Phase 1/2 Study of Oral Nuvisertib (TP-3654) in Patients with Myelofibrosis

Estado	Tipo de Participantes	Rangos de Edad
Reclutando	No aportado	Mayores de 64 , Adultos (18-64 años)
Género	**Fases**	**Participantes esperados**
Ambos	Fase I , Fase II	204
Resultados	**Bajo nivel intervención**	**Enfermedad rara**
Sin resultados	No	Si
Cobertura geográfica	**Ámbitos del ensayo**	**Terapia avanzada**
Sin determinar	seguridad, eficacia, farmacocinética, farmacodinamica	NO

Información

Identificador
2022-502597-16-00 (CTIS)

Cod. Protocolo
BBI-TP-3654-102

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

Enfermedad investigada
Intermediate or High-risk Primary or Secondary Myelofibrosis

Título Científico
A Phase 1/2, Open-label, Dose-escalation, Safety, Pharmacokinetic, and Pharmacodynamic Study of Oral Nuvisertib (TP-3654) in Patients with Intermediate or High-risk Primary or Secondary Myelofibrosis

Justificación

No aportado

Objetivo Principal

- Nuvisertib Monotherapy (Arm 1) - Phase 1: To identify the recommended Phase 2 dose (RP2D) of Nuvisertib monotherapy. - Nuvisertib Monotherapy (Arm 1) - Phase 1: To determine the overall safety of Nuvisertib monotherapy.(Note: this objective is secondary in Phase 2) - Nuvisertib Monotherapy (Arm 1) - Phase 2: To assess any preliminary clinical activity of Nuvisertib monotherapy.
- Nuvisertib + Momelotinib (Arm 3) Phase 1: To identify the recommended Phase 2 dose (RP2D) of Nuvisertib when administered in combination with momelotinib.
- Nuvisertib + Momelotinib (Arm 3) Phase 1: To determine the overall safety of Nuvisertib and momelotinib combination.(Note: this objective is secondary in Phase 2) - Nuvisertib + Momelotinib (Arm 3) Phase 2: To assess any preliminary clinical activity of Nuvisertib and momelotinib combination.

Variables de Evaluación Primaria

Nuvisertib Monotherapy (Arm 1) - Phase 1: Dose-limiting toxicity (DLT) at escalated doses of Nuvisertib.
Nuvisertib Monotherapy (Arm 1) - Phase 1: Adverse events (AEs) as characterized by type, frequency, severity, seriousness, and relationship to study drugs. (Note: This endopoint is secondary in Phase 2)
Nuvisertib Monotherapy (Arm 1) - Phase 2: Spleen volume response: 35% spleen volume reduction (SVR35) at any time.
Nuvisertib + Momelotinib (Arm 3) Phase 1: Dose-limiting toxicity (DLT) at escalated doses of Nuvisertib when administered in combination with momelotinib.
Nuvisertib + Momelotinib (Arm 3) Phase 1: Adverse events (AEs) as characterized by type, frequency, severity, seriousness, and relationship to study drugs. [Note: This endpoint is secondary in Phase 2]
Nuvisertib + Momelotinib (Arm 3) Phase 2: Spleen volume response: 35% spleen volume reduction (SVR35) at any time.

Momentos temporales de evaluación primaria

No aportado

Objetivo Secundario

Nuvisertib Monotherapy (Arm 1) - Phase 1 and 2: To assess any preliminary clinical activity of Nuvisertib monotherapy.
Nuvisertib Monotherapy (Arm 1) - Phase 1 and 2: To determine the cardiac safety of Nuvisertib.
Nuvisertib Monotherapy (Arm 1) - Phase 1 and 2: To establish the pharmacokinetic (PK) profile of orally administered Nuvisertib monotherapy.
Nuvisertib + Momelotinib (Arm 3) Phase 1 and 2: To assess any preliminary clinical activity of Nuvisertib and momelotinib combination.
Nuvisertib + Momelotinib (Arm 3) Phase 1 and 2: To establish the pharmacokinetic (PK) profile of Nuvisertib and momelotinib at steady state when administered concomitantly.

