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Trial record **5 of 6** for: aplastic anaemia | eltrombopag

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Eltrombopag With Standard Immunosuppression for Severe Aplastic Anemia

This study is currently recruiting participants.

Verified March 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:
NCT01623167

First received: June 14, 2012
Last updated: August 2, 2013
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History of Changes

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

Purpose

Background:

- Severe **aplastic anemia** is a rare and serious blood disorder. It happens when the immune system starts to attack the bone marrow cells. This causes the bone marrow to stop making red blood cells, platelets, and white blood cells. Standard treatment for this disease is horse-ATG and cyclosporine, which suppress the immune system and stop it from attacking the bone marrow. However, this treatment does not work in all people. Some people still have poor blood cell counts even after treatment.
- Eltrombopag is a drug designed to mimic a protein in the body called thrombopoietin. It helps the body to make more platelets. It may also cause the body to make more red and white blood cells. Studies have shown that eltrombopag may be useful when added to standard treatment for severe **aplastic anemia**. It may help improve poor blood cell counts.

Objectives:

- To test the safety and effectiveness of adding eltrombopag to standard immunosuppressive therapy for severe **aplastic anemia**.

Eligibility:

- Individuals at least 2 years of age who have severe **aplastic anemia** that has not yet been treated.

Design:

- Participants will be screened with a physical exam, medical history, and blood tests. Blood and urine samples will be collected.
- Participants will start treatment with horse-ATG and cyclosporine. Treatment will be given according to the standard of care for the disease.
- After 14 days, participants will start taking eltrombopag. They will take eltrombopag for up to 6 months.
- Participants may receive other medications to prevent infections during treatment.
- Treatment will be monitored with frequent blood tests. Participants will also fill out questionnaires about their symptoms and their quality of life.

Condition	Intervention	Phase
Aplastic Anemia Neutropenia Pancytopenia **Anemia** Thrombocytopenia	Drug: **Eltrombopag** Drug: Horse Anti-Thymocyte Globulin (ATG) Drug: Cyclosporine A (CSA)	Phase 1 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: **Eltrombopag** Added to Standard Immunosuppression in Treatment-Naive Severe **Aplastic Anemia**

Resource links provided by NLM:

Genetics Home Reference related topics: cyclic neutropenia

MedlinePlus related topics: Anemia Aplastic Anemia

Drug Information available for: Cyclosporine Antilymphocyte Serum Eltrombopag

U.S. FDA Resources

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

Primary Outcome Measures:

- The primary endpoint will be the rate of complete hematologic response at six months.

Secondary Outcome Measures:

- Secondary endpoints are relapse, robust hematologic blood count recovery at 3, 6, and 12 months, survival, clonal evolution to myelodysplasia and leukemia, and marrow stem cell content.

Estimated Enrollment: 31
Study Start Date: June 2012
Estimated Study Completion Date: May 2015
Estimated Primary Completion Date: May 2015 (Final data collection date for primary outcome measure)

Intervention Details:

Drug: **Eltrombopag**
N/A
Drug: Horse Anti-Thymocyte Globulin (ATG)
N/A
Drug: Cyclosporine A (CSA)

N/A

Detailed Description:

Severe aplastic anemia (SAA) is a life-threatening bone marrow failure disorder characterized by pancytopenia and a hypocellular bone marrow. Allogeneic bone marrow transplantation offers the opportunity for cure in younger patients, but most are not suitable candidates for transplantation due to advanced age or lack of a histocompatible donor. Comparable long-term survival in SAA is attainable with immunosuppressive treatment with horse anti-thymocyte globulin (ATG) and cyclosporine (CsA). However, of those patients treated with horse ATG (h-ATG)/CsA, one quarter to one third will not respond, and 30-40% of responders relapse. The majority of the hematologic responses observed following initial h-ATG/CsA are partial, with only a few patients achieving normal blood counts. Furthermore, analysis of our own extensive clinical data suggests that poor blood count responses to a single course of ATG (non-robust responders), even when transfusion-independence is achieved, predicts a worse prognosis than when robust hematologic improvement is achieved (protocol 90-H-0146). The explanation for partial recovery and relapse are not fully understood, but incomplete elimination of auto-reactive T cells and insufficient stem cell reserve are both possible. Furthermore, 10-15% of SAA patients treated with standard immunosuppression will develop an abnormal karyotype in follow-up, with monosomy 7 being most common, which portends progression to myelodysplasia and leukemia. In contrast, malignant clonal evolution is rare in complete responders to immunosuppression. Although horse ATG/CsA represented a major advance in the treatment of SAA, refractoriness, incomplete responses, relapse, and clonal evolution limit the success of this modality. Thus, newer regimens are needed to address these limitations, and provide a better alternative to stem cell transplantation.

