4 weeks of unmodified anticoagulant therapy prior to the first administration of study treatment. History of HLH/MAS Trauma or major surgery within 28 days of first dose Administration of live attenuated vaccine within 4 weeks of first dose Active or chronic HBV or HCV infection Body weight is <40 kg at screening and/or at the time of their first dose Toxicities from previous anticancer therapies that have not resolved to baseline levels, or to Grade 1 or less, or to Grade 2 for alopecia, peripheral neuropathy, and vitiligo Any serious underlying medical or psychiatric condition (eg, alcohol or drug abuse), dementia or altered mental status; or any issue that would impair the ability of the participant to receive or tolerate the planned treatment at the investigational site, to understand informed consent, or that in the opinion of the investigator would contraindicate the participation in the study or confound the protocol-specified assessments or results of the study A prohibited medication that cannot be discontinued or substituted, or temporally interrupted during the study. Prohibited therapies are described in Section 6.8.4

Calendario

(Última actualización: 04/05/2026)

Autorización	Inicio de Ensayo	Inclusión Primer Paciente	Interrumpido	Reiniciado
16/02/2024	21/10/2024	21/10/2024	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

Janssen - Cilag International Belgium

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Contact Person

CTIS Point of Contact

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Monetary support: N/A

Tipo de promotor: Comercial

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Centros

Activo (11/03/2024)

Hospital Clinico Universitario De Valencia

Valencia

VALENCIA

Hematology

Activo (09/05/2024)

Institut Catala D'oncologia

Badalona

BARCELONA

Hematology

Medicamentos

JNJ-88549968
SOLUTION FOR INJECTION
SUBCUTANEOUS USE

-

Principios Activos: N/A

Experimental

Sin resultados

A Phase 1 Study of JNJ-88549968, a T-cell Redirecting Antibody, for CALR-mutated Myeloproliferative Neoplasms

State	Type of participants	Age Ranges
Recruiting	Not provided	Older than 64 , Adults (18-64 years)
Gender	**Phases**	**Expected Participants**
Both	Phase I	170
Results	**Low level of intervention**	**Rare disease**
No results	No	No
Geographic coverage	**Areas of the study**	**Advanced therapy**
Undetermined	diagnosis, treatment, safety, effectiveness, pharmacokinetics, pharmacodynamics, dose	NO

Information

Identifier
2023-505584-36-00 (CTIS)

Protocol Code
88549968MPN1001

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

Investigated Disease
CALR-mutated Myeloproliferative Neoplasms

Scientific Title
A First-in-Human Study of the Safety, Pharmacokinetics, and Pharmacodynamics of JNJ-88549968, a T-cell Redirecting Bispecific Antibody for CALR-mutated Myeloproliferative Neoplasms

Rationale

Not provided

Main Objective

Part 1 (Dose Escalation)
To characterize safety and to determine the putative RP2D(s) and optimal dosing schedule(s) of JNJ-88549968 in monotherapy (ET and MF) and in combination with ruxolitinib or momelotinib (MF only)
Part 2 (Cohort Expansion)
To further characterize the safety of JNJ-88549968 at the putative RP2D(s) in monotherapy (ET and MF) and in combination with ruxolitinib or momelotinib (MF only)

Primary Endpoints

For Part 1 (Dose Escalation) Frequency and severity of AEs (including DLTs)
For Part 2 (Cohort Expansion) Frequency and severity of AEs

Temporary moments of secondary assessment

Not provided

Secondary Objective

Not provided

Secondary Endpoints

Not provided

Temporary moments of secondary assessment

Not provided

Inclusion criteria

18 years of age 2.1. Criterion modified per EEA-4: 2.2 Have a diagnosis of either ET or MF as defined by the 2022 WHO criteria (WHO Classification of Tumours Editorial Board 2022) that meets the stated risk criteria: Essential Thrombocythemia High-risk of thrombosis or hemorrhage, defined as any 1 of the following: - Age >60 years - Platelet count >1500 x 10^9 /L at any point during the participants disease - Previous documented thrombosis

