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Trial record **3 of 10** for: revolade anemia

Previous Study | Return to List | Next Study

A Pilot Study of a Thrombopoietin-Receptor Agonist (TPO-R Agonist), Eltrombopag, in Aplastic Anemia Patients With Immunosuppressive-Therapy Refractory Thrombocytopenia

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:
NCT00922883

First received: June 16, 2009
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

Severe aplastic **anemia** (SAA) is a life-threatening blood disease which can be effectively treated with immunosuppressive drug regimens or allogeneic stem cell transplantation. However, 20-40% of patients without transplant options do not respond to immunosuppressive therapies, and have persistent severe thrombocytopenia. Even patients that respond to immunosuppressive therapies with an improvement in their life-threatening neutropenia sometimes have persistent thrombocytopenia. Both groups of patients (i.e. nonresponders to immunosuppressive therapy and responders with persistent thrombocytopenia) require regular platelet transfusions, which are expensive and inconvenient, and are a risk for further serious bleeding complications.

Thrombopoietin (TPO) is the principal endogenous regulator of platelet production. On binding to the megakaryocyte progenitor TPO receptor, TPO initiates a number of signal transduction events to increase the production of mature megakaryocytes and platelets. Thrombopoietin also has stimulatory effects on more primitive multilineage progenitors and stem cells in vitro and in animal models. A 2nd generation small molecule TPO-agonist, **eltrombopag** (**Promacta**(Registered Trademark)) has been shown to increase platelets in healthy subjects and in thrombocytopenic patients with chronic immune thrombocytopenic purpura (ITP) and hepatitis C virus (HCV) infection. **Eltrombopag** is administered orally and has been well-tolerated in clinical trials. Unlike recombinant TPO, it has not been found to induce autoantibodies. **Eltrombopag** received FDA accelerated approval on Nov 20, 2008 for the treatment of thrombocytopenia in patients with chronic immune (idiopathic) thrombocytopenic purpura who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy. Because a paucity of megakaryocytes and decreased platelet production is responsible for thrombocytopenia in aplastic **anemia** patients, we now propose this Phase 2, non-randomized pilot study of **eltrombopag** in aplastic **anemia** patients with immunosuppressive therapy refractory thrombocytopenia.

Subjects will initiate study medication at an oral dose of 50 mg/day (25 mg/day for East Asians), which will be increased or decreased as clinically indicated to the lowest dose that maintains a stable platelet count 20,000/(micro)L above baseline while maximizing tolerability. Treatment response is defined as platelet count increases to 20,000/(micro)L above baseline at three months. Subjects with response at 3 months may continue study medication (extended access) until they meet an off study criteria.

Condition	Intervention	Phase
Anemia, Aplastic **Anemia**, Hypoplastic Thrombocytopenia	Drug: **Eltrombopag** (**Promacta**) 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 Aplastic **Anemia** Patients With Immunosuppressive-Therapy Refractory Thrombocytopenia

Resource links provided by NLM:

MedlinePlus related topics: Anemia Aplastic Anemia

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 and the toxicity profile as measured at 12 weeks using the CTCAE criteria. [Time Frame: 12 weeks] [Designated as safety issue: Yes]

Secondary Outcome Measures:

- Incidence of bleeding; changes in serum thrombopoietin level (as measured by enzyme-linked immunosorbent assay, R& D Systems), and health related quality of life (as measured by the Medical Outcomes Study 36-item Short Form General Health Su...

Estimated Enrollment:	50
Study Start Date:	May 2009
Estimated Study Completion Date:	December 2015
Estimated Primary Completion Date:	December 2013 (Final data collection date for primary outcome measure)

Intervention Details:

Drug: **Eltrombopag** (**Promacta**)

N/A

Drug: **Eltrombopag**

N/A

Show Detailed Description

Eligibility

Ages Eligible for Study:	12 Years and older
Genders Eligible for Study:	Both
Accepts Healthy Volunteers:	No

Criteria

- INCLUSION CRITERIA:
  a. Diagnosis of aplastic anemia, with refractory thrombocytopenia following at least one treatment course of horse or rabbit ATG/cyclosporine.
  b. Platelet count less than or equal to 30,000/microL
  c. Age greater than or equal to 12 years old

EXCLUSION CRITERIA:

1. Diagnosis of Fanconi anemia
2. Infection not adequately responding to appropriate therapy
3. Patients with a PNH clone size in neutrophils of greater than or equal to 50%
4. HIV positivity
5. Creatinine > 2.5
6. Bilirubin > 2.0
7. SGOT or SGPT > 5 times the upper limit of normal
8. Hypersensitivity to eltrombopag or its components
9. Female subjects who are nursing or pregnant or are unwilling to take oral contraceptives or refrain from pregnancy if of childbearing potential
10. 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)
11. Unable to understand the investigational nature of the study or give informed consent
12. History of congestive heart failure arrhythmia requiring chronic treatment, arterial or venous thrombosis (not excluding line thrombosis) within the last 1 year, or myocardial infarction within 3 months before enrollment
13. ECOG Performance Status of 3 or greater
14. Treatment with horse or rabbit ATG or Campath within 6 months of study entry. Concurrent stable treatment with cyclosporine or G-CSF is permitted.

Contacts and Locations

Please refer to this study by its ClinicalTrials.gov identifier: NCT00922883

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 EXIT

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.

Emmons RV, Reid DM, Cohen RL, Meng G, Young NS, Dunbar CE, Shulman NR. Human thrombopoietin levels are high when thrombocytopenia is due to megakaryocyte deficiency and low when due to increased platelet destruction. Blood. 1996 May 15;87(10):4068-71.

Additional publications automatically indexed to this study by ClinicalTrials.gov Identifier (NCT Number):

Olnes MJ, Scheinberg P, Calvo KR, Desmond R, Tang Y, Dumitriu B, Parikh AR, Soto S, Biancotto A, Feng X, Lozier J, Wu CO, Young NS, Dunbar CE. Eltrombopag and improved hematopoiesis in refractory aplastic anemia. N Engl J Med. 2012 Jul 5;367(1):11-9.

Responsible Party:	National Institutes of Health Clinical Center (CC) (National Heart, Lung, and Blood Institute (NHLBI))
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Study First Received:	June 16, 2009
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Health Authority:	United States: Federal Government

Keywords provided by National Institutes of Health Clinical Center (CC):
Promacta
SAA
Aplastic **Anemia**
Thrombocytopenia

Additional relevant MeSH terms:

Anemia	Blood Platelet Disorders
Anemia, Aplastic	Immunosuppressive Agents
Thrombocytopenia	Immunologic Factors
Hematologic Diseases	Physiological Effects of Drugs
Bone Marrow Diseases	Pharmacologic Actions

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