Variables de Evaluación Secundaria

Nuvisertib Monotherapy (Arm 1) - Phase 1 and 2: Spleen volume response: - 25% spleen volume reduction [SVR25] at any time; - Duration of spleen volume response.
Nuvisertib Monotherapy (Arm 1) - Phase 1 and 2: Total symptom score response assessed by MFSAF v4.0; - 50% improvement in total symptom score (TSS50) at Week 24; - Duration of TSS50 over time during the study; - Absolute TSS change from baseline at Week 24.
Nuvisertib Monotherapy (Arm 1) - Phase 1 and 2: Patient Global Impression of Change (PGIC) at Week 24 and at any time.
Nuvisertib Monotherapy (Arm 1) - Phase 1 and 2: Response evaluation per the revised IWG-MRT criteria: Complete remission (CR), partial remission (PR), clinical improvement (CI), stable disease (SD), and progressive disease (PD).
Nuvisertib Monotherapy (Arm 1) - Phase 1 and 2: QT interval changes.
Nuvisertib Monotherapy (Arm 1) - Phase 1 and 2: PK parameters of Nuvisertib: Cmax, tmax, AUC, t½, and others as data permits.
Nuvisertib + Momelotinib (Arm 3) Phase 1 and 2: Spleen volume response: - 25% spleen volume reduction [SVR25] at any time; - Duration of spleen volume response.
Nuvisertib + Momelotinib (Arm 3) Phase 1 and 2: Total symptom score response assessed by MFSAF v4.0: - 50% improvement in total symptom score (TSS50) at Week 24; - Duration of TSS50 over time during the study; - Absolute TSS change from baseline at Week 24.
Nuvisertib + Momelotinib (Arm 3) Phase 1 and 2: Patient Global Impression of Change (PGIC) at Week 24 and at any time.
Nuvisertib + Momelotinib (Arm 3) Phase 1 and 2: Response evaluation per the revised IWG-MRT criteria: - Complete remission (CR), partial remission (PR), clinical improvement (CI), stable disease (SD), and progressive disease (PD).
Nuvisertib + Momelotinib (Arm 3) Phase 1 and 2: PK parameters of TP-3654 and momelotinib: Cmax, tmax, AUC, t½ and others as data permits.

Momentos temporales de evaluación secundaria

No aportado

Criterios de Inclusión

Arm 1: Adult (18 years of age). Arm 3: Fulfills the following clinical laboratory parameters: a. Anemic, defined as Hb <10 g/dL; b. Platelet count 50 × 109 /L (without the assistance of growth factors or platelet transfusions); c. ANC 1 × 10^9 /L without the assistance of granulocyte growth factors; d. Peripheral blood blast count < 5% at screening; e. Adequate renal function, as determined by clinical laboratory tests: serum creatinine 1.5 × ULN or calculated creatinine clearance 30 mL/min (using Cockcroft-Gault formula); f. Adequate hepatic function: ALT and AST 3 × ULN (ALT and AST 5 × ULN if there is liver involvement secondary to MF); direct bilirubin 2 × ULN; g. Adequate coagulation function: PT and PTT 1.5 × ULN; INR 1.2 × ULN (INR < 2.5 × ULN permitted if on chronic anticoagulant therapy). Arm 3: Splenomegaly, defined as spleen volume of 450 cm3 by MRI/CT scan within 2 weeks prior to Cycle 1 Day 1. Arm 1: Capable of providing signed informed consent as described in Section 10.1.3 of the study protocol which includes compliance with the requirements and restrictions listed in the informed consent form (ICF) and in this protocol. Arm 3: At least 2 symptoms measurable with each score of 3 or a total average score of 10 per MFSAF v4.0. Arm 3: ECOG performance status 1. Arm 3: Life expectancy 6 months. Arm 3: Non-fertile or agree to use an adequate method of contraception. Arm 3: Capable of providing signed informed consent which includes compliance with the requirements and restrictions listed in the ICF and in this protocol. Arm 3: Able to swallow orally administered medication. Arm 1: Non-fertile or agrees to use an adequate method of contraception. Arm 1: Previously treated with an approved JAK inhibitor(s) and is intolerant, resistant, refractory or has lost response to an approved the JAK inhibitor(s), or is ineligible to be treated with an approved JAK inhibitor as determined by the Investigator in accordance with the local product labels. Note: Intolerant is considered as requiring a transfusion of 4 units of red blood cells in 8 weeks, or Grade 3/4 AEs of thrombocytopenia, anemia, or hematoma for ruxolitinib and

