Dose Ranging Pharmacokinetics and Pharmacodynamics Study With Mepolizumab in Asthma Patients With Elevated Eosinophils

This study is currently recruiting participants.

Verified on June 2011 by GlaxoSmithKline

First Received on May 12, 2011. Last Updated on June 23, 2011 History of Changes

Sponsor:	GlaxoSmithKline
Information provided by:	GlaxoSmithKline
ClinicalTrials.gov Identifier:	NCT01366521

Purpose

A multi-center, randomized, open-label, parallel-group, repeat dose study in asthma patients with elevated eosinophils. Eligible subjects will receive 3 doses (28 days apart) of **mepolizumab** given intravenous (IV) or subcutaneously (SC). Blood samples for safety, pharmacokinetics (PK), pharmacodynamics (PD) and immunogenicity analysis, as well as safety/tolerability assessments will be collected throughout the study

Condition	Intervention	Phase
Asthma	Biological: **Mepolizumab** 250 mg subcutaneous (SC) Biological: **Mepolizumab** 125 mg subcutaneous (SC) Biological: **Mepolizumab** 12.5 mg subcutaneous (SC)	Phase II

Study Type: Interventional

Study Design: Allocation: Randomized
Endpoint Classification: Pharmacokinetics/Dynamics Study
Intervention Model: Parallel Assignment
Masking: Open Label
Primary Purpose: Treatment

Official Title: A Multicenter, Open-label, Dose Ranging Study to Determine the Pharmacokinetics and Pharmacodynamics of **Mepolizumab** Administered Intravenously or Subcutaneously to Adult Asthmatic Subjects With Elevated Blood Eosinophil Levels

Resource links provided by NLM:

MedlinePlus related topics: Asthma

Drug Information available for: Mepolizumab

U.S. FDA Resources

Further study details as provided by GlaxoSmithKline:

Primary Outcome Measures:

- Change from baseline in blood eosinophil levels
  [Time Frame: 140 days] [Designated as safety issue: No]
- Area under the blood eosinophil time curve (AUC)
  [Time Frame: 140 days] [Designated as safety issue: No]
- maximum change from baseline in blood eosinophils (Emax)
  [Time Frame: 140 days] [Designated as safety issue: No]
- time to maximum change in blood eosinophil levels (Tmaxeos)
  [Time Frame: 140 days] [Designated as safety issue: No]
- time to 50% eosinophil repletion (Trep) [Time Frame: 140 days]
  [Designated as safety issue: No]
- Area under the plasma-concentration time curve (AUC) of **mepolizumab** [Time Frame: 140 days]
  [Designated as safety issue: No]
- maximum plasma concentration (Cmax) of **mepolizumab**
  [Time Frame: 140 days] [Designated as safety issue: No]
- time to Cmax (Tmax) of **mepolizumab** [Time Frame: 140 days]
  [Designated as safety issue: No]
- terminal half-life (t½) of **mepolizumab** [Time Frame: 140 days]
  [Designated as safety issue: No]

Secondary Outcome Measures:

- area under the curve (AUC) of **mepolizumab** [Time Frame: 140 days] [Designated as safety issue: No]

  To assess the relative bioavailability of mepolizumab administered subcutaneously, as compared to mepolizumab administered intravenously

- maximum plasma concentration (Cmax) of **mepolizumab**
  [Time Frame: 140 days] [Designated as safety issue: No]

  To assess the relative bioavailability of mepolizumab administered subcutaneously, as compared to mepolizumab administered intravenously

- Levels of anti-**mepolizumab** antibodies [Time Frame: 140 days] [Designated as safety issue: No]

  To assess the immunogenicity of repeat doses of mepolizumab

- Spontaneous and elicited adverse events (AEs)
  [Time Frame: 140 days] [Designated as safety issue: No]

  safety assessment

- change from baseline in vital signs [Time Frame: 140 days]
  [Designated as safety issue: No]

  safety assessment

- change from baseline in electrocardiogram (ECG)
  [Time Frame: 140 days] [Designated as safety issue: No]

  safety assessment

- change from baseline in clinical laboratory [Time Frame: 140 days] [Designated as safety issue: No]

  safety assessment

Estimated Enrollment:	65
Study Start Date:	February 2011
Estimated Study Completion Date:	November 2011
Estimated Primary Completion Date:	October 2011 (Final data collection date for primary outcome measure)