(including transient ischemic attack [TIA]), erythromelalgia, or migraine (severe, recurrent, requiring medications, and felt to be secondary to the MPN) either after diagnosis or within 10 years before diagnosis and considered to be disease-related. -Previous hemorrhage or coagulopathy related to ET -Diabetes mellitus or hypertension requiring pharmacological therapy >6 months. AND Intolerant or resistant or refractory to HU (unless contraindicated), defined as any 1 of the following according to NCCN Guidelines Version 1.2023: - Platelet count >600 x 10^9 /L after 3 months of at least 2 g/day or MTD of HU (2.5 g/day in participants with a body weight >80 kg) - Platelet count >400 x 10^9 /L and WBC 400 x 10^9 /L and hemoglobulin <10 g/dL at any dose of HU (for a period of at least 3 months) - Presence of leg ulcers or other unacceptable mucocutaneous manifestations at any dose of HU - HU-related fever. Myelofibrosis (primary or post-ET) Primary Myelofibrosis: DIPSS -Intermediate 1-2 or High-Risk with a blast percentage not consistently exceeding 20% in blood or bone marrow. Post-ET MYSEC-PM Intermediate 1-2 or High-Risk with a blast percentage not consistently exceeding 20% in blood or bone marrow AND Ineligible for Hematopoietic Stem Cell Transplantation (HSCT) AND EITHER Ineligible or intolerant or resistant / refractory to JAKi therapy Positive for CALR mutation Criterion modified per Amendment EEA-4: 4.1. Have received prior therapy(ies): ET: have received at least 2 (unless unavailable or contraindicated) lines of prior cytoreductive therapy Have discontinued concurrent use of the following therapies: ET: Interferon- (pegylated or standard preparation), anagrelide, busulfan. Exception: HU is permitted. MF: JAKi, immunomodulatory drug therapy (such as thalidomide), danazol, or other therapy intended to lead to disease modification Have an ECOG performance status grade of 0 or 1 Required clinical hematology laboratory values predose: o Hemoglobin 8.0 g/dL o Neutrophils 0.75 x 10^9/L without the assistance of granulocyte growth factors within 4 weeks of the first dose of study drug o Platelets 50 x 10^9/L without the assistance of thrombopoietic factors or transfusions Criterion modified per Amendment EEA-3: 8.1 Participants should have the following clinical chemistry laboratory values predose: a. ALT: 3 x ULN b. AST: 3 x ULN c. Direct bilirubin: 1.5 x ULN d. Renal function: Estimated or measured glomerular filtration rate 40 mL/min per CKD-EPI (Creatinine) or BIS1 formula (See Appendix 9.) Known HIV-positive participants are eligible if they meet all of the following at screening: o No detectable viral load o CD4+ count >300 cells/mm^3 o No AIDS-defining opportunistic infection within 6 months o Receiving HAART.

Exclusion criteria

Chemo, targeted therapy, immunotherapy or cytoreductive therapy at 5 half-lives prior planned first study treatment Any prior treatment with CALRmut-targeted therapy. Concurrent or recently diagnosed or treated malignancies present at the time of screening Prior solid organ transplant HSCT restriction: HSCT6mo, GVHD that requires chronic immunosuppressant therapy Active autoimmune disease that requires systemic immunosuppressive medication Uncontrolled CV disease within 6 months of first dose Clinically significant pulmonary compromise Reported temperature > 38ºC within 48 hours of first dose Evidence of active viral (including chronic EBV), bacterial, or uncontrolled systemic fungal infection requiring systemic treatment within 14 days before the first dose of study treatment. History of pneumonitis or interstitial lung disease. Active or uncontrolled infection within 14 days of first dose Those without evidence of stable anticoagulant therapy, defined as 4 weeks of unmodified anticoagulant therapy prior to the first administration of study treatment. History of HLH/MAS Trauma or major surgery within 28 days of first dose Administration of live attenuated vaccine within 4 weeks of first dose Active or chronic HBV or HCV infection Body weight is <40 kg at screening and/or at the time of their first dose Toxicities from previous anticancer therapies that have not resolved to baseline levels, or to Grade 1 or less, or to Grade 2 for alopecia, peripheral neuropathy, and vitiligo Any serious underlying medical or psychiatric condition (eg, alcohol or drug abuse), dementia or altered mental status; or any issue that would impair the ability of the participant to receive or tolerate the planned treatment at the investigational site, to understand informed consent, or that in the opinion of the investigator would contraindicate the participation in the study or confound the protocol-specified assessments or results of the study A prohibited medication that cannot be discontinued or substituted, or temporally interrupted during the study. Prohibited therapies are described in Section 6.8.4

Calendar

(Last Update: 04/05/2026)

Authorization	Start of Trial	First patient inclusion	Halted	Restarted
16/02/2024	21/10/2024	21/10/2024	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

Janssen - Cilag International Belgium

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Contact Person

CTIS Point of Contact

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Monetary support: N/A

Sponsor type: Commercial

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Sites

Active (11/03/2024)

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Valencia

VALENCIA

Hematology

Active (09/05/2024)

Institut Catala D'oncologia

Badalona

BARCELONA

Hematology

Medication

JNJ-88549968
SOLUTION FOR INJECTION
SUBCUTANEOUS USE

-

Active Principles: N/A

Experimental

No results