PLEASE NOTE: *This study has been imported from ClinicalTrials.gov without additional data checks.*

Trial Description

Title

Study MEA117113: Mepolizumab vs. Placebo as Add-on Treatment for Frequently Exacerbating COPD Patients Characterized by Eosinophil Level

Trial Acronym

[---]*

URL of the trial

[---]*

Brief Summary in Lay Language

**This is a multi-centered, randomized, placebo-controlled, double-blind, parallel group,
trial evaluating 2 doses of mepolizumab against placebo given every 4 weeks through
subcutaneous (SC) injection. In severe COPD subjects, sputum eosinophils levels are elevated
to similar levels as those seen in severe asthmatics. It is hypothesized that the reduction
of eosinophils with mepolizumab in COPD subjects would translate into a reduction of COPD
exacerbations. The study will evaluate the efficacy and safety of mepolizumab, in subjects
who are at or above the baseline blood eosinophil count of at least 150 cells/microliters
who exacerbate despite regular use of maximal tolerated therapy, appropriate for severe COPD
subjects, in the 12 months prior to study start. In total, 660 subjects will be randomized
in 1:1:1 ratio to receive mepolizumab 300 mg, mepolizumab 100mg, or placebo administered SC.
The total duration of subject participation will be approximately 62 weeks, consisting of a
1 to 2 week screening period, 52-week treatment period and 8-week follow-up period.**

Brief Summary in Scientific Language

[---]*

Organizational Data

- DRKS-ID: **DRKS00007259**
- Date of Registration in DRKS: **2016/03/04**
- Date of Registration in Partner Registry or other Primary Registry: **2014/04/03**
- Investigator Sponsored/Initiated Trial (IST/IIT): **no**
- Ethics Approval/Approval of the Ethics Committee: **[---]***
- (leading) Ethics Committee Nr.: **[---]***

Secondary IDs

- Primary Registry-ID: **NCT02105961 (ClinicalTrials.gov)**
- Sponsor-ID: **117113 (GlaxoSmithKline)**

Health condition or Problem studied

- Free text: **Pulmonary Disease, Chronic Obstructive**
- ICD10: **J44.1 - Chronic obstructive pulmonary disease with acute exacerbation, unspecified**

Interventions/Observational Groups

- Arm 1: **Drug: Mepolizumab**
- Arm 2: **Drug: Placebo**

Characteristics

- Study Type: **Interventional**
- Study Type Non-Interventional: **[---]***
- Allocation: **Randomized controlled trial**
- Blinding: **[---]***
- Who is blinded: **patient/subject, investigator/therapist, assessor**
- Control: **Placebo**
- Purpose: **Treatment**
- Assignment: **Parallel**
- Phase: **III**
- Off-label use (Zulassungsüberschreitende Anwendung eines Arzneimittels): **[---]***

Primary Outcome

- Frequency of moderate/severe exacerbations; time frame: Up to Week 52; Moderate exacerbations are defined as COPD exacerbations that require either systemic corticosteroids (intramuscular (IM), intravenous, or oral) and/or antibiotics. Severe exacerbations are defined as COPD exacerbations requiring hospitalization or result in death.

Secondary Outcome

- Time to first moderate/severe exacerbation; time frame: Up to Week 52; The endpoint will be measured as the first instance of a moderate or severe exacerbation. Severe exacerbations are defined per protocol as clinically significant exacerbations that require in-patient hospitalization (i.e.>=24 hours) or result in death
- Frequency of COPD exacerbations requiring emergency department (ED) visits and/or hospitalizations; time frame: Up to Week 52; The endpoint will be the measurement of number of times COPD exacerbations results in an emergency department visits and/ or hospitalizations during the study.
- Change from baseline in mean total St. George's Respiratory Questionnaire-COPD (SGRQ-C) score; time frame: Baseline to Week 52; The SGRQ-C is a 40-item subject questionnaire, designed to measure health impairment by addressing the frequency of respiratory symptoms and the subject's current state.
- Change from baseline in COPD assessment test (CAT) score; time frame: Baseline to Week 52; CAT is an 8-item questionnaire used for measuring the health status of subjects with COPD. Subjects will rate their experience on a 6-point scale, ranging from 0 (no impairment) to 5 (maximum impairment) with a scoring range of 0-40, wherein higher scores indicate greater disease impact.

