A Study of Avapritinib in Patients with Indolent and Systemic Mastocytosis

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	137
Resultados	**Bajo nivel intervención**	**Enfermedad rara**
Sin resultados	No	Si
Cobertura geográfica	**Ámbitos del ensayo**	**Terapia avanzada**
Sin determinar	tratamiento, seguridad, eficacia, farmacocinética, farmacodinamica, dosis	NO

Información

Identificador
2024-512585-34-00 (CTIS)

Cod. Protocolo
BLU-285-2203

Transicionado 2018-000588-99

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

Enfermedad investigada
Indolent Systemic Mastocytosis (ISM)

Título Científico
A 3-Part, Randomized, Double-Blind, Placebo-Controlled Phase 2 Study to Evaluate Safety and Efficacy of Avapritinib (BLU 285), a Selective KIT Mutation-Targeted Tyrosine Kinase Inhibitor, in Indolent and Smoldering Systemic Mastocytosis with Symptoms Inadequately Controlled with Standard Therapy

Justificación

No aportado

Objetivo Principal

Part 1- To determine the RP2D of avapritinib in patients with ISM for use in Part 2 and Part 3 of the study.
Part 2- To determine mean change in ISM-SAF TSS from baseline to C7D1, compared to placebo.
Part 3- To assess the long-term safety and efficacy of avapritinib in ISM patients.

Variables de Evaluación Primaria

Part 1 The RP2D in patients with ISM. Part 2 Mean change in ISM-SAF TSS, from Baseline to C7D1. Part 3 The long-term safety and efficacy of avapritinib.

Momentos temporales de evaluación primaria

No aportado

Objetivo Secundario

Key Secondary (Part2 Only) To determine the proportion of avapritinib-treated patients with ISM, from baseline to C7D1, compared to placebo: - with a 50% reduction in serum tryptase - with a 50% reduction in peripheral blood KIT D816V allele fraction or undetectable (<0.02%) for patients with detectable mutation at Baseline - achieving 50% reduction in ISM-SAF TSS - achieving 30% reduction in ISM-SAF TSS - with a 50% reduction in bone marrow mast cells or no aggregates for patients with aggregates at Baseline Additional Secondary Assess change in: - measures of mast cell burden in each treatment cohort (serum tryptase, KIT D816V allele burden in blood, bone marrow mast cells) - best supportive care usage for SM symptoms Assess change in other Patient-Reported Outcomes and Quality of Life measures Assess the safety and tolerability of avapritinib, as assessed by AEs, vital signs, electrocardiograms, and laboratory tests. Assess the PK of avapritinib (Part 1 & 2 only)

Variables de Evaluación Secundaria

Change in measures of mast cell burden: serum tryptase, KIT D816V allele burden in blood, bone marrow mast cells. Change in best supportive care usage. Change in MC-QoL, PGIS, SF-12, PGIC, and EQ-5D-5L. Safety and tolerability of avapritinib, as assessed by AEs, vital signs, electrocardiograms, and laboratory tests. Pharmacokinetics of avapritinib (Part 1 and 2 only)

Momentos temporales de evaluación secundaria

No aportado

Criterios de Inclusión

1. Patients must be 18 years of age.
2. Patient must have SM, confirmed by Central Pathology Review of BM biopsy, and central review of B- and C-findings by WHO diagnostic criteria.
3. Patient must have moderate-to- severe symptoms based on minimum mean TSS over the 14-day eligibility screening period for assessment of TSS. Minimum TSS for eligibility is 28.
4. Patient must have failed to achieve adequate symptom control for 1 or more Baseline symptoms, as determined by the Investigator, with at least 2 of the following symptomatic therapies: H1 blockers, H2 blockers, proton-pump inhibitors, leukotriene inhibitors, cromolyn sodium, corticosteroids, or omalizumab.
5. The patient's symptomatic SM therapies (e.g., H1 and H2 blockers) must be stable (same dose, no new medications 14 days before beginning the 14-day ISM-SAF eligibility TSS assessment).
6. If the patient is receiving corticosteroids, the dose must be 20 mg/day prednisone or equivalent, and the dose must be stable for 14 days before beginning the 14-day ISM-SAF eligibility TSS assessment.
7. Patient must have an ECOG-PS of 0 to 2.
8. Patient must be able to give written informed consent.

