KRT-232 in Subjects With PMF, Post-PV MF, or Post-ET MF Who Have Failed a JAK Inhibitor

ClinicalTrials.gov Identifier: NCT03662126

Recruitment Status : Recruiting
First Posted : September 7, 2018
Last Update Posted : November 26, 2019

See **Contacts and Locations**

Sponsor:
Kartos Therapeutics, Inc.

Information provided by (Responsible Party):
Kartos Therapeutics, Inc.

Study Details | Tabular View | No Results Posted | Disclaimer | How to Read a Study Record

Study Description

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Brief Summary:

This study evaluates KRT-232, a novel oral small molecule inhibitor of MDM2, for the treatment of patients with myelofibrosis (MF) who no longer benefit from treatment with JAK inhibitor. Inhibition of MDM2 is a novel mechanism of action in MF.

This study is a global, open-label Phase 2 study to determine the efficacy and safety of KRT-232 in patients with primary MF, post-polycythemia vera MF, or post-essential thrombocythemia MF who have failed previous treatment with JAK inhibitor (Part A), or Ruxolitinib (Part B). In Part A of the study, patients will be randomly assigned to 2 different doses and 3 different dosing schedules of KRT-232. In Part B of the study, patients will be treated at the recommended dose and schedule from Part A.

Condition or disease	Intervention/treatment	Phase
Primary Myelofibrosis (PMF) Post-Polycythemia Vera MF (Post-PV-MF) Post-Essential Thrombocythemia MF (Post-ET-MF)	Drug: KRT-232	Phase 2

Study Design

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Study Type :	Interventional (Clinical Trial)
Estimated Enrollment :	203 participants
Allocation:	Randomized
Intervention Model:	Parallel Assignment
Masking:	None (Open Label)
Primary Purpose:	Treatment
Official Title:	An Open-Label, Phase 2a/2b Study of KRT-232 in Subjects With Primary Myelofibrosis (PMF), Post-Polycythemia Vera MF (Post-PV-MF), Or Post-Essential Thrombocythemia MF (Post-ET-MF) Who Have Failed a JAK Inhibitor
Actual Study Start Date :	January 15, 2019
Estimated Primary Completion Date :	August 1, 2021
Estimated Study Completion Date :	February 28, 2023

Resource links provided by the National Library of Medicine NIH NLM

Genetics Home Reference related topics: Essential thrombocythemia

Polycythemia vera Primary myelofibrosis

Genetic and Rare Diseases Information Center resources: Myelofibrosis
Polycythemia Vera Essential Thrombocythemia
Chronic Myeloproliferative Disorders

U.S. FDA Resources

Arms and Interventions

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Arm	Intervention/treatment
Experimental: Part A Cohort 1 KRT-232 120mg by mouth once daily for Days 1-7, off treatment for Days 8-21 (21-day cycles)	Drug: KRT-232 KRT-232, administered by mouth
Experimental: Part A Cohort 2 KRT-232 240mg by mouth once daily for Days 1-7, off treatment for Days 8-21 (21-day cycles)	Drug: KRT-232 KRT-232, administered by mouth
Experimental: Part A Cohort 3 KRT-232 240mg by mouth once daily for Days 1-7, off treatment for Days 8-28 (28-day cycles)	Drug: KRT-232 KRT-232, administered by mouth
Experimental: Part B Recommended KRT-232 dose and schedule from Part A	Drug: KRT-232 KRT-232, administered by mouth
Experimental: Part A Cohort 4b KRT-232 240mg by mouth once daily for Days 1-5, off treatment for Days 6-28 (28-day cycles)	Drug: KRT-232 KRT-232, administered by mouth

Outcome Measures

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Primary Outcome Measures :

1. To determine spleen response [Time Frame: 24 weeks]

   The proportion of patients achieving a ≥ 35% spleen volume reduction from Baseline to Week 24, as assessed by magnetic resonance imaging (MRI) or computed tomography (CT) scan

Secondary Outcome Measures :

1. To determine the change in modified MPN-SAF Total Symptom Score (TSS) at Week 24 and Week 48 [Time Frame: 48 weeks]

   Proportion of patients who have at least a 50% reduction from Baseline to Week 24 and Week 48 in the total symptom score as measured by the modified MPN-SAF v2.0

2. RBC transfusion independence at Week 24 [Time Frame: 24 weeks]

   Proportion of patients who have RBC transfusion independence at week 24

3. Complete remission and partial remission defined according to International Working Group-Myeloproliferative Neoplasms Research and Treatment and modified European LeukemiaNet criteria [Time Frame: 24 weeks]

   Proportion of patients who have complete remission and partial remission at week 24

Eligibility Criteria

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Information from the National Library of Medicine

Choosing to participate in a study is an important personal decision. Talk with your doctor and family members or friends about deciding to join a study. To learn more about this study, you or your doctor may contact the study research staff using the contacts provided below. For general information, Learn About Clinical Studies.

Ages Eligible for Study:	18 Years and older (Adult, Older Adult)
Sexes Eligible for Study:	All
Accepts Healthy Volunteers:	No

Criteria

Inclusion Criteria:

- Confirmed diagnosis of PMF, post-PV MF or post-ET MF (WHO)
- High, intermediate-2, or intermediate-1 risk Dynamic International Prognostic System (DIPSS)
- Failure of prior treatment with JAK inhibitor (Part A) or ruxolitinib (Part B)
- ECOG ≤ 2

Exclusion Criteria:

- Prior splenectomy
- Splenic irradiation within 3 months prior to the first dose of KRT-232
- Active or chronic bleeding within 4 weeks prior to the first dose of KRT-232
- Prior MDM2 inhibitor therapy or p53-directed therapy
- Prior treatment with HDAC or BCL-2 inhibitors
- Grade 2 or higher QTc prolongation (> 480 milliseconds per NCI-CTCAE criteria, version 5.0)

Contacts and Locations

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Information from the National Library of Medicine NIH NLM

To learn more about this study, you or your doctor may contact the study research staff using the contact information provided by the sponsor.

Please refer to this study by its ClinicalTrials.gov identifier (NCT number): ***NCT03662126***

Contacts

Contact: John Mei 650-542-0136 jmei@kartosthera.com

Locations

Show 65 study locations

Sponsors and Collaborators

Kartos Therapeutics, Inc.

More Information

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Responsible Party:	Kartos Therapeutics, Inc.
ClinicalTrials.gov Identifier:	NCT03662126 History of Changes
Other Study ID Numbers:	KRT-232-101
First Posted:	September 7, 2018 Key Record Dates
Last Update Posted:	November 26, 2019
Last Verified:	November 2019

Studies a U.S. FDA-regulated Drug Product:	Yes
Studies a U.S. FDA-regulated Device Product:	No
Product Manufactured in and Exported from the U.S.:	Yes

Additional relevant MeSH terms:

Polycythemia Vera	Neoplasms by Site
Primary Myelofibrosis	Neoplasms
Polycythemia	Blood Platelet Disorders
Thrombocytosis	Blood Coagulation Disorders
Thrombocythemia, Essential	Hemorrhagic Disorders
Myeloproliferative Disorders	Janus Kinase Inhibitors
Bone Marrow Diseases	Protein Kinase Inhibitors
Hematologic Diseases	Enzyme Inhibitors
Bone Marrow Neoplasms	Molecular Mechanisms of Pharmacological Action
Hematologic Neoplasms	