Trial Description

Title

A double-blind, placebo-controlled, randomized, multi-center phase II trial to assess the efficacy of Sorafenib-maintenance therapy in Flt3-ITD positive AML in complete hematological remission after allogenic stem cell transplantation

Trial Acronym

SORMAIN

URL of the trial

[---]*

Brief Summary in Lay Language

The aim of this clinical trial is to investigate the effect of a drug on the relapse in acute myeloid leukaemia after treatment of the patients with chemotherapy and additional stem cell transplantation.
Remaining of leukaemia-cells in the bone marrow can lead to relapse, what is tried to prevent by giving oral application of Sorafenib. Sorafenib is an “inhibitor of kinases”, what are a class of proteins that are involved in the growth of cells. One member of this class is the so called Flt3 ITD protein what is the product of a genetic damage which leads to uncontrolled growth of leukaemia-cells.
Because Sorafenib inhibits effectively Flt3-ITD, leukaemia-cells but not other blood-cells are eliminated. Therefore only patients who have shown the Flt3-ITD protein are chosen for treatment.
Due to the fact that the therapy with Sorafenib is without the adverse event like chemotherapy, it can be realised continuously and so decrease more and more the number of leukaemia-cells. Together with the outcome by the new immune-system given by the transplanted cells the Sorafenib-therapy give hope of a minimised rate of relapse.

Brief Summary in Scientific Language

The aim of this study is the comparison of the relapse free survival (RFS) of Flt3-ITD+ AML patients in complete hematological remission after allo-SCT receiving Sorafenib maintenance therapy versus placebo.
The following differences between the Sorafenib and placebo branches are to be investigated: a) the median of Overall survival (OS), b) the mean value of RFS and OS depending on the status of NPM1 mutations, c) the mean value of RFS and OS depending on the level of Flt3 expression at baseline and d) the toxicity.
It should proceed a longitudinally examination of biomarkers that are associated with response or resistance for Sorafenib and the correlation of these biomarkers to RFS and OS.
The safety of Sorafenib should be analysed in regard to the nature and severity (according to NCI CTC 4.02).

Organizational Data

- DRKS-ID: **DRKS00000591**
- Date of Registration in DRKS: **2010/10/26**
- Date of Registration in Partner Registry or other Primary Registry: **[---]***
- Investigator Sponsored/Initiated Trial (IST/IIT): **yes**
- Ethics Approval/Approval of the Ethics Committee: **Approved**
- (leading) Ethics Committee Nr.: **138/10 (A) , Ethik-Kommission des Fachbereichs Medizin der Philipps-Universität Marburg**

Secondary IDs

- EudraCT-No.
  (for studies acc. to Drug Law): **2010-018539-16**
- BfArM-No.: **4036508**

Health condition or Problem studied

- ICD10: **C92.11 - [generalization C92.1: Chronic myeloid leukaemia]**

Interventions/Observational Groups

- Arm 1: **Product:**
  Sorafenib, 200mg / tablet
  Mode of administration:
  Oral, tablet
  Dosing schedule:
  Dose level 1 (starting dose) : 2 tablets / day (1-0-1)
  Dose level 2 (escalated dose): 3 tablets / day (1-0-2)
  Dose level 3 (targeted dose) : 4 tablets / day (2-0-2)
  •Dose level 1 will be given for 2 weeks
- Arm 2: **Product: matching placebo**
  Mode of administration:
  Oral, tablet
  Dosing schedule:
  Dose level 1 (starting dose) : 2 tablets / day (1-0-1)
  Dose level 2 (escalated dose): 3 tablets / day (1-0-2)
  Dose level 3 (targeted dose) : 4 tablets / day (2-0-2)

starting 6 weeks after treatment initiation

•Placebo will be administered up to 2 years or until relapse

Characteristics

- Study Type: **Interventional**
- Study Type Non-Interventional: **[---]***
- Allocation: **Randomized controlled trial**
- Blinding: **[---]***
- Who is blinded: **patient/subject, investigator/therapist, caregiver**
- Control: **Placebo**
- Purpose: **Treatment**
- Assignment: **Parallel**
- Phase: **II**
- Off-label use (Zulassungsüberschreitende Anwendung eines Arzneimittels): **[---]***

Primary Outcome

Relapse free survival (RFS), 50 events (relapse)
RFS is defined as time interval from randomization until relapse of AML or death from any cause, which ever occurs first. Relapse is defined as any blast appearance in the peripheral blood, in the bone marrow (> 5%) or extramedullary blasts (chloroma). For a patient with no relapse before the end of study follow-up, observation of RFS will be censored at the date of his or her last follow-up examination.