Criterios de Exclusión

1. Patient has been diagnosed with any of the following WHO SM subclassifications: Cutaneous mastocytosis only, SM-AHN, SSM, ASM, MCL, MC sarcoma. 10. Patient has a history of a cerebrovascular accident or transient ischemic attacks within 12 months before the first dose of study drug. 11. Patient has a known risk or recent history (12 months before the first dose of study drug) of ICB (eg, brain aneurysm). 12. Patient has a primary brain malignancy or metastases to the brain. 13. Patient has clinically significant, uncontrolled cardiovascular disease, including Grade III or Grade IV congestive heart failure greater than New York Heart Association classification II; myocardial infarction or unstable angina within the previous 6 months; clinically significant, uncontrolled arrhythmias, or uncontrolled hypertension. 14. Female patients who are unwilling, if not postmenopausal or surgically sterile, to abstain from sexual intercourse or employ highly effective contraception during the study drug administration period and for at least 6 weeks after the last dose of study drug. Men who are unwilling, if not surgically sterile, to abstain from sexual intercourse or employ highly effective contraception during the study drug administration period and for at least 6 weeks after the last dose of study drug. 15. Pregnant women, as documented by a -hCG pregnancy test consistent with pregnancy obtained within 7 days before the first dose of study drug. 16. Women who are breastfeeding. 2. Patient has been diagnosed with another myeloproliferative disorder. 3. Patient has any of the following organ damage C-findings attributable to SM: Cytopenia, Hepatomegaly with ascites and impaired liver function, Palpable splenomegaly with hypersplenism, Malabsorption with hypoalbuminemia and significant weight loss, Skeletal lesions: large osteolytic lesions with pathologic fractures, Life-threatening organ damage in other organ systems that is caused by MC infiltration in tissues. 4. Patient meets any of the following laboratory criteria: Aspartate aminotransferase or alanine aminotransferase > 3.0 × ULN, Total bilirubin > 1.5 × ULN; > 3.0 × ULN if due to Gilbert's disease. (In the case of Gilbert's disease, a direct bilirubin > 2.0 × ULN is an exclusion.) Albumin < 1 × LLN, eGFR < 30 mL/min/1.73 m^2 or creatinine clearance or creatinine > 1.5 × ULN Absolute neutrophil count < 1.5 × 10^9/L, Hemoglobin < 10 g/dL, Platelet count < 100,000/L 5. Patient has received any of the following medications, therapies, or procedures in the timeframes listed: Any prior treatment with avapritinib, Any TKI, including but not limited to masitinib and midostaurin, or investigational agent for < 14 days or 5 half-lives of the drug (whichever is longer) before beginning the 14-day ISM-SAF eligibility TSS assessment, Any antineoplastic drug therapy < 28 days or 5 half-lives of the drug (whichever is longer) before beginning the 14- day ISM-SAF eligibility TSS assessment, Radiotherapy or PUVA therapy < 14 days before beginning the 14-day ISM-SAF eligibility TSS assessment, Any hematopoietic growth factor < 14 days before beginning the 14-day ISM-SAF eligibility TSS assessment, Any major surgical procedure < 14 days before starting the ISM-SAF for determination of eligibility. 6. Patient requires therapy with a concomitant medication that is a strong inhibitor, strong inducer, or moderate inducer of CYP3A4 (see Appendix 9). 7. Patient has a history of a malignancy that has been diagnosed or required therapy within 3 years before the first dose of study drug. Patients with a prior or concurrent malignancy whose natural history or treatment does not have the potential to interfere with the safety or efficacy assessment of the investigational agent may be included after approval by medical monitor. 8. Patient has a QTcF > 480 msec. 9. Patient has a history of a seizure

disorder (eg, epilepsy) or requires antiseizure medication.

Calendario

(Última actualización: 21/04/2026)

Autorización	Inicio de Ensayo	Inclusión Primer Paciente	Interrumpido	Reiniciado
23/01/2019	17/06/2019	05/07/2019	No aportado	No aportado

Fin de reclutamiento	Fin prematuro (España)	Fin prematuro (Global)	Fin del ensayo en España	Fin del ensayo global
21/09/2021	No aportado	No aportado	20/03/2022	No aportado

Promotor

Blueprint Medicines Corp. United States

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Contact Person

Medical Information

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Monetary support: N/A

Tipo de promotor: Comercial

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Centros

Cerrado (20/03/2022)

HOSPITAL GERIÁTRICO VIRGEN DEL VALLE

Toledo

TOLEDO

Instituto de Mastocitosis de Castilla-La Mancha

Cerrado (20/03/2022)

HOSPITAL UNIVERSITARI VALL D'HEBRON

Barcelona

BARCELONA

No iniciado (--/--/----)

