A Study to Evaluate Efficacy and Safety of Vismodegib (Erivedge) in Combination With Ruxolitinib for the Treatment of Intermediate- or High-Risk Myelofibrosis (MF)

This study is currently recruiting participants. (see Contacts and Locations)

Verified February 2016 by *Hoffmann-La Roche*

Sponsor:
Hoffmann-La Roche

Information provided by (Responsible Party):
Hoffmann-La Roche

ClinicalTrials.gov Identifier:
NCT02593760

First received: October 29, 2015
Last updated: February 1, 2016
Last verified: February 2016
History of Changes

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

Purpose

This multicenter, randomized, double-blind, placebo-controlled study will evaluate the efficacy and safety of vismodegib plus (+) ruxolitinib versus placebo + ruxolitinib in participants with intermediate- or high-risk MF. The study will be divided into 2 components. The Phase 1b portion of the study will be started with 6-week safety run-in period with 10 participants who will receive vismodegib (150 milligrams [mg] orally [PO] once daily [QD]) + ruxolitinib (PO twice daily [BID]) for the assessment of acute safety events associated with this combined therapy. After getting confirmation about the safety and toxicity of this combination, the Phase 3 randomization portion of the study will begin during which approximately 84 participants will randomly assign in 1:1 ratio to receive either vismodegib (150 mg PO QD) plus ruxolitinib (PO BID) or placebo (PO QD) plus ruxolitinib (PO BID) for up to 48 weeks or until withdrawal or discontinuation, whichever occurs first.

Condition	Intervention	Phase
Myelofibrosis	Other: Placebo Drug: Ruxolitinib Drug: Vismodegib	Phase 1 Phase 2

Study Type: Interventional
Study Design: Allocation: Randomized
Endpoint Classification: Safety/Efficacy Study
Intervention Model: Parallel Assignment
Masking: Double Blind (Subject, Investigator)
Primary Purpose: Treatment

Resource links provided by NLM:

Genetics Home Reference related topics: primary myelofibrosis

Drug Information available for: Vismodegib Ruxolitinib Ruxolitinib phosphate

Genetic and Rare Diseases Information Center resources: Chronic Myeloproliferative Disorders Myelofibrosis

U.S. FDA Resources

Further study details as provided by Hoffmann-La Roche:

Primary Outcome Measures:

- Percentage of participants who achieve a greater than equal to (>=) 35% reduction in spleen volume at Week 24, as determined by an IRC using IWG-MRT revised response criteria [Time Frame: Week 24] [Designated as safety issue: No]
- Percentage of participants with complete response (CR) and partial response (PR) at Week 24, as determined by an IRC using IWG-MRT revised response criteria [Time Frame: Week 24] [Designated as safety issue: No]

Secondary Outcome Measures:

- Plasma vismodegib concentration at steady state [Time Frame: Predose, Weeks 6, 12, 24, 36, and 48] [Designated as safety issue: No]
- Percentage of participants who achieve a >=35% reduction in spleen volume, as determined by an IRC using IWG-MRT revised response criteria at Week 48 and by an Investigator at Weeks 24 and 48 [Time Frame: Weeks 24 and 48] [Designated as safety issue: No]
- Percentage of participants with CR and PR, as determined by an IRC using IWG-MRT revised response criteria at Week 48 and by an Investigator at Weeks 24 and 48 [Time Frame: Weeks 24 and 48] [Designated as safety issue: No]
- Percentage of Participants with objective response rate (CR, PR and clinical improvement) at Weeks 24 and 48, as determined by an IRC and the investigator using IWG-MRT revised response criteria [Time Frame: Weeks 24 and 48] [Designated as safety issue: No]
- Percentage of participants who achieve anemia response at Weeks 24 and 48, as determined by the Investigator using IWG-MRT revised response criteria

[Time Frame: Weeks 24 and 48] [Designated as safety issue: No]

- Percentage of participants w ith symptom response rate (participants w ho achieve a >=50% reduction in the Myeloproliferative Neoplasm Symptom Assessment Form Total Symptom Score [MPN-SAF TSS]) [Time Frame: Baseline, Weeks 24 and 48] [Designated as safety issue: No]
- Duration of response, determined by the Investigator and an IRC using IWG-MRT revised response criteria or death from any cause during the study [Time Frame: 28 days after the last dose of study drug (52 w eeks)] [Designated as safety issue: No]
- Percentage of participants w ith improvement in bone marrow fibrosis at Weeks 24 and 48, as determined by the Investigator and independent pathology review using the European consensus grading system [Time Frame: Weeks 24 and 48] [Designated as safety issue: No]
- Progression free survival [Time Frame: up to the end of the study (up to 1 year after completing 48 w eeks of treatment by the last participant)] [Designated as safety issue: No]
- Percentage of participants w ho achieve a >=50% reduction in fatigue from baseline to Weeks 24 \nand 48 [Time Frame: Baseline, Weeks 24 and 48] [Designated as safety issue: No]
- Percentage of participants w ho achieve a >=50% reduction in other symptom and impact item scores from baseline to Weeks 24 and 48, as measured by the MPN-SAF [Time Frame: Baseline, Weeks 24 and 48] [Designated as safety issue: No]
- Percentage of participants w ho achieved a meaningful improvement on the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC QLQ-C30) scale scores from baseline to Weeks 24 and 48 [Time Frame: Baseline, Weeks 24 and 48] [Designated as safety issue: No]
- Overall survival [Time Frame: up to the end of the study (up to 1 year after completing 48 w eeks treatment by the last participant)] [Designated as safety issue: No]