Countries of recruitment

- US **United States**
- AR **Argentina**
- CL **Chile**
- DK **Denmark**
- DE **Germany**
- JP **Japan**
- KR **Korea, Republic of**
- NL **Netherlands**
- RO **Romania**
- SK **Slovakia**
- TW **Taiwan, Province of China**
- UA **Ukraine**
- UK **United Kingdom**

Locations of Recruitment

- **GSK Investigational Site, Stuttgart**
- **GSK Investigational Site, Frankfurt**
- **GSK Investigational Site, Frankfurt**
- **GSK Investigational Site, Neu-Isenburg**
- **GSK Investigational Site, Magdeburg**
- **GSK Investigational Site, Dresden**
- **GSK Investigational Site, Leipzig**
- **GSK Investigational Site, Luebeck**
- **GSK Investigational Site, Berlin**
- **GSK Investigational Site, Hamburg**

Recruitment

- Planned/Actual: **[---]***
- (Anticipated or Actual) Date of First Enrollment: **2014/04/30**
- Target Sample Size: **660**
- Monocenter/Multicenter trial: **Multicenter trial**
- National/International: **International**

Inclusion Criteria

- Gender: **Both, male and female**
- Minimum Age: **40 Years**
- Maximum Age: **no maximum age**

Additional Inclusion Criteria

- COPD diagnosis: Subjects with a clinically documented history of COPD for at least 1 year in accordance with the following definition by the American Thoracic Society/European Respiratory Society

- Severity of COPD: Subjects must present with the following: a measured pre and post-salbutamol Forced expiratory volume in one second/ Forced vital capacity (FEV1/FVC) ratio of <0.70 at Visit 1 to confirm the diagnosis of COPD; a measured post-salbutamol FEV1> 20 percent and <=80 percent of predicted normal values

calculated using National Health and Nutrition Examination Survey (NHANES) III reference equations at Visit 1

- History of exacerbations: A well documented history (e.g., medical record verification) in the 12 months prior to Visit 1 of ; at least two moderate COPD exacerbations. Moderate is defined as the use of systemic corticosteroids (intramuscular (IM), intravenous, or oral) and/or treatment with antibiotics or; at least one severe COPD exacerbation. Severe is defined as having required hospitalization. Note: At least one exacerbation must have occurred while the subject was taking Inhaled corticosteroid (ICS) plus long acting beta2-agonist (LABA) plus long acting muscarinic antagonist (LAMA). Prior use of antibiotics alone does not qualify as a moderate exacerbation unless the use was specifically for the treatment of worsening symptoms of COPD.

- Concomitant COPD therapy: A well documented requirement for optimized standard of care background therapy that includes Inhaled corticosteroid (ICS) plus 2 additional COPD medications (i.e., triple therapy) for the 12 months prior to Visit 1 and meets the following criteria: Immediately prior to Visit 1, minimum of 3 months of use of an; Inhaled corticosteroid at a dose >= 500 micrograms (mcg)/day fluticasone propionate dose equivalent plus; LABA and LAMA.

For subjects who are not continually maintained on ICS plus LABA plus LAMA for the entire 12 months prior to Visit 1 use of following is allowed (but not in the 3 months immediately prior to Visit 1); inhaled corticosteroid at a dose >=500 mcg/day fluticasone propionate dose equivalent plus; a LABA or a LAMA and; use of at least one other class of COPD medication (i.e., phosphodiesterase-4-inhibitors, methylxanthines, or a combination of short acting beta2-agonist and short acting muscarinic antagonist).

- Informed Consent: Able to give written informed consent prior to participation in the study, which will include the ability to comply with the requirements and restrictions listed in the consent form. Subjects must be able to read, comprehend, and write at a level sufficient to complete study related materials.

- Gender: Male or Eligible Female; To be eligible for entry into the study females of child bearing potential must commit to consistent and correct use of an acceptable

method of birth control from the time of consent, for the duration of the trial, and
for 4 months after last study drug administration.

- Age: At least 40 years of age at Visit 1

- Smoking status: Subject with confirmed COPD are eligible to participate independent
of their smoking status and smoking history, i.e. current smokers, never smokers or
ex-smokers can be enrolled into the study. Current smokers are defined as those with
a history of cigarette smoking of >=10 pack-years [number of pack years = (number of
cigarettes per day / 20) x number of years smoked (e.g., 20 cigarettes per day for 10
years, or 10 cigarettes per day for 20 years)]. Former smokers are defined as those
who meet the definition of a current smoker but have stopped smoking for at least 6
months prior to Visit 1. Never smokers are those that do not meet the definition of a
current or former smoker.