One approach to augment the quality of hematologic responses is to improve underlying stem cell function. Previous attempts to improve responses in SAA with hematopoietic cytokines including erythropoietin, G-CSF, and stem cell factor, have failed. Thrombopoietin (TPO) is the principal endogenous regulator of platelet production. In addition, TPO also has stimulatory effects on more primitive multilineage progenitors and stem cells in vitro and in animal models. Eltrombopag (Promacta(Registered Trademark)), an oral 2nd generation small molecule TPO-agonist, is currently approved for treatment of chronic immune thrombocytopenic purpura (ITP). Eltrombopag increases platelets in healthy subjects and in thrombocytopenic patients with chronic ITP and hepatitis C virus (HCV)-infection. Our Branch recently completed a pilot study of eltrombopag in refractory SAA. We saw encouraging clinical results in a cohort of patients who have failed on average two prior immunosuppressive regimens(Olnes et al. ASH Annual Meeting Abstracts, San Diego, CA, 2011, oral presentation). Of the twenty-five SAA patients treated with eltrombopag by mouth for three months, eleven (44%) patients met protocol criteria of clinically meaningful hematologic responses, without significant toxicity. Nine patients demonstrated an improvement in thrombocytopenia (> 20k/mL increase or transfusion independence), hemoglobin improved in two patients (> 1.5g/dL or achieved transfusion independence, and four patients had a significant response in their neutrophil count. When responders continued the drug beyond three months, the hematologic response to eltrombopag increased; a trilineage response was observed in four patients, and a bilineage response occurred in another four, with median follow-up of 13 months. These results suggest that stem cell depletion, a major component of the pathophysiology of SAA, might be directly addressed by eltrombopag administration. The aim of the current study would be to improve the hematologic response rate and its quality, as well as prevent late complications such as relapse and clonal progression, by addition of eltrombopag to standard immunosuppressive therapy.

This trial will evaluate the safety and efficacy of combining eltrombopag with standard hATG/CSA as first line therapy in patients with SAA. The primary endpoint will be the rate of complete hematologic response at six months. Secondary endpoints are relapse, robust hematologic blood count recovery at 3, 6, and 12 months, survival, clonal evolution to myelodysplasia and leukemia, and marrow stem cell content.

Eligibility

Ages Eligible for Study:	2 Years and older
Genders Eligible for Study:	Both
Accepts Healthy Volunteers:	No

Criteria

-INCLUSION CRITERIA:

1. Severe aplastic anemia characterized by Bone marrow cellularity less than 30 percent (excluding lymphocytes) AND At least two of the following:
   - Absolute neutrophil count less than 500/microL
   - Platelet count less than 20,000/microL

   Absolute reticulocyte count less than 60,000/microL
2. Age greater than or equal to 2 years old
3. Weight greater than 12 kg

EXCLUSION CRITERIA:

1. Diagnosis of Fanconi anemia
2. Evidence of a clonal disorder on cytogenetics performed within 12 weeks of study entry. Patients with super severe neutropenia (ANC less than 200 /microL) will not be excluded initially if cytogenetics are not available or pending. If evidence of a clonal disorder consistent with myelodysplasia is later identified, the patient will go off study.
3. Prior immunosuppressive therapy with any ATG, alemtuzumab, or high dose cyclophosphamide
4. SGOT or SGPT greater than 3 times the upper limit of normal
5. Subjects with liver cirrhosis
6. Hypersensitivity to eltrombopag or its components
7. Infection not adequately responding to appropriate therapy
8. Moribund status or concurrent hepatic, renal, cardiac, neurologic, pulmonary, infectious, or metabolic disease of such severity that it would preclude the patient's ability to tolerate protocol therapy, or that death within 7-10 days is likely
9. Potential subjects with cancer who are on active chemotherapeutic treatment or who take drugs with hematological effects will not be eligible
10. Current pregnancy, or unwillingness to take oral contraceptives or use a barrier method of birth control or practice abstinence to refrain from pregnancy if of childbearing potential during the course of this study

11. Inability to understand the investigational nature of the study or to give informed consent

Contacts and Locations

Please refer to this study by its ClinicalTrials.gov identifier: NCT01623167

Contacts

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Locations

United States, Maryland

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Contact: For more information at the NIH Clinical Center contact Patient Recruitment and Public Liaison Office (PRPL) 800-411-1222 ext TTY

Sponsors and Collaborators

National Heart, Lung, and Blood Institute (NHLBI)

Investigators

Principal Investigator: Danielle M Townsley, M.D. National Heart, Lung, and Blood Institute (NHLBI)

More Information

Additional Information:

NIH Clinical Center Detailed Web Page EXIT

Publications:

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.

Zoumbos NC, Gascon P, Djeu JY, Trost SR, Young NS. Circulating activated suppressor T lymphocytes in aplastic anemia. N Engl J Med. 1985 Jan 31;312(5):257-65.

Young NS, Leonard E, Platanias L. Lymphocytes and lymphokines in aplastic anemia: pathogenic role and implications for pathogenesis. Blood Cells. 1987;13(1-2):87-100. Review.

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Keywords provided by National Institutes of Health Clinical Center (CC):
T-Cells
Immunosuppression
Hematopoesis
Autoimmunity
Thrombocytopenia

Additional relevant MeSH terms:

Anemia
Anemia, **Aplastic**
Neutropenia
Pancytopenia
Thrombocytopenia
Hematologic Diseases
Bone Marrow Diseases
Agranulocytosis
Leukopenia
Leukocyte Disorders
Blood Platelet Disorders
Antilymphocyte Serum
Cyclosporins
Cyclosporine
Immunosuppressive Agents
Immunologic Factors
Physiological Effects of Drugs
Pharmacologic Actions
Enzyme Inhibitors
Molecular Mechanisms of Pharmacological Action
Antifungal Agents
Anti-Infective Agents
Therapeutic Uses
Dermatologic Agents
Antirheumatic Agents

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