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Eltrombopag for Moderate Aplastic Anemia

This study is currently recruiting participants.

Verified January 2013 by National Institutes of Health Clinical Center (CC)

Sponsor:
National Heart, Lung, and Blood Institute (NHLBI)

Information provided by (Responsible Party):
National Institutes of Health Clinical Center (CC) (National Heart, Lung, and Blood Institute (NHLBI))

ClinicalTrials.gov Identifier:
NCT01328587

First received: April 1, 2011
Last updated: May 1, 2013
Last verified: January 2013
History of Changes

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

Purpose

Background:

- Moderate **aplastic anemia** is a blood disease which may require frequent blood and platelet transfusions. Sometimes patients with this disease can be treated with immunosuppressive drugs. Not all patients respond and not all patients are suitable for this treatment.
- Thrombopoietin (TPO) is a protein made by the body. The bone marrow needs TPO to produce platelets. TPO may also be able to stimulate bone marrow stem cells to produce red cells and white cells. However, TPO cannot be given by mouth. This has led researchers to develop the drug eltrombopag, which acts in the same way and can be given by mouth. Eltrombopag has been shown to safely increase platelet numbers in healthy volunteers and in patients with other chronic blood diseases, including severe **aplastic anemia**. Researchers are interested in looking at whether eltrombopag can be given to people with moderate **aplastic anemia** and significantly low blood cell counts.

Objectives:

- To evaluate the safety and effectiveness of eltrombopag in people with moderate **aplastic anemia** who need treatment for significantly low blood cell counts.

Eligibility:

- People at least 18 years of age who have moderate **aplastic anemia** and significantly low blood cell counts.

Design:

- Patients will be screened with a physical examination, medical history, blood tests, a bone marrow biopsy, and an eye exam.
- Patients will receive eltrombopag by mouth once a day.
- Patients will have weekly blood tests to monitor the effectiveness of the treatment and adjust the dose in response to possible side effects.
- Patients may continue to take eltrombopag if their platelet count or hemoglobin increases, their requirement for platelet or blood transfusion decreases after 90 days of treatment, and there have been no serious side effects. Access to the drug will continue until the study is closed. Patients will have followup visits for 6 months after the last dose of medication.

Condition	Intervention	Phase
Eltrombopag **Aplastic Anemia** **Aplastic Anemia** Treatment Moderate **Aplastic Anemia** Moderate **Aplastic Anemia** Treatment	Drug: **Eltrombopag**	Phase 2

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

Official Title: A Pilot Study of a Thrombopoietin-Receptor Agonist (TPO-R Agonist), **Eltrombopag**, in Moderate **Aplastic Anemia** Patients

Resource links provided by NLM:

MedlinePlus related topics: Anemia Aplastic Anemia Blood Transfusion and Donation

Drug Information available for: Eltrombopag

U.S. FDA Resources

Further study details as provided by National Institutes of Health Clinical Center (CC):

Primary Outcome Measures:

- The portion of drug responders as defined by changes in the platelet count and/or platelet transfusion requirements or hemoglobin and/or PRBC transfusion requirements and the toxicity profile as measured using the CTCAE criteria. [Time Frame: 16 weeks]
  [Designated as safety issue: Yes]

Secondary Outcome Measures:

- Incidence of bleeding, changes in serum thrombopoietin level, and health related quality of life (as measured by the Medical Outcomes Study 36-Item Short Form General Health Survey, version 2 [SF36v2] Quality-Metric) measured at 16 weeks. [Time Frame: 16 weeks]
  [Designated as safety issue: Yes]

Estimated Enrollment:	38
Study Start Date:	March 2011
Estimated Study Completion Date:	December 2014
Estimated Primary Completion Date:	December 2014 (Final data collection date for primary outcome measure)

Intervention Details:

Drug: **Eltrombopag**

N/A

Detailed Description:

Moderate aplastic anemia (MAA) is a blood disease which can be effectively treated with immunosuppressive drug regimens. However, a significant number of patients have persistent cytopenias. Currently, the treatment of these patients is regular transfusion, which are expensive, inconvenient, and associated with serious side effects related to iron overload, or cytokines such as erythropoietin or G-CSF, which are expensive, and not effective in many patients.

Thrombopoietin (TPO) is a protein made by the body that is important for normal production of platelets by the bone marrow. TPO may also be able to stimulate bone marrow stem cells to produce red cells and white cells. TPO cannot be given by mouth, and as an alternative, a drug, eltrombopag, has been designed that acts in the same way as TPO but is stable and active when given by mouth. Eltrombopag has been shown to safely increase platelet numbers in healthy volunteers and in patients with chronic immune thrombocytopenic purpura (ITP). It has been recently granted accelerated approval by FDA on November 20, 2008 for the treatment of patients with chronic immune thrombocytopenic purpura (ITP) who have had an insufficient response to standard therapies.

We have previously shown encouraging results when eltrombopag is used to treat patients with severe aplastic anemia, with some patients responding with increases in platelets, red cells and white cells. Given these encouraging early preliminary results in our clinical trial using eltrombopag in SAA, and low toxicity and ease of administration of this drug, we now propose a non-randomized pilot phase II study of eltrombopag in moderate aplastic anemia patients with clinically significant thrombocytopenia or anemia. Patients with MAA may not reach criteria for SAA, but none the less may be transfusion-dependent or have significant symptoms from cytopenias. We hypothesize that patients with MAA as compared to SAA may have a better chance of response, due to better residual marrow function in MAA patients compared to SAA.