Estimated Enrollment:	94
Study Start Date:	December 2015
Estimated Study Completion Date:	January 2019
Estimated Primary Completion Date:	January 2019 (Final data collection date for primary outcome measure)

Arms	Assigned Interv entions
Active Comparator: Placebo + Ruxolitinib Participants w ill receive placebo (PO QD) in combination w ith ruxolitinib (dose w ill depend on the participant's baseline platelet count) for up to 48 w eeks.	Other: Placebo Placebo w ill be administered PO QD for up to 48 w eeks. Drug: Ruxolitinib Ruxolitinib w ill be administered PO BID at a starting dose depending on the participants's baseline platelet count for up to 48 w eeks.
Experimental: Vismodegib + Ruxolitinib Participants w ill receive vismodegib (150 mg PO QD) in combination w ith ruxolitinib (dose w ill depend on the participant's baseline platelet count) for up to 48 w eeks.	Drug: Ruxolitinib Ruxolitinib w ill be administered PO BID at a starting dose depending on the participants's baseline platelet count for up to 48 w eeks. Drug: Vismodegib Vismodegib w ill be administered at a dose of 150 mg PO QD) for up to 48 w eeks. Other Name: Erivedge

Eligibility

Ages Eligible for Study:	18 Years and older
Genders Eligible for Study:	Both
Accepts Healthy Volunteers:	No

Criteria

Inclusion Criteria:

- Pathologically confirmed diagnosis of primary MF, post-polycythemia vera MF, or post-essential thrombocythemia MF, according to the 2008 revised World Health Organization criteria
- Intermediate-1, intermediate-2, or high-risk according to the International Working Group- Myeloproliferative Neoplasms Research and Treatment (IWG-MRT) Dynamic International Prognostic Scoring System (DIPSS)
- Participants aged greater than or equal to (>=) 18 years
- Life expectancy >=6 months
- Peripheral blood blast count of less than (<) 10%
- Palpable splenomegaly of greater than (>) 5 centimeters (cm) below the left costal margin
- Eastern Cooperative Oncology Group (ECOG) Performance Status of 0 to 2
- Adequate hepatic and renal function as assessed by:

Total bilirubin less than or equal to (<=) 2.0*upper limit of normal (ULN), unless resulting from hemolysis and Gilbert's Syndrome Aspartate transaminase and alanine transaminase <=2.5*ULN (<=5*ULN if liver is involved by extramedullary hematopoiesis as determined by investigator) Serum creatinine <=1.5*ULN and creatinine clearance greater than (>) 30 milliliters per minute (mL/min)

Exclusion Criteria:

- Prior treatment w ith a Hedgehog or Janus kinase (JAK) pathw ay inhibitor
- Treatment w ith strong cytochrome P450 (CYP) 3A4 inhibitors/inducers w ithin 28 days prior to Day 1
- Prior therapy for the treatment of intermediate- or high-risk MF including chemotherapy, interferon, thalidomide, busulfan, lenalidomide, anagrelide, or androgens w ithin 28 days prior to Day 1
- Prior splenectomy or splenic irradiation
- Inadequate bone marrow reserve as follow s:

Absolute neutrophil count of <=1000/microliters (mcL) Platelet count of <100,000/mcL w ithout the assistance of grow th factors, thrombopoietic factors, or

platelet transfusions

- Participants with any history of platelet counts of <50,000/mccL or ANC of <500/mL, except during treatment for myeloproliferative neoplasm (MPN) or treatment with cytotoxic therapy for any other reason
- Planned allogeneic bone marrow transplant during the study

Contacts and Locations

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, see Learn About Clinical Studies.

Please refer to this study by its ClinicalTrials.gov identifier: NCT02593760

Contacts

Contact: Reference Study ID Number: **WO29806** www.roche.com/about_roche/roche_worldwide.htm 888-662-6728 (U.S. Only) global.rochegenentechtrials@roche.co

Show 22 Study Locations

Sponsors and Collaborators

Hoffmann-La Roche

Investigators

Study Director: Clinical Trials Hoffmann-La Roche

More Information

No publications provided

Responsible Party:	Hoffmann-La Roche
ClinicalTrials.gov Identifier:	NCT02593760 History of Changes
Other Study ID Numbers:	**WO29806** 2015-001620-33
Study First Received:	October 29, 2015
Last Updated:	February 1, 2016
Health Authority:	United States: Food and Drug Administration

Additional relevant MeSH terms:
Primary Myelofibrosis
Bone Marrow Diseases
Hematologic Diseases
Myeloproliferative Disorders

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