PLEASE NOTE: *This study has been imported from ClinicalTrials.gov without additional data checks.*

Trial Description

Title

A Two-part Study to Assess the Safety and Preliminary Efficacy of Givinostat in Patients With Polycythemia Vera

Trial Acronym

[---]*

URL of the trial

[---]*

Brief Summary in Lay Language

This is a two-part, multicenter, open label, non-randomized, phase Ib/II study to assess the safety and tolerability, Maximum Tolerated Dose and preliminary efficacy of Givinostat in patients with JAK2V617F positive Polycythemia Vera. Part A is the dose finding part while Part B is assessing the preliminary efficacy. Patients will be enrolled either in Part A or Part B and transition from one part to the other is not allowed.

Eligible patients for this study will have a confirmed diagnosis of Polycythemia Vera according to the revised World Health Organization criteria. Only if the enrolment in Part A is slow (i.e. < 5 patients enrolled in 3 months), eligibility for this part of the study may be expanded to all patients with chronic myeloproliferative neoplasms.

Study therapy will be administered in 28 day cycles (4 weeks of treatment). Disease response will be evaluated according to the European LeukemiaNet criteria after 3 and 6 cycles (i.e. at weeks 12 and 24, respectively) of treatment with Givinostat for both parts of the study.
All phlebotomies performed in the first 3 weeks of treatment will not be counted to assess the clinico-haematological response.

The study will last up to a maximum of 24 weeks of treatment. However, after completion of the trial, all patients achieving clinical benefit will be allowed to continue treatment

with Givinostat (at the same dose and schedule) in a long-term study.

Safety will be monitored at each visit throughout the entire duration of the study.
Treatment will be administered on an outpatient basis and patients will be followed
regularly with physical and laboratory tests, as specified in the protocol; in case of
hospitalization, the treatment will be continued or interrupted according to the Investigators' decision.

Brief Summary in Scientific Language

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Organizational Data

- DRKS-ID: **DRKS00005325**
- Date of Registration in DRKS: **2013/10/24**
- Date of Registration in Partner Registry or other Primary Registry: **2013/07/10**
- Investigator Sponsored/Initiated Trial (IST/IIT): **no**
- Ethics Approval/Approval of the Ethics Committee: **[---]***
- (leading) Ethics Committee Nr.: **[---]***

Secondary IDs

- EudraCT-No.
  (for studies acc. to Drug Law): **2013-000860-27**
- Primary Registry-ID: **NCT01901432 (ClinicalTrials.gov)**
- Sponsor-ID: **DSC/12/2357/45 (Italfarmaco)**

Health condition or Problem studied

- Free text: **Polycythemia Vera**
- ICD10: **D45 - Polycythaemia vera**

Interventions/Observational Groups

- Arm 1: **Drug: Givinostat**

Characteristics

- Study Type: **Interventional**
- Study Type Non-Interventional: **[---]***
- Allocation: **Single arm study**
- Blinding: **[---]***
- Who is blinded: **[---]***
- Control: **Uncontrolled/Single arm**
- Purpose: **Treatment**
- Assignment: **Single (group)**
- Phase: **I-II**
- Off-label use (Zulassungsüberschreitende Anwendung eines Arzneimittels): **[---]***

Primary Outcome

- Part A: Maximum Tolerated Dose; time frame: 168 days (i.e. 6 cycles); Determination of the Maximum Tolerated Dose of Givinostat based on cycle 1 Dose Limiting Toxicity's.
- Part B: Preliminary efficacy after 3 cycles of treatment; time frame: 84 days (i.e. 3 cycles); Overall response rate - i.e. Complete Response and Partial Response - of Givinostat at the Maximum Tolerated Dose after 3 cycles; the response will be evaluated according to the clinico-haematological European LeukemiaNet response criteria.
- Part A: Safety and tolerability; time frame: 168 days (i.e. 6 cycles); Safety and tolerability evaluated as following:
Number of patients experiencing adverse events;
Type, incidence, and severity of treatment-related adverse events.
- Part B: Safety and tolerability after 3 cycles of treatment; time frame: 84 days (i.e. 3 cycles); Safety and tolerability of Givinostat at the Maximum Tolerated Dose after 3 cycles evaluated as following:
Number of patients experiencing adverse events;
Type, incidence, and severity of treatment-related adverse events.

Secondary Outcome

- Part A: characterization of pharmacokinetic; time frame: 84 and 168 days (i.e. clycles 3 and 6); Individual Givinostat concentrations tabulated by dose cohort along with descriptive statistics.
- Part B: characterization of pharmacokinetic; time frame: 168 days (i.e. 6 cycles); Individual Givinostat concentrations tabulated with descriptive statistics.
- Part A: preliminary efficacy after 3 and 6 cycles of treatment; time frame: 84 and 168 days (i.e. clycles 3 and 6); Overall response rate - i.e. Complete Response and Partial Response - of Givinostat at the Maximum Tolerated Dose after 3 and 6 cycles; the response will be evaluated according to the clinico-haematological European LeukemiaNet response criteria.
- Part B: preliminary efficacy of Givinostat at the Maximum Tolerated Dose after 6 cycles.; time frame: 168 days (i.e. 6 cycles); Overall response rate - i.e. Complete Response and Partial Response - of Givinostat at the Maximum Tolerated Dose after 6 cycles; the response will be evaluated according to the clinico-

haematological European LeukemiaNet response criteria.
- Part B: safety and tolerability after 6 cycles; time frame: 168 days (i.e. 6 cycles); Safety and tolerability of Givinostat at the Maximum Tolerated Dose after 6 cycles evaluated as following:
Number of patients experiencing adverse events;
Type, incidence, and severity of treatment-related adverse events.