fedratinib; Grade 2 peripheral neuropathy for momelotinib. Arm 1: Splenomegaly, defined as spleen volume of 450 cm3 by magnetic resonance Imaging (MRI) or computerized tomography (CT) scan, within 2 weeks prior to Cycle 1 Day 1. Arm 1: Dose Escalation: at least 2 symptoms measurable (score 1) using the MFSAF v4.0. Dose Expansion: at least 2 symptoms measurable with each score of 3 or a total average score of 10 per MFSAF v4.0. Arm 1: Able to swallow orally administered medication. Arm 3: Confirmed pathological diagnosis of PMF or post-PV-MF/post ET-MF as per WHO diagnostic criteria (Section 10.2.4), and intermediate or high-risk primary or secondary MF based on the DIPSS. Arm 1: Confirmed pathological diagnosis of primary myelofibrosis (PMF) or post-polycythemia vera (PV)-MF/post-ET-MF as per World Health Organization (WHO) diagnostic criteria, and intermediate or high-risk primary or secondary MF based on the Dynamic International Prognostic Scoring System (DIPSS). Arm 3: Adult (18 years of age). Arm 1: Fulfills the following laboratory parameters: a. Platelet count 25 × 10^9 /L without the assistance of growth factors or platelet transfusions; b. Absolute neutrophil count (ANC) 1 × 10^9 /L without the assistance of granulocyte growth factors. Arm 1: Peripheral blood blast count < 5%. Arm 1: Eastern Cooperative Oncology Group (ECOG) performance status 1. Arm 1: Life expectancy 6 months. Arm 1: Adequate renal function, as determined by clinical laboratory tests: serum creatinine 1.5 x upper limit of normal (ULN), or calculated creatinine clearance 30 mL/min (using Cockcroft-Gault formula). Arm 1: Adequate hepatic function: ALT and AST 3 × ULN, (ALT and AST 5 × ULN, if liver involvement secondary to MF); direct bilirubin 2 × ULN; and coagulation function: PT and PTT 1.5 × ULN; INR 1.2 × ULN (INR < 2.5 × ULN permitted if on chronic anticoagulant therapy). Arm 3: Previously treated with an approved JAK inhibitor (except momelotinib) for PMF or Post-PV/ET MF for 12 weeks, or 4 weeks if JAK inhibitor therapy was complicated by a transfusion requirement of 4 units of red blood cells in 8 weeks, or Grade 3/4 AEs of thrombocytopenia, anemia, or hematoma.

Criterios de Exclusión

Arm 1: Received previous systemic antineoplastic therapy or any experimental therapy within 2 weeks or 5 half-lives, whichever is longer, prior to Cycle 1 Day 1. Notes: In patients with ongoing JAK inhibitor therapy, ie, ruxolitinib, at screening, JAK inhibitor therapy must be tapered over a period of at least 1 week. Patients on a low dose of ruxolitinib (eg, 5 mg QD) may have a reduced taper period or no taper. Hydroxyurea or anagrelide are allowed up to 24 hours prior to Cycle 1 Day 1. Arm 3: Splenic irradiation within 6 months prior to screening or prior splenectomy. Arm 3: Prior allogenic stem cell transplant within the last 6 months. Note: Patients who have relapsed after 6 months post-transplant and do not have active GVHD are eligible. Arm 1: Prior or concurrent malignancy whose natural history or treatment would have a significant potential to interfere with the safety or efficacy assessments of the investigational regimen. Arm 1: Splenic irradiation within 6 months prior to screening or prior splenectomy. Arm 1: Prior allogeneic stem cell transplant within the last 6 months. Note: Patients who have relapsed after 6 months post-transplant and do not have active graft versus host disease (GVHD) are eligible. Arm 1: Eligible for allogeneic bone marrow or stem cell transplantation. Note: Patients who are willing to undergo transplantation, or for whom a suitable donor is not available are considered transplant ineligible. Arm 1: Currently receiving treatment with a prohibited medication that cannot be discontinued at least 1 week prior to Cycle 1 Day 1. Arm 1: Unresolved Grade 2 non-hematological toxicity related to prior treatment (however, stable Grade 2 exceptions may be permitted if discussed in advance with the Sponsor). Arm 1: History of symptomatic congestive heart failure or myocardial infarction, or uncontrolled arrhythmia within the 6 months prior to Cycle 1 Day 1; left ventricular ejection fraction (LVEF) < 45% by echocardiogram within 4 weeks prior to Cycle 1 Day 1. Arm 1: Corrected QT interval (using Fridericia's correction formula; QTcF) of > 470. Arm 1: Systemic steroid therapy (>10 mg/day prednisone or equivalent) within 1 week prior to the first dose of study treatment (Note: topical, inhaled, nasal, and ophthalmic steroids are not prohibited). Arm 3: Eligible for allogeneic bone marrow or stem cell transplantation. Note: Patients who are not willing to undergo transplantation or for whom a suitable donor is not available are considered as transplant ineligible. Arm 3: Major surgery within 4 weeks prior to Cycle 1 Day 1 and/or have not recovered adequately from complications of any surgical intervention prior to first dose. Arm 3: Active, uncontrolled bacterial, viral, or fungal infections, requiring systemic antimicrobial within 14 days prior to Cycle 1 Day 1. Arm 1: Known history of chronic liver disease (eg, portal hypertension or any of its complications, cirrhosis, Child-Pugh C, auto-immune hepatitis, alpha-1 anti-trypsin deficiency, Wilsons disease, etc). Note: Abnormal liver morphology at baseline imaging may require additional testing, as needed. Arm 3: Chronic active or acute viral hepatitis A, B, or C infection (testing for hepatitis B and C are required). Arm 3: Known history of chronic liver disease (eg, portal hypertension or any of its complications, cirrhosis, Child-Pugh C, auto-immune hepatitis, alpha-1 anti-trypsin deficiency, Wilsons disease, etc) Note: Abnormal liver morphology at baseline imaging may require additional testing, as needed. Arm 3: Unresolved Grade 2 non-

