Trial Description

Title

Clinical study to investigate safety, tolerability, efficacy, pharmacokinetics and pharmacodynamics of inhaled multiple doses of the human GATA-3-specific DNAzyme solution SB010 in patients with moderate to severe COPD
– A randomised, double-blind, parallel group, multicenter, phase IIa pilot study –

Trial Acronym

SB010-COPD

URL of the trial

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Brief Summary in Lay Language

Main Purpose : In patients who suffer from moderate to severe COPD shall be investigated whether the inhalation of the solution SB010 over 28 days leads to an improvement of symptoms .
Background: the solution SB010 is able to downregulate certain inflammatory parameters (Eosinophile), therefor one can assume, that the solution may improve the symptoms of COPD patients who have eosinophils in the sputum. .
Procedure: Through28 days (BID at a distance of 12h) the patients inhale SB010 or a placebo (solution without drug); Regular investigations (eg lung function test) will be performed to estimate the effect at the end of the study .
Aims / hypothesis : One aim of this study, which includes a low number of patients,

Brief Summary in Scientific Language

Aim: To assess the safety, tolerability, efficacy, pharmacokinetics and pharmacodynamics of inhaled multiple doses of the human GATA-3-specific DNAzyme solution SB010 in patients with moderate to severe COPD
Background: SB010 is able to downregulate eosinophiles and therefore it can be assumed, that inahlation of SB010 in patients with eosinophilic COPD may improve the symptoms.
Objectives:
Primary objective
• To assess the feasibility of conducting a larger phase II trial of SB010 in patients with moderate to severe, stable COPD
Secondary objectives
• Efficacy of inhaled multiple doses of SB010 in improving:
- lung function (FEV1, FVC)
- eosinophil count in sputum
- FeNO

- symptom scores
- exploratory biomarkers (IL-5, IL-13, ECP, tryptase, but not limited to)
• Safety and tolerability of inhaled multiple doses of SB010
• Pharmacokinetics
Study procedure: BID (12h distance) inhalation of SB010 or Placebo on 28 consecutive days for each patient and following analysis of study parameters.
Inidication: moderate to severe, stable COPD

Organizational Data

- DRKS-ID: **DRKS00006087**
- Date of Registration in DRKS: **2014/06/05**
- Date of Registration in Partner Registry or other Primary Registry: **[---]***
- Investigator Sponsored/Initiated Trial (IST/IIT): **yes**
- Ethics Approval/Approval of the Ethics Committee: **Approved**
- (leading) Ethics Committee Nr.: **149/13 A-ff , Ethik-Kommission des Fachbereichs Medizin der Philipps-Universität Marburg**

Secondary IDs

- EudraCT-No.
(for studies acc. to Drug Law): **2013-002332-24**

Health condition or Problem studied

- ICD10: **J44.9 - Chronic obstructive pulmonary disease, unspecified**

Interventions/Observational Groups

- Arm 1: **Inhalation: Verum (10 mg hgd40 in 2ml solution, = SB010), BID for 27 days, OD at day 28**
- Arm 2: **Inhalation: Placebo (2ml solution), BID for 27 days, OD at day 28**

Characteristics

- Study Type: **Interventional**
- Study Type Non-Interventional: **[---]***
- Allocation: **Randomized controlled trial**
- Blinding: **[---]***
- Who is blinded: **patient/subject, investigator/therapist, data analyst**
- Control: **Placebo**

Study Type: **Interventional**

Study Type Non-Interventional: **[---]***

Allocation: **Randomized controlled trial**

Blinding: **[---]***

Who is blinded: **patient/subject, investigator/therapist, data analyst**

Control: **Placebo**

- Purpose: **Treatment**
- Assignment: **Parallel**
- Phase: **IIa**
- Off-label use (Zulassungsüberschreitende Anwendung eines Arzneimittels): **Yes**

Primary Outcome

Assessment of feasibility of conducting a larger phase II trial as determined by:
- number of eligible patients / screening failures in light of specific inclusion / exclusion criteria;
- duration of recruiting period;
- number of randomized patients not evaluable due to, e.g. non-evaluable sputum;
- suitability of inhalation device, patient compliance, and device handling
- compliance to schedule for screening procedures (Day -28 to -7)

Secondary Outcome

Efficacy and pharmacodynamics
- treatment effect after 28 days in reducing percentage of eosinophils in sputum;
- treatment effect after 28 days in reducing FeNO;
- treatment effect after 28 days in improving lung function (FEV1, FVC)
- treatment effect after 28 days in improving symptom scores;
- impact on exploratory biomarker analysis
Pharmacokinetics
Safety and tolerability

Countries of recruitment

- DE **Germany**

Locations of Recruitment

- University Medical Center **Universitätsklinikum Gießen u. Marburg GmbH, Standort Marburg Klinik für Pneumologie Baldingerstraße D-35043 Marburg, Marburg**

- other **Fraunhofer-Institut für Toxikologie und Experimentelle Medizin Klinische Atemwegsforschung Nikolai-Fuchs-Strasse 1 D-30625 Hannover, Hannover**
- other **LungenClinic Grosshansdorf Pneumologisches Forschungsinstitut (PRI) Wöhrendamm 80 D-22927 Großhansdorf, Großhannsdorf**