- French subjects: In France, a subject will be eligible for inclusion in this study
only if either affiliated to or a beneficiary of a social security category.

Exclusion criteria

- Subjects with Asthma: Current and Former Smokers: Subjects with a current diagnosis
of asthma (those with a prior history are eligible if they meet inclusion criteria
for a current diagnosis of COPD); Never-Smokers: Subjects with any history of asthma.

- Other respiratory disorders: The investigator must judge that COPD is the primary
diagnosis accounting for the clinical manifestations of the lung disease. Subjects
with alpha1-antitrypsin deficiency as the underlying cause of COPD are excluded.
Also, excluded are subjects with active tuberculosis, lung cancer, bronchiectasis,
sarcoidosis, lung fibrosis, primary pulmonary hypertension, interstitial lung
diseases or other active pulmonary diseases. Subjects are also excluded if
maintenance use of bi-level positive airway pressure is required for the treatment of
respiratory disorder.

- COPD stability: Subjects with pneumonia, exacerbation, lower respiratory infection
within the 4 weeks prior to Visit 1.

- Lung resection: Subjects with lung volume reduction surgery within the 12 months prior to Visit 1.

- Pulmonary rehabilitation program: Participation in the acute phase of a pulmonary rehabilitation program within 4 weeks prior to Visit 1. Subjects who are in the maintenance phase of a pulmonary rehabilitation program are not excluded.

- Oxygen: Subjects receiving treatment with oxygen more than 4.0 liters/minute (L/min). While breathing supplemental oxygen, subjects should demonstrate an oxyhemoglobin saturation greater than or equal to 89 percent.

- 12-lead Electrocardiography (ECG) finding: An abnormal and significant ECG finding from the 12-lead ECG conducted at Visit 1, if considered to be clinically significant by the Investigator. 12-lead ECGs will be over-read by a centralized independent cardiologist to assist in consistent evaluation of subject eligibility. Results from the 12-lead ECG over-read must be received prior to assessing eligibility at Visit 2.

- Unstable or life threatening cardiac disease: Subjects with any of the following would be excluded: Myocardial infarction or unstable angina in the last 6 months ; Unstable or life threatening cardiac arrhythmia requiring intervention in the last 3 months ; New York Heart Association (NYHA) Class IV Heart failure

- Other diseases/abnormalities: Subjects with (historical or) current evidence of clinically significant, neurological, psychiatric, renal, hepatic, immunological, endocrine (including uncontrolled diabetes or thyroid disease) or haematological abnormalities that are uncontrolled. Significant is defined as any disease that, in the opinion of the investigator, would put the safety of the subject at risk through participation, or which would affect the efficacy or safety analysis if the disease/condition exacerbated during the study.

- Eosinophilic disease: Subjects with other conditions that could lead to elevated eosinophils such as Hypereosinophilic syndromes including Eosinophilic Granulomatosis with Polyangiitis (EGPA, also known as Churg-Strauss Syndrome), or Eosinophilic

Esophagitis.

- Parasitic infection: Subjects with a pre-existing helminthes infestation within 6 months prior to Visit 1 are also excluded.

- Malignancy: A current malignancy or previous history of cancer in remission for less than 12 months prior to Visit 1 (Subjects that had localized carcinoma of the skin or cervix which was resected for cure will not be excluded). South Korea subjects with a diagnosis of malignancy within 5 years of Visit 1 are excluded.

- Immunodeficiency: A known immunodeficiency (e.g. human immunodeficiency virus HIV), other than that explained by the use of corticosteroids taken for COPD.

- Liver disease: 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). Chronic stable hepatitis B and C are acceptable if subject otherwise meets entry criteria (e.g., presence of hepatitis B surface antigen or positive hepatitis C test result within 3 months of screening)

- Monoclonal antibodies: Subjects who have received any monoclonal antibody within 5 half-lives of Visit 1.

- Investigational medications: Subjects who have received an investigational drug within 30 days of Visit 1, or within 5 drug half-lives of the investigational drug, whichever is longer (this also includes investigational formulations of a marketed product).

- Hypersensitivity: Subjects with a known allergy or intolerance to another monoclonal antibody or biologic including history of anaphylaxis to another biologic

- Inability to read: In the opinion of the investigator, any subject who is unable to read and/or would not be able to complete study related materials.