hematological adverse events related to prior treatment (stable Grade 2 conditions may be permitted in consultation with the Sponsor). Arm 3: Presence of Grade 2 peripheral neuropathy. Arm 3: History of myocardial infarction or symptomatic congestive heart failure or uncontrolled arrhythmia within 6 months prior to Cycle 1 Day 1; LVEF < 45% by echocardiogram within 4 weeks prior to Cycle 1 Day 1. Arm 3: Corrected QTcF of > 470 msec. Arm 1: Known clinically significant anemia due to iron, vitamin B12, or folate deficiencies, or autoimmune or hereditary hemolytic anemia, or thalassemia, or severe GI bleeding. Arm 3: Prior or concurrent malignancy whose natural history or treatment has a significant potential to interfere with the safety or efficacy assessment of the study intervention. Arm 3: History of a medical condition or GI tract surgery that could impair absorption or could result in short bowel syndrome with diarrhea. Arm 3: Known clinically significant anemia due to iron, vitamin B12, or folate deficiencies, or autoimmune or hereditary hemolytic anemia, or thalassemia, or severe GI bleeding. Arm 3: Pregnant (as evidenced by a positive serum or urine pregnancy test) or is breastfeeding. Arm 1: Active, uncontrolled bacterial, viral, or fungal infections, requiring systemic antimicrobial within 14 days prior to Cycle 1 Day 1. Arm 1: Chronic active or acute viral hepatitis A, B, or C infection (testing for hepatitis B and C are required). Arm 1: Currently receiving any other investigational agent. Arm 1: Exhibited allergic reactions or sensitivity to Nuvisertib, or any structurally similar compound, biological agent, or to any component of the formulation. Arm 1: Medical condition or gastrointestinal (GI) tract surgery that could impair absorption or result in short bowel syndrome with diarrhea. Arm 1: Major surgery within 4 weeks prior to first dose of either study drug and/or have not recovered adequately from complications of any surgical intervention prior to first dose. Arm 1: Pregnant (as evidenced by a positive serum or urine pregnancy test) or is breastfeeding. Arm 3: Received previous systemic antineoplastic therapy or any experimental therapy within 2 weeks or 5 half-lives, whichever is longer, prior to Cycle 1 Day 1. Notes: - Prior treatment with momelotinib is not allowed; - Prior treatment with Nuvisertib is not allowed; - In patients with ongoing JAK inhibitor therapy, ie, ruxolitinib, at screening, JAK inhibitor therapy must be tapered over a period of at least 1 week. Patients on a low dose of ruxolitinib (eg, 5 mg QD) may have a reduced taper period or no taper; - Hydroxyurea or anagrelide are allowed up to 24 hours prior to Cycle 1 Day 1. Arm 3: Received systemic steroid therapy (>10 mg daily prednisone or equivalent) within 1 week prior to Cycle 1 Day 1. Note: Topical, inhaled, nasal, and ophthalmic steroids are not prohibited. Arm 3: Currently receiving treatment with a prohibited medication that cannot be discontinued at least 1 week prior to Cycle 1 Day 1. Arm 3: Known allergic reactions or sensitivity to Nuvisertib, momelotinib, or any structurally similar drug, or to any component of the formulations of either study intervention.

Calendario

(Última actualización: 18/06/2026)

Autorización	Inicio de Ensayo	Inclusión Primer Paciente	Interrumpido	Reiniciado
02/01/2026	22/04/2026	No aportado	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

Sumitomo Pharma America Inc. United States

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Contact Person

Clinical Development

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Monetary support: N/A

Tipo de promotor: Comercial

Ceim

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Centros

Activo (02/06/2026)

Hospital Universitario De Salamanca

Salamanca

SALAMANCA

ES046A: Hematología

Activo (23/04/2026)

Hospital Universitario Y Politecnico La Fe

Valencia

VALENCIA

ES044A: Hematología

Activo (06/04/2026)