Recruitment

- Planned/Actual: **Actual**
- (Anticipated or Actual) Date of First Enrollment: **2014/07/15**
- Target Sample Size: **20**
- Monocenter/Multicenter trial: **Multicenter trial**
- National/International: **National**

Inclusion Criteria

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

Additional Inclusion Criteria

Adult male and female Caucasian patients aged ≥ 40.
2. Clinical diagnosis of moderate to severe, stable COPD, defined as a postbronchodilator Forced Expiratory Volume in One Second (FEV1) greater than 30 % of the predicted normal value and less than 80 % of the predicted normal value, and post-bronchodilator FEV1/FVC less than 0.7.
3. Patients on stable COPD medication at least 4 weeks prior to screening
4. Sputum eosinophils ≥ 2.5% at screening.
5. Current or ex-smoker with a smoking history of ≥ 10 packyears
6. Ability to inhale in an appropriate manner (patients will be trained to inhale from the AKITA2 APIXNEB® device with a placebo medication at the screening visit)
7. Only men who do not want to father children for six months after the last dose of SB010
8. Only women who don’t plan pregnancy for six months after the last dose of SB010
9. WOCBP must use a double barrier method of contraception during the study and for 6 months following the last dose of study medication. WOCBP are defined as sexually mature women who have not undergone a hysterectomy or surgical sterilization or who have not been naturally postmenopausal for at least 12 consecutive months (i.e., who has had menses any time in the preceding 12 consecutive months).
10. Male subjects whose sexual partners are WOCBP must use a double barrier method of contraception, one of which includes a condom, during the study and for 6 months after the end of treatment.
11. Patient is able to understand and give written informed consent
12. Provision of a written informed consent on participation in the trial prior to trial start and any trial-related procedures

Exclusion criteria

1. Presence of clinically significant diseases other than COPD and known COPD comorbidities (cardiovascular, renal, hepatic, gastrointestinal, haematological, neurological, genitourinary, autoimmune, endocrine, metabolic, etc.), which, in the opinion of the investigator, may put the patient at risk because of participation in the trial
2. Diseases which may influence the results of the study or the patient's ability to take part in it
3. Presence of relevant pulmonary diseases or history of thoracic surgery, such as:
- known active tuberculosis,
- history of interstitial lung or pulmonary thromboembolic disease,
- pulmonary resection during the past 12 months,
- history of asthma
- history of bronchiectasis secondary to respiratory diseases (e.g. cystic fibrosis, Kartagener's syndrome, etc.),
- history of allergic bronchopulmonary aspergillosis or respiratory infection within the 4 preceding weeks of the first morning IMP administration
4. Clinically relevant acute infections in the last 4 weeks prior to randomization
5. Clinically relevant chronic infections
6. known clinically relevant allergies or idiosyncrasy to oligonucleotide based drugs
7. History of allergic reactions to any active or inactive ingredients of the nebulizer solution
8. Proneness to orthostatic dysregulation, faintings, or blackouts
9. History of malignancy within the past 5 years, except excised basaliomas
10. Clinically relevant abnormalities (except of known COPD / comorbidity related abnormalities) in clinical chemical, haematological or in any other laboratory variables as judged by the investigator
11. Positive results in any of the virology tests of acute or chronic infectious human immunodeficiency virus (HIV) and hepatitis B/C virus infections
12. Positive drug screen
13. Abuse of alcohol or drugs
14. Treatment with any known enzyme inducing or inhibiting agents (St. John's Wort (Johanniskraut), barbiturates, phenothiazines, cimetidine, ketoconazole etc.) within 30 days before first administration of trial medication or during treatment period of the trial
15. Treatment with any biologicals within three months before first administration of trial medication or during treatment period of the trial (only allowed by judgement of principal investigator)
16. Surgery of the gastrointestinal tract which may interfere with drug absorption of swallowed fraction (Note: this is not applicable for minor abdominal surgery such as appendectomy or herniotomy),
17. Planned lung transplantation
18. Blood donation within the last 30 days before screening
19. Planned donation of germ cells, blood, organs or bone marrow during the course of the trial or within 6 months thereafter
20. Participation in another clinical trial with an investigational drug or device within the last month or within 10 times the half-life of the respective drug. For biologics the minimum period is 10 times the half-life of the respective drug before inclusion in this trial
21. Lack of ability or willingness to give informed consent or inability to cooperate adequately
22. Anticipated non-availability for trial visits/procedures
23. Vulnerable subjects (e.g., persons kept in detention)
24. Employee at the investigational site, relative or spouse of the investigator.
25. Pregnancy or breast feeding

Addresses

■ **Primary Sponsor**

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Sources of Monetary or Material Support

- **Public funding institutions financed by tax money/Government funding body (German Research Foundation (DFG), Federal Ministry of Education and Research (BMBF), etc.)**

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  E-mail: **postmaster at dfg.de**
  URL: **www.dfg.de**
- **Commercial (pharmaceutical industry, medical engineering industry, etc.)**

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Status

- Recruitment Status: **Recruiting complete, follow-up complete**
- Study Closing (LPLV): **2016/12/22**

Trial Publications, Results and other documents

- Paper **A GATA3-specific DNAzyme attenuates sputum eosinophilia in eosinophilic COPD patients: a feasibility randomized clinical trial**

** 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.*