ForPatients
by Roche

Polycythemia Vera

A Study to Evaluate the Efficacy, Safety, Pharmacokinetics and Pharmacodynamics of Idasanutlin Monotherapy in Participants With Hydroxyurea-Resistant/Intolerant Polycythemia Vera

Trial Status	Trial Runs In	Trial Identifier
Terminated	4 Countries	NCT03287245 2017-000861-58 NP39761

The information is taken directly from public registry websites such as ClinicalTrials.gov, EuClinicalTrials.eu, ISRCTN.com, etc., and has not been edited.

Official Title:

A Phase II, Single-Arm, Open-Label Study to Evaluate the Efficacy, Safety, Pharmacokinetics and Pharmacodynamics of Idasanutlin Monotherapy in Patients With Hydroxyurea-Resistant/Intolerant Polycythemia Vera

Trial Summary:

This is an open-label, single-arm study of idasanutlin monotherapy in participants with hydroxyurea (HU)-resistant/intolerant Polycythemia vera (PV). The study will include two phases: initial phase and expansion phase. The initial phase will assess the safety and efficacy of idasanutlin monotherapy in ruxolitinib naïve and ruxolitinib-resistant or intolerant patients, respectively. If the initial phase shows promising results for ruxolitinib-resistant or intolerant patients, an expansion phase will be opened to further characterize the efficacy of idasanutlin.

Hoffmann-La Roche
Sponsor

Phase 2
Phase

NCT03287245 2017-000861-58 NP39761
Trial Identifiers

Eligibility Criteria:

Gender	Age	Healthy Volunteers
All	# 18 Years	No

Inclusion Criteria:

- Documentation that the participant has met the revised 2016 World Health Organization (WHO) criteria for the diagnosis of polycythemia vera (PV)
- Hematocrit at screening and at initiation of idasanutlin greater than (>)40%
- Phlebotomy-dependent participants with splenomegaly by magnetic resonance imaging (MRI) or computerized tomography (CT) imaging (greater than or equal to [#]450 cubic centimeters [cm^3]) or without splenomegaly (less than [<]450 cm^3 or prior splenectomy)
- Resistance to/intolerance to hydroxyurea according to modified European Leukemia Net (ELN) criteria
- For participants in the ruxolitinib intolerant or resistant group, in addition to previous hydroxyurea intolerance/resistance: Therapy-resistant PV after at least 6 months of treatment with ruxolitinib, as defined in the protocol; Ruxolitinib intolerance, as defined in the protocol; and Documentation of adverse events likely caused by ruxolitinib (assessment of attending physician) and that are of a severity that preclude further treatment with ruxolitinib (as per judgment of the attending physician and the patient)
- Eastern Cooperative Oncology Group (ECOG) performance status of 0 to 1
- Participants must be willing to submit the blood sampling and bone marrow sampling for the pharmacokinetic (PK) and pharmacodynamic analyses and exploratory biomarkers
- Adequate hepatic and renal function
- Ability and willingness to comply with the study protocol procedures, including clinical outcome assessment measures
- For women of childbearing potential: agreement to use contraceptive methods that result in a failure rate of less than (<)1% per year during the treatment period and for at least 6 weeks after the last dose of idasanutlin
- For men: Agreement to use contraceptive measures, and agreement to refrain from donating sperm during the treatment period and for at least 90 days after the last dose of idasanutlin

Exclusion Criteria:

- Meets the criteria for post-PV myelofibrosis as defined by the International Working Group-Myeloproliferative Neoplasms Research and Treatment (IWG-MRT)
- Blast phase disease (>20% blasts in the marrow or peripheral blood)
- Clinically-significant thrombosis within 3 months of screening
- Participants who must receive CYP2C8 inhibitors, substrates and inducers, strong CYP3A4 inducers, or OATP1B1/3 substrates while on study. These must be discontinued 7 days (inhibitors and substrates) or 14 days (inducers) prior to start of study medication
- Previously treated with murine double minute 2 (MDM2) antagonist therapies or receiving interferon-alpha, anagrelide, or ruxolitinib within 28 days or 5 half-lives (whichever is shorter), or hydroxyurea within 1 day, or receiving any other cytoreductive or investigational agents within 28 days or 5 half-lives (whichever is shorter) of initial dose. Aspirin is permitted per treatment guidelines for PV unless medically contraindicated
- Patients with evidence of electrolyte imbalance such as hypokalemia, hyperkalemia, hypocalcemia, hypercalcemia, hypomagnesemia, and hypermagnesemia of Grade >1 intensity, as per the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE), version 4.0, prior to dosing on Cycle 1 Day 1. Treatment for correction of electrolyte imbalances is permitted to meet eligibility
- Neutrophil count <1.5 × 10^9/Liter (L) prior to dosing on Cycle 1 Day 1
- Platelet count less than or equal to (#)150 × 10^9/L prior to dosing on Cycle 1 Day 1
- Women who are pregnant or breastfeeding
- Ongoing serious non-healing wound, ulcer, or bone fracture
- History of major organ transplant
- Uncontrolled intercurrent illness including, but not limited to hepatitis, concurrent malignancy that could affect compliance with the protocol or interpretation of results, hepatitis A, B, and C, human immunodeficiency virus (HIV)-positive, ongoing or active infection, clinically significant cardiac disease

(New York Heart Association Class III or IV), symptomatic congestive heart failure, unstable angina pectoris, ventricular arrhythmia, or psychiatric illness/social situations that would limit compliance with study requirements. Concurrent malignancy exceptions include: Curatively treated carcinoma in situ of the cervix, good-prognosis ductal carcinoma in situ of the breast, basal- or squamous-cell skin cancer, Stage I melanoma, or low-grade, early-stage localized prostate cancer. Any previously treated early-stage non-hematological malignancy that has been in remission for at least 2 years is also permitted.

- Patients with active gastrointestinal conditions (Crohn's disease, ulcerative colitis, diverticulosis associated colitis, and Behçet's disease)
- Clinically significant toxicity (other than alopecia) from prior therapy that has not resolved to Grade #1 (according to the NCI CTCAE, v4.0) prior to Cycle 1 Day 1
- Cardiovascular disease, such as: uncontrolled arterial hypertension; symptomatic congestive heart failure or ejection fraction below 55% at screening, or left ventricular hypertrophy; any significant structural abnormality of the heart at screening echocardiogram; unstable angina pectoris; presence or history of any type of supraventricular and ventricular arrhythmias, including lone atrial fibrillation or flutter