Institut Catala D´oncologia

Badalona

BARCELONA

ES001A: Hematología

Medicamentos

Nuvisertib
CAPSULE
ORAL

-
Principios Activos: N/A
Experimental

Nuvisertib
CAPSULE
ORAL

-
Principios Activos: N/A
Experimental

PRD11032047
TABLET
ORAL

-
Principios Activos: N/A
Huérfano
Experimental

PRD11032121
TABLET
ORAL

-
Principios Activos: N/A
Huérfano
Experimental

PRD11032087
TABLET
ORAL

-
Principios Activos: N/A
Huérfano
Experimental

Nuvisertib
CAPSULE
ORAL

-
Principios Activos: N/A
Experimental

Sin resultados

Phase 1/2 Study of Oral Nuvisertib (TP-3654) in Patients with Myelofibrosis

State	**Type of participants**	**Age Ranges**
Recruiting	Not provided	Older than 64 , Adults (18-64 years)
Gender	**Phases**	**Expected Participants**
Both	Phase I , Phase II	204
Results	**Low level of intervention**	**Rare disease**
No results	No	Yes
Geographic coverage	**Areas of the study**	**Advanced therapy**
Undetermined	safety, effectiveness, pharmacokinetics, pharmacodynamics	NO

Information

Identifier
2022-502597-16-00 (CTIS)

Protocol Code
BBI-TP-3654-102

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

Investigated Disease
Intermediate or High-risk Primary or Secondary Myelofibrosis

Scientific Title
A Phase 1/2, Open-label, Dose-escalation, Safety, Pharmacokinetic, and Pharmacodynamic Study of Oral Nuvisertib (TP-3654) in Patients with Intermediate or High-risk Primary or Secondary Myelofibrosis

Rationale

Not provided

Main Objective

- Nuvisertib Monotherapy (Arm 1) - Phase 1: To identify the recommended Phase 2 dose (RP2D) of Nuvisertib monotherapy. - Nuvisertib Monotherapy (Arm 1) - Phase 1: To determine the overall safety of Nuvisertib monotherapy.(Note: this objective is secondary in Phase 2) - Nuvisertib Monotherapy (Arm 1) - Phase 2: To assess any preliminary clinical activity of Nuvisertib monotherapy.
- Nuvisertib + Momelotinib (Arm 3) Phase 1: To identify the recommended Phase 2 dose (RP2D) of Nuvisertib when administered in combination with momelotinib.
- Nuvisertib + Momelotinib (Arm 3) Phase 1: To determine the overall safety of Nuvisertib and momelotinib combination.(Note: this objective is secondary in Phase 2) - Nuvisertib + Momelotinib (Arm 3) Phase 2: To assess any preliminary clinical activity of Nuvisertib and momelotinib combination.

Primary Endpoints

Nuvisertib Monotherapy (Arm 1) - Phase 1: Dose-limiting toxicity (DLT) at escalated doses of Nuvisertib.
Nuvisertib Monotherapy (Arm 1) - Phase 1: Adverse events (AEs) as characterized by type, frequency, severity, seriousness, and relationship to study drugs. (Note: This endopoint is secondary in Phase 2)
Nuvisertib Monotherapy (Arm 1) - Phase 2: Spleen volume response: 35% spleen volume reduction (SVR35) at any time.
Nuvisertib + Momelotinib (Arm 3) Phase 1: Dose-limiting toxicity (DLT) at escalated doses of Nuvisertib when administered in combination with momelotinib.
Nuvisertib + Momelotinib (Arm 3) Phase 1: Adverse events (AEs) as characterized by type, frequency, severity, seriousness, and relationship to study drugs. [Note: This endpoint is secondary in Phase 2]
Nuvisertib + Momelotinib (Arm 3) Phase 2: Spleen volume response: 35% spleen volume reduction (SVR35) at any time.

Temporary moments of secondary assessment

Not provided

Secondary Objective

Nuvisertib Monotherapy (Arm 1) - Phase 1 and 2: To assess any preliminary clinical activity of Nuvisertib monotherapy.
Nuvisertib Monotherapy (Arm 1) - Phase 1 and 2: To determine the cardiac safety of Nuvisertib.
Nuvisertib Monotherapy (Arm 1) - Phase 1 and 2: To establish the pharmacokinetic (PK) profile of orally administered Nuvisertib monotherapy.
Nuvisertib + Momelotinib (Arm 3) Phase 1 and 2: To assess any preliminary clinical activity of Nuvisertib and momelotinib combination.
Nuvisertib + Momelotinib (Arm 3) Phase 1 and 2: To establish the pharmacokinetic (PK) profile of Nuvisertib and momelotinib at steady state when administered concomitantly.