Arms	Assigned Interventions

Mepolizumab: Experimental Monoclonal antibody Interventions: • Biological: **Mepolizumab** 250 mg subcutaneous (SC) • Biological: **Mepolizumab** 125 mg subcutaneous (SC) • Biological: **Mepolizumab** 12.5 mg subcutaneous (SC)	Biological: **Mepolizumab** 250 mg subcutaneous (SC) 250 mg subcutaneous (SC) Biological: **Mepolizumab** 125 mg subcutaneous (SC) 125 mg subcutaneous (SC) Biological: **Mepolizumab** 12.5 mg subcutaneous (SC) 12.5 mg subcutaneous (SC)

Detailed Description:

Mepolizumab (SB-240563) is a humanized monoclonal antibody that blocks human interleukin 5 (IL-5) from binding to its receptor. Mepolizumab is currently under development for severe refractory asthma and a Phase IIB dose-ranging study using the IV route of administration is currently on-going. This study will be a multi-center, randomized, open-label, parallel-group, repeat dose study conducted in approximately 65 subjects with established asthma and elevated blood eosinophil levels. Dosing will occur on three occasions, every four weeks [Day 1, Day 28 (+/- 3 days) and Day 56 (+/- 3 days)]. Blood samples for safety, pharmacodynamics (PD), pharmacokinetics (PK) and immunogenicity analysis, as well safety and tolerability assessments will be collected/assessed throughout the study. Each subject will participate in the study for up to approximately 22 weeks, including screening, dosing and follow-up.

Eligibility

Ages Eligible for Study: 18 Years to 65 Years
Genders Eligible for Study: Both
Accepts Healthy Volunteers: No

Criteria

Inclusion Criteria:

- Males or eligible females between 18 and 65 years of age inclusive, at the time of signing the informed consent; Non-childbearing potential is defined as pre-menopausal females with a documented tubal ligation or hysterectomy; or postmenopausal defined as 12 months of spontaneous amenorrhea [in questionable cases a blood sample with simultaneous follicle stimulating hormone (FSH) > 40 MlU/ml and estradiol < 40 pg/ml (<147 pmol/L) is confirmatory]. To be eligible for entry into the study, females of child-bearing potential and females whose menopausal status is in question must commit to consistent and correct use of an acceptable method of birth control as defined in Section 7.1.1 from one month prior to the first dose of investigational product until 4 months after the last dose of investigational product.
- History of asthma for at least one year.
- Subjects must be on a stable dose of an inhaled corticosteroid or combination (ICS+LABA) therapy for at least 12 weeks prior to screening.

- FEV1≥45% and <90 % of predicted normal value during screening (obtained between 6:00 AM and 1:00 PM).
- Evidence of airway reversibility (FEV1≥12%) within 30 minutes of inhalation of albuterol OR airway hyperresponsiveness (PC20 of <8mg/mL or PD20 of <7.8 µ mol methacholine/histamine) documented in the 12 months prior to randomization.
- Subjects with documented evidence of elevated blood eosinophilia levels (>0.3 cells 109/L) within 12 months of screening and evidence of elevated blood eosinophilia levels (>0.3 cells 109/L) at screening.
- Capable of giving written informed consent, which includes compliance with the requirements and restrictions listed in the consent form.