Countries of recruitment

- FR **France**
- DE **Germany**
- IT **Italy**
- PL **Poland**
- UK **United Kingdom**

Locations of Recruitment

- **Charite Research Organisation GmbH, Berlin**
- **Klinikum Darmstadt GmbH, Darmstadt**
- **Universitaetsklinikum Carl Gustav Carus TU Dresden, Dresden**
- **Universitaetsklinikum Freiburg, Freiburg**
- **Universitaetsklinikum Koeln, Koeln**

Recruitment

- Planned/Actual: **[---]***
- (Anticipated or Actual) Date of First Enrollment: **2013/10/31**
- Target Sample Size: **52**
- Monocenter/Multicenter trial: **Multicenter trial**
- National/International: **International**

Inclusion Criteria

- Gender: **Both, male and female**
- Minimum Age: **18 Years**
- Maximum Age: **no maximum age**

Additional Inclusion Criteria

1. Patients must be able to provide informed consent and be willing to sign an informed consent form;

2. Patients must have an age ≥18 years;

3. Patients must have a confirmed diagnosis of Polycythemia Vera according to the revised World Health Organization criteria;

4. Patients must have mutated Janus Kinase 2 (mutation V617F) positive disease;

5. Patients must have an active/not controlled disease defined as

1. hematocrit ≥ 45% or hematocrit <45% in need of phlebotomy, and

2. platelet count > 400 x109/L, and

3. white blood cell count > 10 x109/L;

6. Patients must have an Eastern Cooperative Oncology Group (ECOG) performance status ≤ 1 in Part A, ECOG performance status ≤ 2 in Part B within 7 days of initiating study drug;

7. Female patient of childbearing potential has a negative serum or urine pregnancy test within 72 hours of the first dose of study therapy;

8. Use of an effective means of contraception for women of childbearing potential and men with partners of childbearing potential;

9. Adequate and acceptable organ function within 7 days of initiating study drug;

10. Willingness and capability to comply with the requirements of the study.

Note that if the enrolment in Part A is slow (i.e. < 5 patients enrolled in 3 months), eligibility for this part of the study may be expanded to all patients with chronic myeloproliferative neoplasms. In this case, the inclusion criteria 5 will be modified as following only for Part A:

5. Patients must have an active/not controlled disease defined as:

1. Essential Thrombocythemia patients: Platelet count > 600 x109/L;

2. Myelofibrosis patients: no response according to European Myelofibrosis Network criteria.

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:

1. Uncontrolled hypertension despite medical treatment, myocardial infarction, unstable angina within 6 months from study start;

2. New York Heart Association Grade II or greater congestive heart failure;

3. History of any cardiac arrhythmia requiring medication (irrespective of its severity);

4. A history of additional risk factors for torsade de pointes;

6. Known positivity for human immunodeficiency;

7. Known active hepatitis B virus and/or hepatitis C virus infection;

8. Platelet count < 100 x109/L within 14 days before enrolment;

9. Absolute neutrophil count < 1.2x109/L within 14 days before enrolment;

10. Serum creatinine > 2 times the upper limit of normal;

11. Total serum bilirubin > 1.5 times the upper limit of normal except in case of Gilbert's disease;

12. Serum aspartate aminotransferase/alanine aminotransferase (AST/ALT) > 3 times the upper limit of normal;

13. History of other diseases (including active tumours), 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 subject at high risk from treatment complications;

14. Prior treatment with a Janus Kinase 2 or Histone Deacetylase inhibitor or participation in an interventional clinical trial for chronic

myeloproliferative neoplasms;

15. Systemic treatment for chronic myeloproliferative neoplasms other than aspirin/cardio aspirin;

16. Hydroxyurea within 28 days before enrolment;

17. Interferon alpha within 14 days before enrolment;

18. Anagrelide within 7 days before enrolment;

19. Any other investigational drug or device within 28 days before enrolment;

20. Patient with known hypersensitivity to the components of study therapy.

Addresses

- **Primary Sponsor**

  Italfarmaco

  Telephone: **[---]***
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Sources of Monetary or Material Support

- **[---]***

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Bitte wenden Sie sich an den Sponsor / Please refer to primary sponsor

Telephone: **[---]***
Fax: **[---]***
E-mail: **[---]***
URL: **[---]***

Status

- Recruitment Status: **Recruiting ongoing**
- Study Closing (LPLV): **[---]***

Trial Publications, Results and other documents

The parameters in ClinicalTrials.gov and DRKS are not identical. Therefore the data import from ClinicalTrials.gov required adjustments. For full details please see the DRKS FAQs.
- Translation on version: 6
- Last processed date by ClinicalTrials.gov: 2013/10/20

** This entry means the parameter is not applicable or has not been set.*

**** This entry means that data is not displayed due to insufficient data privacy clearing.*