Secondary Endpoints

Nuvisertib Monotherapy (Arm 1) - Phase 1 and 2: Spleen volume response: - 25% spleen volume reduction [SVR25] at any time; - Duration of spleen volume response.
Nuvisertib Monotherapy (Arm 1) - Phase 1 and 2: Total symptom score response assessed by MFSAF v4.0; - 50% improvement in total symptom score (TSS50) at Week 24; - Duration of TSS50 over time during the study; - Absolute TSS change from baseline at Week 24.
Nuvisertib Monotherapy (Arm 1) - Phase 1 and 2: Patient Global Impression of Change (PGIC) at Week 24 and at any time.
Nuvisertib Monotherapy (Arm 1) - Phase 1 and 2: Response evaluation per the revised IWG-MRT criteria: Complete remission (CR), partial remission (PR), clinical improvement (CI), stable disease (SD), and progressive disease (PD).
Nuvisertib Monotherapy (Arm 1) - Phase 1 and 2: QT interval changes.
Nuvisertib Monotherapy (Arm 1) - Phase 1 and 2: PK parameters of Nuvisertib: Cmax, tmax, AUC, t½, and others as data permits.
Nuvisertib + Momelotinib (Arm 3) Phase 1 and 2: Spleen volume response: - 25% spleen volume reduction [SVR25] at any time; - Duration of spleen volume response.
Nuvisertib + Momelotinib (Arm 3) Phase 1 and 2: Total symptom score response assessed by MFSAF v4.0: - 50% improvement in total symptom score (TSS50) at Week 24; - Duration of TSS50 over time during the study; - Absolute TSS change from baseline at Week 24.
Nuvisertib + Momelotinib (Arm 3) Phase 1 and 2: Patient Global Impression of Change (PGIC) at Week 24 and at any time.
Nuvisertib + Momelotinib (Arm 3) Phase 1 and 2: Response evaluation per the revised IWG-MRT criteria: - Complete remission (CR), partial remission (PR), clinical improvement (CI), stable disease (SD), and progressive disease (PD).
Nuvisertib + Momelotinib (Arm 3) Phase 1 and 2: PK parameters of TP-3654 and momelotinib: Cmax, tmax, AUC, t½ and others as data permits.

Temporary moments of secondary assessment

Not provided

Inclusion criteria

Arm 1: Adult (18 years of age). Arm 3: Fulfills the following clinical laboratory parameters: a. Anemic, defined as Hb <10 g/dL; b. Platelet count 50 × 109 /L (without the assistance of growth factors or platelet transfusions); c. ANC 1 × 10^9 /L without the assistance of granulocyte growth factors; d. Peripheral blood blast count < 5% at screening; e. Adequate renal function, as determined by clinical laboratory tests: serum creatinine 1.5 × ULN or calculated creatinine clearance 30 mL/min (using Cockcroft-Gault formula); f. Adequate hepatic function: ALT and AST 3 × ULN (ALT and AST 5 × ULN if there is liver involvement secondary to MF); direct bilirubin 2 × ULN; g. Adequate coagulation function: PT and PTT 1.5 × ULN; INR 1.2 × ULN (INR < 2.5 × ULN permitted if on chronic anticoagulant therapy). Arm 3: Splenomegaly, defined as spleen volume of 450 cm3 by MRI/CT scan within 2 weeks prior to Cycle 1 Day 1. Arm 1: Capable of providing signed informed consent as described in Section 10.1.3 of the study protocol which includes compliance with the requirements and restrictions listed in the informed consent form (ICF) and in this protocol. Arm 3: At least 2 symptoms measurable with each score of 3 or a total average score of 10 per MFSAF v4.0. Arm 3: ECOG performance status 1. Arm 3: Life expectancy 6 months. Arm 3: Non-fertile or agree to use an adequate method of contraception. Arm 3: Capable of providing signed informed consent which includes compliance with the requirements and restrictions listed in the ICF and in this protocol. Arm 3: Able to swallow orally administered medication. Arm 1: Non-fertile or agrees to use an adequate method of contraception. Arm 1: Previously treated with an approved JAK inhibitor(s) and is intolerant, resistant, refractory or has lost response to an approved the JAK inhibitor(s), or is ineligible to be treated with an approved JAK inhibitor as determined by the Investigator in accordance with the local product labels. Note: Intolerant is considered as requiring a transfusion of 4 units of red blood cells in 8 weeks, or Grade 3/4 AEs of thrombocytopenia, anemia, or hematoma for ruxolitinib and