Hospital Virgen Del Valle

Toledo

TOLEDO

Instituto de Estudios de Mastocitosis de Castilla La Mancha

Medicamentos

Avapritinib
FILM-COATED TABLET
ORAL USE

-

Principios Activos: N/A

Huérfano Experimental

Avapritinib
FILM-COATED TABLET
ORAL USE

-

Principios Activos: N/A

Huérfano Experimental

Sin resultados

A Study of Avapritinib in Patients with Indolent and Systemic Mastocytosis

State	Type of participants	Age Ranges
Finished CT	Not provided	Older than 64 , Adults (18-64 years)
Gender	**Phases**	**Expected Participants**
Both	Phase II	137
Results	**Low level of intervention**	**Rare disease**
No results	No	Yes
Geographic coverage	**Areas of the study**	**Advanced therapy**
Undetermined	treatment, safety, effectiveness, pharmacokinetics, pharmacodynamics, dose	NO

Information

Identifier
2024-512585-34-00 (CTIS)

Protocol Code
BLU-285-2203

Transitioned 2018-000588-99

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

Investigated Disease
Indolent Systemic Mastocytosis (ISM)

Scientific Title
A 3-Part, Randomized, Double-Blind, Placebo-Controlled Phase 2 Study to Evaluate Safety and Efficacy of Avapritinib (BLU 285), a Selective KIT Mutation-Targeted Tyrosine Kinase Inhibitor, in Indolent and Smoldering Systemic Mastocytosis with Symptoms Inadequately Controlled with Standard Therapy

Rationale

Not provided

Main Objective

Part 1- To determine the RP2D of avapritinib in patients with ISM for use in Part 2 and Part 3 of the study.
Part 2- To determine mean change in ISM-SAF TSS from baseline to C7D1, compared to placebo.
Part 3- To assess the long-term safety and efficacy of avapritinib in ISM patients.

Primary Endpoints

Part 1 The RP2D in patients with ISM. Part 2 Mean change in ISM-SAF TSS, from Baseline to C7D1. Part 3 The long-term safety and efficacy of avapritinib.

Temporary moments of secondary assessment

Not provided

Secondary Objective

Key Secondary (Part2 Only) To determine the proportion of avapritinib-treated patients with ISM, from baseline to C7D1, compared to placebo: - with a 50% reduction in serum tryptase - with a 50% reduction in peripheral blood KIT D816V allele fraction or undetectable (<0.02%) for patients with detectable mutation at Baseline - achieving 50% reduction in ISM-SAF TSS - achieving 30% reduction in ISM-SAF TSS - with a 50% reduction in bone marrow mast cells or no aggregates for patients with aggregates at Baseline Additional Secondary Assess change in: - measures of mast cell burden in each treatment cohort (serum tryptase, KIT D816V allele burden in blood, bone marrow mast cells) - best supportive care usage for SM symptoms Assess change in other Patient-Reported Outcomes and Quality of Life measures Assess the safety and tolerability of avapritinib, as assessed by AEs, vital signs, electrocardiograms, and laboratory tests. Assess the PK of avapritinib (Part 1 & 2 only)

Secondary Endpoints

Change in measures of mast cell burden: serum tryptase, KIT D816V allele burden in blood, bone marrow mast cells. Change in best supportive care usage. Change in MC-QoL, PGIS, SF-12, PGIC, and EQ-5D-5L. Safety and tolerability of avapritinib, as assessed by AEs, vital signs, electrocardiograms, and laboratory tests. Pharmacokinetics of avapritinib (Part 1 and 2 only)

Temporary moments of secondary assessment

Not provided

Inclusion criteria

1. Patients must be 18 years of age.
2. Patient must have SM, confirmed by Central Pathology Review of BM biopsy, and central review of B- and C-findings by WHO diagnostic criteria.
3. Patient must have moderate-to- severe symptoms based on minimum mean TSS over the 14-day eligibility screening period for assessment of TSS. Minimum TSS for eligibility is 28.
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5. The patient's symptomatic SM therapies (e.g., H1 and H2 blockers) must be stable (same dose, no new medications 14 days before beginning the 14-day ISM-SAF eligibility TSS assessment).
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7. Patient must have an ECOG-PS of 0 to 2.
8. Patient must be able to give written informed consent.