Exclusion Criteria:

- QTcF ≥450 msec; or QTcF ≥ 480 msec in subjects with Bundle Branch Block.
- AST, ALT, alkaline phosphatase and bilirubin ≥ 1.5xULN (isolated bilirubin <1.5xULN is acceptable if bilirubin is fractionated and direct bilirubin ≥35%).
- Subjects with elevated blood eosinophil levels which is not related to asthma
- Current smokers (any subject who has smoked within the six months prior to screening or has a positive urine cotinine at screening) or subjects with a smoking history of >10 pack years calculated as follows:

Number of cigarettes per day X number of years smoked 20

- Presence of a clinically important lung condition other than asthma including current infection, bronchiectasis, pulmonary fibrosis, bronchopulmonary aspergillosis, Churg-Strauss syndrome, or diagnoses of emphysema or chronic bronchitis (chronic obstructive pulmonary disease other than asthma) or a history of lung cancer.
- An asthma exacerbation or respiratory tract infection within six weeks prior to screening (an exacerbation is defined as worsening asthma requiring the use of systemic corticosteroids and/or emergency department visit, hospitalisation).
- Subjects with a parasitic infestation within six months of screening.
- A current malignancy or previous history of cancer in remission for less than five years prior screening (except for localized carcinoma of the skin that has been resected for cure).
- Subjects who have clinically significant cardiovascular, endocrine, autoimmune, metabolic, neurological, renal, gastrointestinal, hepatic, haematological or any other system abnormalities that are uncontrolled with standard treatment.
- Unstable liver disease (as defined by the presence of ascites, encephalopathy, coagulopathy, hypoalbuminaemia, esophageal or

gastric varices or persistent jaundice), cirrhosis, and known biliary abnormalities (with the exception of Gilbert's syndrome or asymptomatic gallstones).

- Subjects with a known immunodeficiency (e.g. human immunodeficiency virus - HIV).
- A positive pre-study Hepatitis B surface antigen or positive Hepatitis C antibody result within three months of screening.
- Subjects who have received omalizumab [Xolair] within 130 days of administration of the first dose of study medication.
- Subjects with recent history (within two years prior to screening) of alcohol misuse or substance abuse prior screening.
- A positive pre-study drug/alcohol test at screening.
- The subject has participated in a clinical trial and has received an investigational product within the following time period prior to the first dosing day in the current study: 30 days, five half-lives or twice the duration of the biological effect of the investigational product (whichever is longer).
- Subjects who have previously participated in a study of mepolizumab and received study medication within 90 days prior to screening.
- Use of prescription or non-prescription drugs, including vitamins, herbal and dietary supplements within seven days (or 14 days if the drug is a potential enzyme inducer) or five half-lives (whichever is longer) prior to the first dose of study medication, unless in the opinion of the Investigator and GSK Medical Monitor the medication will not interfere with the study procedures or compromise subject safety.
- Exposure to live vaccine within the four weeks prior to screening and no intention to receive live vaccine during the study.
- History of sensitivity to the study medications (or components thereof) or a history of drug or other allergy that, in the opinion of the investigator or GSK Medical Monitor, contraindicates their participation.
- Pregnant or lactating females; pregnancy as determined by positive pregnancy test at screening or prior to dosing.

Contacts and Locations

Please refer to this study by its ClinicalTrials.gov identifier: NCT01366521

Contacts

Contact: US GSK Clinical Call Center	877-379-3718	GSKClinicalSupportHD@gsk.com

Locations

United States, North Carolina

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Sponsors and Collaborators
GlaxoSmithKline
Investigators

Study Director: GSK Clinical Trials GlaxoSmithKline

More Information

No publications provided

Responsible Party:	GSK Clinical Disclosure (Cheri Hudson; Clinical Disclosure Advisor)
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Other Study ID Numbers:	114092
Study First Received:	May 12, 2011
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Health Authority:	Estonia: State Agency of Medicines; France: Afssaps - French Health Products Safety Agency; United States: Food and Drug Administration; Germany: Pau-Ehrlich Institute

Additional relevant MeSH terms:

Asthma
Bronchial Diseases
Respiratory Tract Diseases
Lung Diseases, Obstructive
Lung Diseases
Respiratory Hypersensitivity
Hypersensitivity, Immediate

Hypersensitivity
Immune System Diseases
Antibodies, Monoclonal
Immunologic Factors
Physiological Effects of Drugs
Pharmacologic Actions

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Back to top of Main Content