fedratinib; Grade 2 peripheral neuropathy for momelotinib. Arm 1: Splenomegaly, defined as spleen volume of 450 cm3 by magnetic resonance Imaging (MRI) or computerized tomography (CT) scan, within 2 weeks prior to Cycle 1 Day 1. Arm 1: Dose Escalation: at least 2 symptoms measurable (score 1) using the MFSAF v4.0. Dose Expansion: at least 2 symptoms measurable with each score of 3 or a total average score of 10 per MFSAF v4.0. Arm 1: Able to swallow orally administered medication. Arm 3: Confirmed pathological diagnosis of PMF or post-PV-MF/post ET-MF as per WHO diagnostic criteria (Section 10.2.4), and intermediate or high-risk primary or secondary MF based on the DIPSS. Arm 1: Confirmed pathological diagnosis of primary myelofibrosis (PMF) or post-polycythemia vera (PV)-MF/post-ET-MF as per World Health Organization (WHO) diagnostic criteria, and intermediate or high-risk primary or secondary MF based on the Dynamic International Prognostic Scoring System (DIPSS). Arm 3: Adult (18 years of age). Arm 1: Fulfills the following laboratory parameters: a. Platelet count 25 × 10^9 /L without the assistance of growth factors or platelet transfusions; b. Absolute neutrophil count (ANC) 1 × 10^9 /L without the assistance of granulocyte growth factors. Arm 1: Peripheral blood blast count < 5%. Arm 1: Eastern Cooperative Oncology Group (ECOG) performance status 1. Arm 1: Life expectancy 6 months. Arm 1: Adequate renal function, as determined by clinical laboratory tests: serum creatinine 1.5 x upper limit of normal (ULN), or calculated creatinine clearance 30 mL/min (using Cockcroft-Gault formula). Arm 1: Adequate hepatic function: ALT and AST 3 × ULN, (ALT and AST 5 × ULN, if liver involvement secondary to MF); direct bilirubin 2 × ULN; and coagulation function: PT and PTT 1.5 × ULN; INR 1.2 × ULN (INR < 2.5 × ULN permitted if on chronic anticoagulant therapy). Arm 3: Previously treated with an approved JAK inhibitor (except momelotinib) for PMF or Post-PV/ET MF for 12 weeks, or 4 weeks if JAK inhibitor therapy was complicated by a transfusion requirement of 4 units of red blood cells in 8 weeks, or Grade 3/4 AEs of thrombocytopenia, anemia, or hematoma.

Exclusion criteria

Arm 1: Received previous systemic antineoplastic therapy or any experimental therapy within 2 weeks or 5 half-lives, whichever is longer, prior to Cycle 1 Day 1. Notes: In patients with ongoing JAK inhibitor therapy, ie, ruxolitinib, at screening, JAK inhibitor therapy must be tapered over a period of at least 1 week. Patients on a low dose of ruxolitinib (eg, 5 mg QD) may have a reduced taper period or no taper. Hydroxyurea or anagrelide are allowed up to 24 hours prior to Cycle 1 Day 1. Arm 3: Splenic irradiation within 6 months prior to screening or prior splenectomy. Arm 3: Prior allogenic stem cell transplant within the last 6 months. Note: Patients who have relapsed after 6 months post-transplant and do not have active GVHD are eligible. Arm 1: Prior or concurrent malignancy whose natural history or treatment would have a significant potential to interfere with the safety or efficacy assessments of the investigational regimen. Arm 1: Splenic irradiation within 6 months prior to screening or prior splenectomy. Arm 1: Prior allogeneic stem cell transplant within the last 6 months. Note: Patients who have relapsed after 6 months post-transplant and do not have active graft versus host disease (GVHD) are eligible. Arm 1: Eligible for allogeneic bone marrow or stem cell transplantation. Note: Patients who are willing to undergo transplantation, or for whom a suitable donor is not available are considered transplant ineligible. Arm 1: Currently receiving treatment with a prohibited medication that cannot be discontinued at least 1 week prior to Cycle 1 Day 1. Arm 1: Unresolved Grade 2 non-hematological toxicity related to prior treatment (however, stable Grade 2 exceptions may be permitted if discussed in advance with the Sponsor). Arm 1: History of symptomatic congestive heart failure or myocardial infarction, or uncontrolled arrhythmia within the 6 months prior to Cycle 1 Day 1; left ventricular ejection fraction (LVEF) < 45% by echocardiogram within 4 weeks prior to Cycle 1 Day 1. Arm 1: Corrected QT interval (using Fridericia's correction formula; QTcF) of > 470. Arm 1: Systemic steroid therapy (>10 mg/day prednisone or equivalent) within 1 week prior to the first dose of study treatment (Note: topical, inhaled, nasal, and ophthalmic steroids are not prohibited). Arm 3: Eligible for allogeneic bone marrow or stem cell transplantation. Note: Patients who are not willing to undergo transplantation or for whom a suitable donor is not available are considered as transplant ineligible. Arm 3: Major surgery within 4 weeks prior to Cycle 1 Day 1 and/or have not recovered adequately from complications of any surgical intervention prior to first dose. Arm 3: Active, uncontrolled bacterial, viral, or fungal infections, requiring systemic antimicrobial within 14 days prior to Cycle 1 Day 1. Arm 1: Known history of chronic liver disease (eg, portal hypertension or any of its complications, cirrhosis, Child-Pugh C, auto-immune hepatitis, alpha-1 anti-trypsin deficiency, Wilsons disease, etc). Note: Abnormal liver morphology at baseline imaging may require additional testing, as needed. Arm 3: Chronic active or acute viral hepatitis A, B, or C infection (testing for hepatitis B and C are required). Arm 3: Known history of chronic liver disease (eg, portal hypertension or any of its complications, cirrhosis, Child-Pugh C, auto-immune hepatitis, alpha-1 anti-trypsin deficiency, Wilsons disease, etc) Note: Abnormal liver morphology at baseline imaging may require additional testing, as needed. Arm 3: Unresolved Grade 2 non-