Secondary Outcome

Overall survival
Overall survival is defined as time from randomization to the day of death. For a patient who is not known to have died by the end of follow-up, observation of OS will be censored on the date the patient was last known to be alive.

Countries of recruitment

- DE **Germany**

Locations of Recruitment

Recruitment

- Planned/Actual: **Actual**
- (Anticipated or Actual) Date of First Enrollment: **2010/10/29**
- Target Sample Size: **200**
- Monocenter/Multicenter trial: **Multicenter trial**
- National/International: **National**

Inclusion Criteria

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

Additional Inclusion Criteria

•Written informed consent

•Age ≥18 y.

• ECOG performance ≤ 1

•FLT3-ITD-positive AML

•Complete hematological remission (CHR) after allo-SCT

CHR must be confirmed by bone marrow analysis within 14 days before randomization (CHR criteria are: ≤ 5% marrow blasts, no peripheral blasts, blood platelet count > 100/nl, WBC count > 3 G/L, ANC > 1000 G/l).

•Allo-SCT with a HLA-identical allo-family donor (FAM) or a matched unrelated donor (MUD) with up to 1 antigen mismatch acceptable (9/10)

Exclusion criteria

- **Any severe concomitant conditions which make it undesirable for the patient to participate in the study or which could jeopardize compliance with the protocol (such as substance abuse, uncontrolled infection, known HIV, HBV, HCV infection**
- **Psychiatric disorder that interferes with ability to understand the study and give informed consent, and/or impacts study participation or follow-up.**
- **Cardiac disease: heart failure NYHA III/IV, unstable coronary artery disease (MI more than 6 months prior to study entry is permitted), serious cardiac ventricular arrhythmias requiring anti-arrhythmic therapy (beta-blockers or digoxin are permitted)**
- **Resting blood pressure consistently higher than systolic 150 mmHg and/or diastolic 90 mmHg despite antihypertensive therapy**
- **Patients undergoing renal dialysis**
- **Evidence or history of severe non-leukemia associated bleeding diathesis or coagulopathy**
- **Patients with uncontrolled seizure disorder despite medication**
- **History of organ allograft (except for allogenic SCTX)**
- **Patients with major surgery, open biopsy, or significant traumatic injury within 4 weeks prior to start of first dose of study drug**
- **Serious non-healing wound, ulcer or bone fracture**
- **Known Flt3-kinase inhibitor resistance**
- **Previous Sorafenib therapy**
- **Active (uncontrolled) graft versus host disease GvHD (> grade I) at time of randomization despite the use of adequate therapeutic measures**
- **Investigational drug therapy outside of this trial during or within 4 weeks of study entry**
- **Pregnancy or breast feeding**
- **Allergy to study medication or compositions of excipients in study medication**
- **Secondary allo-SCT**
- **Previous or concurrent cancer curatively treated ≤ 3 years prior to study entry**

Addresses

■ **Primary Sponsor**

Philipps-Universität-Marburg (vertreten durch KKS Marburg der Universität Marburg, Karl-von-Frisch-Str.4, 35043 Marburg)
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■ **Contact for Scientific Queries**

Klinik für Hämatologie, Onkologie und Immunologie
Philipps-Universität Marburg

Contact for Scientific Queries

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Sources of Monetary or Material Support

- **Commercial (pharmaceutical industry, medical engineering industry, etc.)**

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URL: **[---]***

Status

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

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Trial Publications, Results and other documents

** 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.*