Long-term Study Evaluating the Effect of Givinostat in Patients With Chronic Myeloproliferative Neoplasms

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

Verified February 2016 by Italfarmaco

Sponsor:
Italfarmaco

Information provided by (Responsible Party):
Italfarmaco

ClinicalTrials.gov Identifier:
NCT01761968

First received: December 18, 2012
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History of Changes

Purpose

This is a multicenter, open label, long-term study testing the long-term safety, tolerability and efficacy of Givinostat in patients with Polycythemia Vera, Essential Thrombocythemia, primary Myelofibrosis, Post-Polycythemia Vera Myelofibrosis, Post-Essential Thrombocythemia Myelofibrosis following core protocols in chronic myeloproliferative neoplasms and/or patient-named compassionate use program (if regulated/allowed by the local regulations, e.g. for Italy D.M. 8/5/2003 "Uso terapeutico di medicinale sottoposto a sperimentazione clinica" published on G.U. n. 173 of 28 July 2003, and the following amendments). Patients will continue at their last tolerable dose and treatment schedule of Givinostat monotherapy. If patients previously received Givinostat in combination with other drugs during a core protocol or a compassionate use program (if regulated/allowed by the local regulations, e.g. for Italy D.M. 8/5/2003 "Uso terapeutico di medicinale sottoposto a sperimentazione clinica" published on G.U. n. 173 of 28 July 2003, and the following amendments), they will be treated at the last tolerable dose of the combination. Assessment of safety and efficacy will be performed at each quarterly visit and each visit will also include laboratory tests and ECG examination. During the visits the clinical benefit will be assessed by Investigator according to the revised European LeukemiaNet response criteria (for PV and ET) and EUMNET response criteria (for MF). The dose of Givinostat will be modified for protocol specified toxicities. The treatment may continue up to Marketing Authorization of Givinostat, currently planned in the next 5 years (note: only for Germany, this long-term study is initially limited up to 2 years of treatment). Patients may discontinue study treatment at any time and remain on study therapy as long as they derive clinical benefit. Safety will be monitored at each visit throughout the entire duration of the study. In case the approved label will not cover the whole study population, Givinostat will be provided by the Sponsor to those patients not fulfilling the criteria for the approved label of the drug that are still deriving benefit from Givinostat at the time of its commercial availability.

Condition	Intervention	Phase
Chronic Myeloproliferative Neoplasms	Drug: Givinostat	Phase 2

Study Type: Interventional
Study Design: Endpoint Classification: Safety/Efficacy Study
Intervention Model: Single Group Assignment
Masking: Open Label
Primary Purpose: Treatment

Official Title: Long-term Study Evaluating the Effect of Givinostat in Patients With JAK2V617F Positive Chronic Myeloproliferative Neoplasms

Resource links provided by NLM:

Genetics Home Reference related topics: essential thrombocythemia polycythemia vera primary myelofibrosis

MedlinePlus related topics: Cancer

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

U.S. FDA Resources

Further study details as provided by Italfarmaco:

Primary Outcome Measures:

- Long-term safety and efficacy [Time Frame: 3 months] [Designated as safety issue: No]

  To obtain information on the long-term efficacy of Givinostat in patients with chronic myeloproliferative neoplasms following core protocols or compassionate use program:

- Number of patients experiencing adverse events;
- Type, incidence, and severity of treatment-related adverse events.

To determine the long term safety and tolerability of Givinostat in patients with chronic myeloproliferative neoplasms following core protocols or compassionate use program:

- For Polycythemia Vera and Essential Thrombocythemia, Complete response and partial response rate according to the revised clinico-haematological European LeukemiaNet response criteria;
- For Myelofibrosis, complete response, major response, moderate response and minor response rate according to European Myelofibrosis Network response criteria.

Note that these assessment will be repeated periodically (each 3 months) during the study. In fact, the treatment will continue up to Marketing Authorisation of Givinostat.

Other Outcome Measures:

- Clinical exploratory endpoint [Time Frame: 1 year] [Designated as safety issue: No]

  To evaluate the effect of Givinostat on each single response parameter according to the revised European LeukemiaNet (for Polycythemia Vera and Essential Thrombocythemia) and European European Myelofibrosis Network response criteria (for Myelofibrosis). Note that this assessment will be repeated periodically (each year) during the study. In fact, the treatment will continue up to Marketing Authorisation of Givinostat.

- Molecular exploratory endpoint [Time Frame: 1 year] [Designated as safety issue: No]

  To evaluate the molecular response (i.e. reduction of the allele burden of the mutated Janus Kinase 2 in the position V617F). Note that this assessment will be repeated periodically (each year) during the study. In fact, the treatment will continue up to Marketing Authorisation of Givinostat.

- Biomolecular exploratory endpoint [Time Frame: 1 year] [Designated as safety issue: No]

  To identify potential other markers predictive of clinical benefit of Givinostat (e.g. potential pharmacodynamic markers). Note that this assessment will be repeated periodically (each year) during the study. In fact, the treatment will continue up to Marketing Authorisation of Givinostat.

