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Eltrombopag Treatment of Thrombocytopenia in Subjects With Advanced Myelodysplastic Syndrome (MDS) or Secondary Acute Myeloid Leukemia After MDS (sAML/MDS)

This study is ongoing, but not recruiting participants.

Sponsor:
GlaxoSmithKline

Information provided by (Responsible Party):
GlaxoSmithKline

ClinicalTrials.gov Identifier:
NCT00903422

First received: May 14, 2009
Last updated: December 19, 2013
Last verified: December 2013
History of Changes

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

Purpose

This study will evaluate the safety and tolerability of eltrombopag in the treatment of low platelet counts in adult subjects with advanced myelodysplastic syndrome (MDS), secondary acute myeloid leukemia after MDS (sAML/MDS), or de novo AML that are relapsed, refractory or ineligible to receive azacitidine, decitabine, intensive chemotherapy or autologous/allogeneic stem cell transplantation. This is a placebo-controlled study in which patients will receive study medication daily for 6 months, during which time the dose of study medication may be adjusted based upon individual platelet counts and bone marrow blast counts. All subjects will receive best standard of care (platelet transfusions, mild chemotherapy, cytokines, valproic acid, all-trans retinoic acid, ESAs or G-CSF) in addition to study medication. Subjects taking placebo may be allowed to crossover to eltrombopag treatment if a clinically and statistically significant improvement in bone marrow blast counts is seen in subjects treated with eltrombopag.

Condition	Intervention	Phase
Myelodysplastic Syndrome	Drug: eltrombopag olamine Other: Placebo	Phase 1

Study Type: Interventional
Study Design: Allocation: Randomized
Endpoint Classification: Safety Study
Intervention Model: Parallel Assignment
Masking: Double Blind (Subject, Caregiver, Investigator)
Primary Purpose: Treatment

Official Title: Study PMA112509, a Phase I/II Study of Eltrombopag in Thrombocytopenic Subjects With Advanced Myelodysplastic Syndrome (MDS) or Secondary Acute Myeloid Leukemia After MDS (sAML/MDS)

Resource links provided by NLM:

Genetics Home Reference related topics: core binding factor acute myeloid leukemia cytogenetically normal acute myeloid leukemia familial acute myeloid leukemia with mutated CEBPA

MedlinePlus related topics: Acute Myeloid Leukemia Leukemia Myelodysplastic Syndromes

Drug Information available for: Eltrombopag Eltrombopag olamine

Genetic and Rare Diseases Information Center resources: Leukemia, Myeloid Myelodysplastic Syndromes Acute Myelocytic Leukemia Acute Non Lymphoblastic Leukemia

U.S. FDA Resources

Further study details as provided by GlaxoSmithKline:

Primary Outcome Measures:

- Safety and tolerability parameters including non-hematological laboratory Grade 3/Grade 4 toxicities, change in bone marrow blast counts from baseline and adverse events reporting. [Time Frame: Approximately 46 months] [Designated as safety issue: No]

Secondary Outcome Measures:

- Proportion of subjects with a baseline platelet count <20 Gi/L and an increase to >20 Gi/L and by at least 2x baseline; or a baseline platelet count between >=20-<30 Gi/L and an absolute platelet count increase to >=50 Gi/L at any time during treatment. [Time Frame: Approx. 46 months] [Designated as safety issue: No]

- Frequency and number of units of platelet transfusions during the treatment and follow-up periods for eltrombopag- and placebo-treated subjects. [Time Frame: approx 46 months] [Designated as safety issue: No]
- The incidence and severity of bleeding events, measured using the World Health Organization (WHO) Bleeding Scale, during the treatment and 4 week follow-up periods for eltrombopag- and placebo-treated subjects. [Time Frame: approx. 46 months] [Designated as safety issue: No]
- Overall survival (OS) of eltrombopag- and placebo-treated subjects. [Time Frame: approx. 46 months] [Designated as safety issue: No]
- Change in health-related quality of life as measured using the EQ-5D questionnaire. [Time Frame: approx. 46 months] [Designated as safety issue: No]

Enrollment: 98
Study Start Date: May 2009
Estimated Study Completion Date: December 2013
Primary Completion Date: June 2012 (Final data collection date for primary outcome measure)

Arms	Assigned Interventions
Active Comparator: Eltrombopag Eltrombopag	Drug: eltrombopag olamine thrombopoietin receptor agonist
Placebo Comparator: Placebo Placebo	Other: Placebo Placebo tablets with no active pharmaceutical ingredient

Detailed Description:

A double-blind, randomized, placebo-controlled phase I/II study to evaluate the safety and tolerability of eltrombopag olamine, a thrombopoietin receptor agonist, administered for 6 months as oral tablets once daily in adult subjects with advanced MDS, sAML/MDS, or de novo AML. Study medication may be increased up to 300 mg (150 mg maximum dose for East Asian subjects), based upon individual platelet counts and bone marrow blast counts.