Exclusion criteria

1. Patient has been diagnosed with any of the following WHO SM subclassifications: Cutaneous mastocytosis only, SM-AHN, SSM, ASM, MCL, MC sarcoma. 10. Patient has a history of a cerebrovascular accident or transient ischemic attacks within 12 months before the first dose of study drug. 11. Patient has a known risk or recent history (12 months before the first dose of study drug) of ICB (eg, brain aneurysm). 12. Patient has a primary brain malignancy or metastases to the brain. 13. Patient has clinically significant, uncontrolled cardiovascular disease, including Grade III or Grade IV congestive heart failure greater than New York Heart Association classification II; myocardial infarction or unstable angina within the previous 6 months; clinically significant, uncontrolled arrhythmias, or uncontrolled hypertension. 14. Female patients who are unwilling, if not postmenopausal or surgically sterile, to abstain from sexual intercourse or employ highly effective contraception during the study drug administration period and for at least 6 weeks after the last dose of study drug. Men who are unwilling, if not surgically sterile, to abstain from sexual intercourse or employ highly effective contraception during the study drug administration period and for at least 6 weeks after the last dose of study drug. 15. Pregnant women, as documented by a -hCG pregnancy test consistent with pregnancy obtained within 7 days before the first dose of study drug. 16. Women who are breastfeeding. 2. Patient has been diagnosed with another myeloproliferative disorder. 3. Patient has any of the following organ damage C-findings attributable to SM: Cytopenia, Hepatomegaly with ascites and impaired liver function, Palpable splenomegaly with hypersplenism, Malabsorption with hypoalbuminemia and significant weight loss, Skeletal lesions: large osteolytic lesions with pathologic fractures, Life-threatening organ damage in other organ systems that is caused by MC infiltration in tissues. 4. Patient meets any of the following laboratory criteria: Aspartate aminotransferase or alanine aminotransferase > 3.0 × ULN, Total bilirubin > 1.5 × ULN; > 3.0 × ULN if due to Gilbert's disease. (In the case of Gilbert's disease, a direct bilirubin > 2.0 × ULN is an exclusion.) Albumin < 1 × LLN, eGFR < 30 mL/min/1.73 m^2 or creatinine clearance or creatinine > 1.5 × ULN Absolute neutrophil count < 1.5 × 10^9/L, Hemoglobin < 10 g/dL, Platelet count < 100,000/L 5. Patient has received any of the following medications, therapies, or procedures in the timeframes listed: Any prior treatment with avapritinib, Any TKI, including but not limited to masitinib and midostaurin, or investigational agent for < 14 days or 5 half-lives of the drug (whichever is longer) before beginning the 14-day ISM-SAF eligibility TSS assessment, Any antineoplastic drug therapy < 28 days or 5 half-lives of the drug (whichever is longer) before beginning the 14- day ISM-SAF eligibility TSS assessment, Radiotherapy or PUVA therapy < 14 days before beginning the 14-day ISM-SAF eligibility TSS assessment, Any hematopoietic growth factor < 14 days before beginning the 14-day ISM-SAF eligibility TSS assessment, Any major surgical procedure < 14 days before starting the ISM-SAF for determination of eligibility. 6. Patient requires therapy with a concomitant medication that is a strong inhibitor, strong inducer, or moderate inducer of CYP3A4 (see Appendix 9). 7. Patient has a history of a malignancy that has been diagnosed or required therapy within 3 years before the first dose of study drug. Patients with a prior or concurrent malignancy whose natural history or treatment does not have the potential to interfere with the safety or efficacy assessment of the investigational agent may be included after approval by medical monitor. 8. Patient has a QTcF > 480 msec. 9. Patient has a history of a seizure

disorder (eg, epilepsy) or requires antiseizure medication.

Calendar

(Last Update: 21/04/2026)

Authorization	Start of Trial	First patient inclusion	Halted	Restarted
23/01/2019	17/06/2019	05/07/2019	Not aported	Not aported

End of recruitment	Premature end (Spain)	Premature End (Global)	Trial end (Spain)	Trial end (Global)
21/09/2021	Not aported	Not aported	20/03/2022	Not aported

Sponsor

Blueprint Medicines Corp. United States

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Contact Person

Medical Information

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Monetary support: N/A

Sponsor type: Commercial

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Sites

Closed (20/03/2022)

HOSPITAL GERIÁTRICO VIRGEN DEL VALLE

Toledo

TOLEDO

Instituto de Mastocitosis de Castilla-La Mancha

Closed (20/03/2022)

HOSPITAL UNIVERSITARI VALL D'HEBRON

Barcelona

BARCELONA

not initialized (--/--/----)

Hospital Virgen Del Valle

Toledo

TOLEDO

Instituto de Estudios de Mastocitosis de Castilla La Mancha

Medication

Avapritinib
FILM-COATED TABLET
ORAL USE

-

Active Principles: N/A

Orphan Experimental

Avapritinib
FILM-COATED TABLET
ORAL USE

-

Active Principles: N/A

Orphan Experimental

No results