Estimated Enrollment:	90
Study Start Date:	March 2013
Estimated Study Completion Date:	December 2020
Estimated Primary Completion Date:	June 2020 (Final data collection date for primary outcome measure)

Arms	Assigned Interventions
Experimental: Givinostat Patients will continue at their last tolerable dose and treatment schedule of Givinostat monotherapy. Givinostat is a histone-deacetylases inhibitor. The product will be supplied as hard gelatine capsules for oral administration at the strength of 50 mg, 75 mg and/or 100 mg each. If patients previously received Givinostat in combination with other drugs during a core protocol or a compassionate use program, they will be treated at their last tolerable dose of this combination.	Drug: Givinostat Patients will continue at their last tolerable dose and treatment schedule of Givinostat monotherapy. Givinostat is a histone-deacetylases inhibitor. The product will be supplied as hard gelatine capsules for oral administration at the strength of 50 mg, 75 mg and/or 100 mg each. If patients previously received Givinostat in combination with other drugs during a core protocol or a compassionate use program, they will be treated at their last tolerable dose of this combination. Other Name: Givinostat (ITF**2357**)

Show Detailed Description

Eligibility

Ages Eligible for Study:	18 Years and older (Adult, Senior)
Genders Eligible for Study:	Both
Accepts Healthy Volunteers:	No

Criteria

Inclusion Criteria:

1. Patients must have completed Givinostat treatment on at least one core study in chronic myeloproliferative neoplasms, or patients must be participating in a compassionate use program with Givinostat AND Patients must have tolerated previous Givinostat treatment and achieved a clinical benefit at the end of core protocols or compassionate use program with Givinostat, assessed by the Investigator according to the revised clinico-haematological ELN response criteria (for PV and ET) and EUMNET response criteria (for MF);
2. Patients must be able to provide informed consent and be willing to sign an informed consent form;
3. Adult patients (age ≥ 18 years) of both genders with established diagnosis of chronic myeloproliferative neoplasms according to the revised WHO criteria;
4. Patients must have an Eastern Cooperative Oncology Group performance status < 3;

5. Acceptable organ function within 7 days of initiating study drug;
6. Use of an effective means of contraception for women of childbearing potential and men with partners of childbearing potential;
7. Willingness and capability to comply with the requirements of the study.

Exclusion Criteria:

1. Active bacterial or mycotic infection requiring antimicrobial treatment;
2. Pregnancy or nursing;
3. A clinically significant corrected QT interval prolongation at baseline;
4. Use of concomitant medications known to prolong the corrected QT interval;
5. Clinically significant cardiovascular disease including:
   - Uncontrolled hypertension, myocardial infarction, unstable angina within 6 months from study start;
   - New York Heart Association Grade II or greater congestive heart failure;
   - History of any cardiac arrhythmia requiring medication (irrespective of its severity);
   - A history of additional risk factors for Torsade de Point;
6. History of virus infection including human immuno deficiency, hepatitis B virus and hepatitis C virus;
7. Platelets count < 100 x109/L within 14 days before enrolment (i.e. the receipt of the Patient ID);
8. Absolute neutrophil count < 1.2 x109/L within 14 days before enrolment (i.e. the receipt of the Patient ID);
9. Serum creatinine > 2 times the upper normal limit;
10. Total serum bilirubin > 1.5 times the upper normal limit;
11. Serum Aspartate aminotransferase/Alanine aminotransferase > 3 times the upper normal limit;
12. History of other diseases, metabolic dysfunctions, physical examination findings, or clinical laboratory findings giving reasonable suspicion of a disease or condition that contraindicates use of an investigational drug or that might affect interpretation of the results of the study or render the patient at high risk from treatment complications;
13. Any investigational drug other than Givinostat within 28 days before enrolment (i.e. the receipt of the Patient ID);
14. Patients with known hypersensitivity to the components of potential study therapy.

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: NCT01761968

Contacts

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Locations

France

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Germany

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Italy

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Sponsors and Collaborators

Italfarmaco

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More Information

Responsible Party:	Italfarmaco
ClinicalTrials.gov Identifier:	NCT01761968 History of Changes
Other Study ID Numbers:	**DSC/11/2357/44** 2012-003499-37
Study First Received:	December 18, 2012
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Health Authority:	Italy: Ethics Committee Italy: The Italian Medicines Agency France: Agence Nationale de Sécurité du Médicament et des produits de santé France: Ethics Committee

Keywords provided by Italfarmaco:
chronic myeloproliferative neoplasms
Polycythemia Vera
Essential Thrombocythemia
Primary Myelofibrosis
Post-Polycythemia Vera Myelofibrosis
Post-Essential Thrombocythemia Myelofibrosis
Givinostat

Additional relevant MeSH terms:
Neoplasms
Myeloproliferative Disorders
Bone Marrow Diseases
Hematologic Diseases
Histone Deacetylase Inhibitors
Enzyme Inhibitors
Molecular Mechanisms of Pharmacological Action

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