- Non-compliance: Subjects at risk of non-compliance, or unable to comply with the study procedures. Any infirmity, disability, or geographic location that would limit

compliance for scheduled visits.

- Questionable validity of consent: Subjects with a history of psychiatric disease,
intellectual deficiency, poor motivation or other conditions that will limit the
validity of informed consent to participate in the study.

- Drug or alcohol abuse: A known or suspected history of alcohol or drug abuse within 2
years prior to Visit 1.

- Previous participation: Subjects who have previously participated in any study of
mepolizumab.

- Affiliation with Investigator Site: Is an investigator, sub-investigator, study
coordinator, employee of a participating investigator or study site, or immediate
family member of the aforementioned that is involved in this study.

Randomization Criteria

In order to be randomized to study drug the subject must meet the following randomization
criteria at Visit 2:

- Blood eosinophils: Documented elevated peripheral blood eosinophil count of >=300
cells/microliter within the past 12 months prior to Visit 1; OR A peripheral baseline
blood eosinophil count of >=150 cells/microliter from haematology conducted at Visit
1

- Electronic Diary Compliance: Compliance with completion of the eDiary defined as
completion of all questions on 5 or more days out of the 7 days immediately preceding
Visit 2.

- 12-lead ECG: No evidence of an abnormal and significant ECG finding from the 12-lead
ECG conducted at Visit 1 as indicated on the over-read provided by the centralized
independent cardiologist. Subjects with a QT interval corrected with Fridericia's
formulas (QTcF)>=450 msec are not eligible. For subjects with a QRS interval
>=120msec, those with QTcF>=480 msec are not eligible. Specific ECG findings that
preclude subject eligibility are listed in the protocol.

- Abnormal chest X-ray (or Computerized Tomography [CT] scan): No chest

X-ray (or CT scan) that reveals evidence of clinically significant abnormalities not believed to be due to the presence of COPD. If a chest X-ray or CT scan is not available within 6 months prior to Visit 1, then a chest X-ray must be taken at Visit 1 and the results reviewed prior to randomization. For sites in Germany: If a chest X-ray (or CT scan) within 6 months prior to Screening (Visit 1) is not available, the subject will not be eligible for the study.

- Laboratory abnormality: No evidence of clinically significant abnormality in the haematological, biochemical, or urinalysis screen at Visit 1, as judged by the investigator.

- Hepatitis B: Subjects who are HBsAg positive or HBcAb positive must not have a HBV DNA level >=2000 International Units (IU)/millilitre (mL).

- Liver function test: Subjects must meet the following based on results from sample taken at Visit 1: Alanine aminotransferase (ALT) <2x ULN (upper limit of normal); Alkaline Phosphatase (Alk Phos) <=2x ULN; Bilirubin <=1.5x ULN (isolated bilirubin>1.5x ULN is acceptable if bilirubin is fractionated and direct bilirubin <35 percent)

- Pregnancy: No subjects who are pregnant or breastfeeding. Subjects should not be enrolled if they plan to become pregnant during the time of study participation.

Addresses

- **Primary Sponsor**

  GlaxoSmithKline

  Telephone: **[---]***
  Fax: **[---]***
  E-mail: **[---]***
  URL: **[---]***

- **Contact for Scientific Queries**

  GlaxoSmithKline
  GSK Clinical Trials

Contact for Scientific Queries

GlaxoSmithKline
GSK Clinical Trials

Telephone: **[---]***
Fax: **[---]***
E-mail: **[---]***
URL: **[---]***

- **Contact for Public Queries**

US GSK Clinical Trials Call Center

Telephone: **877-379-3718**
Fax: **[---]***
E-mail: **GSKClinicalSupportHD at gsk.com**
URL: **[---]***

Sources of Monetary or Material Support

- **[---]***

Bitte wenden Sie sich an den Sponsor / Please refer to primary sponsor

Telephone: **[---]***
Fax: **[---]***
E-mail: **[---]***
URL: **[---]***

Status

- Recruitment Status: **Recruiting ongoing**
- Study Closing (LPLV): **[---]***

Trial Publications, Results and other documents

The parameters in ClinicalTrials.gov and DRKS are not identical. Therefore the data import from ClinicalTrials.gov required adjustments. For full details please see the DRKS FAQs.
- Translation on version: 1
- Last processed date by ClinicalTrials.gov: 2014/11/05

** This entry means the parameter is not applicable or has not been set.*

**** This entry means that data is not displayed due to insufficient data privacy clearing.*