Eligibility

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

Criteria

Inclusion Criteria:

- Adult subjects (18 years of age or older) with advanced MDS, sAML/MDS, or de novo AML with >=10% and <=50% blasts in bone marrow. Peripheral blood blast change over time should not be suggestive of highly proliferative disease (as judged by the investigator).
- Subjects must be dependent on regular platelet transfusions or have a platelet count taken within the 4 weeks prior to randomization that is <30 Gi/L.
- Subjects must be relapsed, refractory or ineligible to receive standard treatment options of azacitidine and decitabine and must be relapsed, refractory or ineligible to receive intensive chemotherapy or autologous/allogeneic stem cell transplantation. A subject may be considered relapsed/refractory to a standard treatment if it is discontinued due to lack of efficacy. For subjects ineligible for standard treatments, it is permissible to start one of these standard treatments while on study medication if the Investigator considers that the subject becomes eligible during the course of the study.
- Prior therapy with demethylating agents (azacitidine or decitabine), lenalidomide or IL-11(oprelvekin) must have been completed at least 4 weeks before Day 1; antithymocyte/antilymphocyte globulin, intensive chemotherapy, or autologous/allogeneic stem cell transplantation must have been completed at least 2 months before Day 1. If a subject must discontinue a course of therapy due to lack of efficacy, the washout periods listed above do not apply (and the patient may be screened and randomized immediately if other eligibility criteria are met).
- Subjects must have platelet count and platelet transfusion data available over a period of 4 weeks prior to randomization.
- Subjects with advanced MDS, sAML/MDS, or de novo AML must have stable disease indicated by a doubling time of peripheral blast counts >7 days during screening.
- During the 4 weeks prior to randomization, subjects must have a baseline bone marrow examination including the following:
- cytomorphology to confirm bone marrow blasts between 10-50%,
- cytogenetics (provide only most prevalent abnormal clone),

The results of the above tests are required prior to subject randomization.

- Supportive/palliative therapies such as cytokines (except for IL-11; oprelvekin), valproic acid, all-trans retinoic acid or mild chemotherapy are allowed if part of the local SOC, provided those therapies have been at a stable dose for 4 weeks. If the subject chooses to discontinue these therapies prior to study entry, they must be completed 4 weeks prior to enrollment into this study, unless the therapy is discontinued due to lack of efficacy. Erythropoiesis-stimulating agents (ESAs) in anemic subjects or granulocyte colony-stimulating factor (G-CSF) in subjects with severe neutropenia and recurrent infections are allowed during the study as per accepted standards. Subjects who enter the study on ESAs or G-CSF should continue at the same dose schedule until the optimal dose of study medication has been established.
- ECOG Status 0-3.
- Subject is able to understand and comply with protocol requirements and instructions.
- Subject has signed and dated informed consent.
- Prothrombin time (PT/INR) and activated partial thromboplastin time (aPTT) must be within 80 to 120% of the normal range at baseline.
- Adequate baseline organ function defined by the criteria below:

- total bilirubin (except for Gilbert's Syndrome) <= 1.5xULN
- ALT and AST <= 3xULN
- creatinine <= 2xULN
- albumin must not be below the lower limit of normal (LLN) by more than 20%.
- Subject is practicing an acceptable method of contraception (documented in chart). Female subjects (or female partners of male subjects) must either be of non-childbearing potential (hysterectomy, bilateral oophorectomy, bilateral tubal ligation or post-menopausal >1 year), or of childbearing potential and use 1 of the following highly effective methods of contraception (i.e., Pearl Index <1.0%) from 2 weeks prior to administration of study medication, throughout the study, and 28 days after completion or premature discontinuation from the study:
- Complete abstinence from intercourse;
- Intrauterine device (IUD);
- Two forms of barrier contraception (diaphragm plus spermicide, and for males condom plus spermicide);
- Male partner is sterile prior to entry into the study and is the only partner of the female;
- Systemic contraceptives (combined or progesterone only).

Exclusion Criteria:

- Subjects with a diagnosis of acute promyelocytic leukemia.
- History of treatment for cancer (other than MDS, sAML/MDS, or de novo AML) with systemic chemotherapy and/or radiotherapy within the last 2 years.
- History of treatment with romiplostim or other TPO-R agonists.
- Pre-existing cardiovascular disease (including congestive heart failure, New York Heart Association [NYHA] Grade III/IV), or arrhythmia known to increase the risk of thromboembolic events (e.g. atrial fibrillation), or subjects with a QTc >450 msec (QTc >480 msec for subjects with Bundle Branch Block).
- Bone marrow fibrosis that leads to an inability to aspirate marrow for assessment.
- Spleen size >14 cm (length as per ultrasound examination).
- Leukocytosis >=25,000/uL prior to Day 1 of study medication.
- Female subjects who are nursing or pregnant (positive serum or urine Beta-human chorionic gonadotropin [B-hCG] pregnancy test) at screening or pre-dose on Day 1.
- Current alcohol or drug abuse.
- Treatment with an investigational drug within 30 days or 5 half-lives (whichever is longer) preceding the first dose of study medication.
- Active and uncontrolled infections.
- Subjects infected with Hepatitis B, C or Human Immunodeficiency Virus (HIV).
- Subjects with liver cirrhosis.

Contacts and Locations

Please refer to this study by its ClinicalTrials.gov identifier: NCT00903422

Show 65 Study Locations

Sponsors and Collaborators

GlaxoSmithKline

Investigators

Study Director: GSK Clinical Trials GlaxoSmithKline

More Information

No publications provided

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ClinicalTrials.gov Identifier:	NCT00903422 History of Changes
Other Study ID Numbers:	112509
Study First Received:	May 14, 2009
Last Updated:	December 19, 2013
Health Authority:	Hong Kong: Department of Health United States: Food and Drug Administration

Keywords provided by GlaxoSmithKline:

Advanced Myelodysplastic Syndrome	Thrombopoietin
Thrombocytopenia	MDS
sAML/MDS	Thrombopoietin receptor agonist
Eltrombopag	secondary Acute Myeloid Leukemia after MDS
TPO-R agonist	Platelets
de novo AML	

Additional relevant MeSH terms:

Leukemia	Neoplasms by Histologic Type
Leukemia, Myeloid, Acute	Neoplasms
Leukemia, Myeloid	Bone Marrow Diseases
Myelodysplastic Syndromes	Hematologic Diseases
Preleukemia	Precancerous Conditions
Thrombocytopenia	Blood Platelet Disorders

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