hematological adverse events related to prior treatment (stable Grade 2 conditions may be permitted in consultation with the Sponsor). Arm 3: Presence of Grade 2 peripheral neuropathy. Arm 3: History of myocardial infarction or symptomatic congestive heart failure or uncontrolled arrhythmia within 6 months prior to Cycle 1 Day 1; LVEF < 45% by echocardiogram within 4 weeks prior to Cycle 1 Day 1. Arm 3: Corrected QTcF of > 470 msec. Arm 1: Known clinically significant anemia due to iron, vitamin B12, or folate deficiencies, or autoimmune or hereditary hemolytic anemia, or thalassemia, or severe GI bleeding. Arm 3: Prior or concurrent malignancy whose natural history or treatment has a significant potential to interfere with the safety or efficacy assessment of the study intervention. Arm 3: History of a medical condition or GI tract surgery that could impair absorption or could result in short bowel syndrome with diarrhea. Arm 3: Known clinically significant anemia due to iron, vitamin B12, or folate deficiencies, or autoimmune or hereditary hemolytic anemia, or thalassemia, or severe GI bleeding. Arm 3: Pregnant (as evidenced by a positive serum or urine pregnancy test) or is breastfeeding. Arm 1: Active, uncontrolled bacterial, viral, or fungal infections, requiring systemic antimicrobial within 14 days prior to Cycle 1 Day 1. Arm 1: Chronic active or acute viral hepatitis A, B, or C infection (testing for hepatitis B and C are required). Arm 1: Currently receiving any other investigational agent. Arm 1: Exhibited allergic reactions or sensitivity to Nuvisertib, or any structurally similar compound, biological agent, or to any component of the formulation. Arm 1: Medical condition or gastrointestinal (GI) tract surgery that could impair absorption or result in short bowel syndrome with diarrhea. Arm 1: Major surgery within 4 weeks prior to first dose of either study drug and/or have not recovered adequately from complications of any surgical intervention prior to first dose. Arm 1: Pregnant (as evidenced by a positive serum or urine pregnancy test) or is breastfeeding. Arm 3: Received previous systemic antineoplastic therapy or any experimental therapy within 2 weeks or 5 half-lives, whichever is longer, prior to Cycle 1 Day 1. Notes: - Prior treatment with momelotinib is not allowed; - Prior treatment with Nuvisertib is not allowed; - In patients with ongoing JAK inhibitor therapy, ie, ruxolitinib, at screening, JAK inhibitor therapy must be tapered over a period of at least 1 week. Patients on a low dose of ruxolitinib (eg, 5 mg QD) may have a reduced taper period or no taper; - Hydroxyurea or anagrelide are allowed up to 24 hours prior to Cycle 1 Day 1. Arm 3: Received systemic steroid therapy (>10 mg daily prednisone or equivalent) within 1 week prior to Cycle 1 Day 1. Note: Topical, inhaled, nasal, and ophthalmic steroids are not prohibited. Arm 3: Currently receiving treatment with a prohibited medication that cannot be discontinued at least 1 week prior to Cycle 1 Day 1. Arm 3: Known allergic reactions or sensitivity to Nuvisertib, momelotinib, or any structurally similar drug, or to any component of the formulations of either study intervention.

Calendar

(Last Update: 18/06/2026)

Authorization	Start of Trial	First patient inclusion	Halted	Restarted
02/01/2026	22/04/2026	Not aported	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

Sumitomo Pharma America Inc. United States

84 Waterford Drive

Contact Person

Clinical Development

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Monetary support: N/A

Sponsor type: Commercial

Ceim

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Sites

Active (02/06/2026)

Hospital Universitario De Salamanca

Salamanca

SALAMANCA

ES046A: Hematología

Active (23/04/2026)

Hospital Universitario Y Politecnico La Fe

Valencia

VALENCIA

ES044A: Hematología

Active (06/04/2026)

Institut Catala D´oncologia

Badalona

BARCELONA

ES001A: Hematología

Medication

Nuvisertib
CAPSULE
ORAL

-
Active Principles: N/A
Experimental

Nuvisertib
CAPSULE
ORAL

-
Active Principles: N/A
Experimental

PRD11032047
TABLET
ORAL

-
Active Principles: N/A
Orphan
Experimental

PRD11032121
TABLET
ORAL

-
Active Principles: N/A
Orphan
Experimental

PRD11032087
TABLET
ORAL

-
Active Principles: N/A
Orphan
Experimental

Nuvisertib
CAPSULE
ORAL

-
Active Principles: N/A
Experimental

No results