Eligible patients can have treated or untreated MAA, as well as counts meeting criteria for MAA following a partial response to treatment with immunosupression for SAA. We will also include patients with bone marrow failure and unilineage cytopenia. Treatment response for the platelet lineage is defined as platelet count increases to 20,000/microL above baseline at 16 weeks, or freedom from platelet transfusions for greater than or equal to 8 weeks in transfusion-dependent patients. For patients with anemia (untransfused hemoglobin less than or equal to 8.5 g/dL), a treatment response will be an increase in Hb by greater than or equal to 1.5g/dl at four months, measured on at least 2 serial measurements and sustained for 1 month or more without transfusion support OR for transfusion dependent patients, reduction of units of RCC transfused by 50 percent/8 weeks compared with the pretreatment transfusion number in the previous 8 weeks or transfusion independence (no transfusions for greater than or equal to 8 weeks).

The primary objective is to assess the safety and efficacy of the oral thrombopoietin receptor agonist (TPO-R agonist) eltrombopag in moderate aplastic anemia patients or patients with bone marrow failure and unilineage cytopenia. Secondary objectives include the analysis of the incidence and severity of bleeding and the impact on quality of life.

Eligibility

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

Criteria

- INCLUSION CRITERIA:

Current diagnosis of moderate aplastic anemia or unilineage bone marrow failure disorders.

Moderate aplastic anemia is defined as aplastic anemia (hypocellular bone marrow for age) with no evidence for other disease processes causing marrow failure, and depression of at least two out of three blood counts below the normal values:

- ANC less than or equal to l200/mm(3)
- platelet count less than or equal to 70,000/mm(3)
- anemia with hemoglobin less than or equal to 8.5 g/dl and absolute reticulocyte count less than or equal to 60,000/mm(3) in transfusion-dependent patients but not fulfilling the criteria for severe disease defined by depression of two of the three peripheral counts:
- ANC less than or equal to 500/mm(3)
- platelet count less than or equal to 20,000/mm(3)
- reticulocyte count less than or equal to 60,000/mm(3)

Unilineage bone marrow failure disorders are defined as hemoglobin less than 8.5 g/dl and reticulocyte count less than 60,000 or red cell transfusion dependent and hypocellular bone marrow for age OR thrombocytopenia less than or equal to 30,000/uL or platelet transfussion dependent with hypocellular bone marrow for age with no evidence of viral or drug suppression of the marrow, dysplasia, or underproduction anemias secondary to B12, folate, iron, or other reversible causes.

One or more of platelet count less than or equal to 30,000/microL, Hemoglobin less than or equal to 8.5g/dl OR platelet and/or red cell transfusion dependent. Platelet transfusion dependent is defined as the need for platelet transfusion due to platelet counts of < 10,000/microL with no bleeding (prophylactic transfusion) or < 20,000/microL with bleeding (therapeutic transfusion). Red cell transfusion dependent is defined as transfusion of greater than 4 units of blood in the 8 weeks prior to study entry.

Age greater than or equal to 18 years old

EXCLUSION CRITERIA:

Diagnosis of Fanconi anemia

Counts that meet criteria for severe aplastic anemia

Infection not adequately responding to appropriate therapy

Patients with a PNH clone size in neutrophils of greater than or equal to 50 percent

HIV positivity

Creatinine > 2.5 mg/dL

Bilirubin > 2.0 mg/dL, including congenital abnormalities in the bilirubin count

SGOT or SGPT > 5 times the upper limit of normal

Hypersensitivity to eltrombopag or its components

Female subjects who are nursing or pregnant or are unwilling to take oral contraceptives or refrain from pregnancy if of childbearing potential

History of malignancy other than localized tumors diagnosed more than one year previously and treated surgically with curative intent (for instance squamous cell or other skin cancers, stage 1 breast cancer, cervical carcinoma in situ, etc) and any clonal abnormality associated with Myelodysplastic Syndrome

Unable to understand the investigational nature of the study or give informed consent (i.e. decisionally impaired)

History of congestive heart failure, arrhythmia requiring chronic treatment, arterial or venous thrombosis (other than line thrombosis) within the last 1 year, or myocardial infarction within 3 months before enrollment

ECOG Performance Status of 3 or greater

Treatment with horse or rabbit ATG or Campath within 6 months of study entry.

Treatment with cytokines such as G-CSF or Erythropoeitin.

Subjects with liver cirrhosis including subjects infected with Hepatitis B or C

Life expectancy of less than 3 months

Contacts and Locations

Please refer to this study by its ClinicalTrials.gov identifier: NCT01328587

Contacts

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Sponsors and Collaborators

National Heart, Lung, and Blood Institute (NHLBI)

Investigators

Principal Investigator: Ronan G Desmond, M.D. National Heart, Lung, and Blood Institute (NHLBI)

More Information

Additional Information:

NIH Clinical Center Detailed Web Page

Publications:

Young NS, Barrett AJ. The treatment of severe acquired aplastic anemia. Blood. 1995 Jun 15;85(12):3367-77. Review. No abstract available.

Young NS, Calado RT, Scheinberg P. Current concepts in the pathophysiology and treatment of aplastic anemia. Blood. 2006 Oct 15;108(8):2509-19. Epub 2006 Jun 15. Review.

Zeng W, Maciejewski JP, Chen G, Risitano AM, Kirby M, Kajigaya S, Young NS. Selective reduction of natural killer T cells in the bone marrow of aplastic anaemia. Br J Haematol. 2002 Dec;119(3):803-9.

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Moderate **Aplastic Anemia**
Moderate **Aplastic Anemia** Treatment

Additional relevant MeSH terms:
Anemia
Anemia, **Aplastic**
Hematologic Diseases
Bone Marrow Diseases

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