A Multicentre, Randomized, Double-blind, Parallel Group, Placebo Controlled, Phase 3 Study to Evaluate the Efficacy and Safety of Tralokinumab in Reducing Oral Corticosteroid Use in Adults and Adolescents with Oral Corticosteroids dependent Asthma (TROPOS)

Published: 27-11-2014
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Primary objective:• To evaluate the effect of tralokinumab compared to placebo in reducing the prescribed, OCS maintenance dose in adult and adolescent subjects with asthma requiring chronic treatment with maintenance OCS in addition to ICS/LABA....

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Bronchial disorders (excl neoplasms)
Study type	Interventional

Summary

ID

NL-OMON44438

Source
ToetsingOnline

Brief title
TROPOS

Condition

- Bronchial disorders (excl neoplasms)

Synonym
oral corticosteroid-dependent asthma, severe asthma

Research involving
Human

Sponsors and support

Primary sponsor: Site Management & Monitoring
Source(s) of monetary or material Support: AstraZeneca BV

Intervention

Keyword: asthma, oral corticosteroids, randomized clinical trial, tralokinumab

Outcome measures

Primary outcome

Primary outcome variable:

Percent change from baseline in the daily, average, OCS dose at week 40 post

randomization while not losing asthma control.

Primary outcome measure:

Percent difference vs placebo at week 40 post randomisation.

Secondary outcome

Secundary outcome variables:

- Difference vs. placebo in the proportion of subjects with final daily average

OCS dose <=5 mg at Week 40 post randomization

- Difference vs. placebo in the proportion of subjects with >=50% reduction in

average daily OCS dose at Week 40 post randomization

Study description

Background summary

Asthma is a syndrome characterized by airway inflammation, reversible airway obstruction and airway hyperresponsiveness, with a global prevalence of approximately 300 million patients (GINA 2014). Approximately 5% to 10% of asthma patients have severe asthma, many of whom may be inadequately controlled by inhaled corticosteroids (ICS) and long-acting β2-agonists (LABA)in combination with additional controller therapies (Bateman et al 2010).
The observed variability in clinical response to currently available asthma therapies appears to be related, in part, to distinctive inflammatory phenotypes (Wenzel 2012). There is considerable evidence that interleukin-13 (IL-13) is a key mediator in the pathogenesis of asthma. Tralokinumab is a human recombinant monoclonal antibody (MAb) that specifically binds human IL-13, blocking interactions with the IL-13 receptor.
OCS are effective agents for controlling airway inflammation in asthma and are indicated for severe persistent asthma, as outlined in Step 5 of the Global Initiative for Asthma (GINA 2014) guidelines. Since long-term treatment with OCS use can result in adverse reactions such as osteoporosis, diabetes, cataract and growth retardation in children, a major objective in this population is to reduce their overall exposure to OCS thereby minimising adverse events. Given the need to reduce the requirement of OCS in patients with severe asthma, treatments that may allow tapering of OCS without loss of control are needed.

Study objective

Primary objective:
• To evaluate the effect of tralokinumab compared to placebo in reducing the prescribed, OCS maintenance dose in adult and adolescent subjects with asthma requiring chronic treatment with maintenance OCS in addition to ICS/LABA.

Secundary objective:
• To evaluate the effect of tralokinumab compared to placebo on the proportion of subjects with the prescribed, OCS maintenance dose <=5 mg (daily) in adult and adolescent subjects with asthma requiring chronic treatment with maintenance OCS in addition to ICS/LABA.

• To evaluate the effect of tralokinumab compared to placebo on the proportion of subjects with at least 50% reduction in their prescribed, OCS maintenance dose in adult and adolescent subjects with asthma requiring chronic treatment with maintenance OCS in addition to ICS/LABA.

Safety objective:
• To evaluate the safety and tolerability of tralokinumab

Exploratory objectives:

• To evaluate the effect of tralokinumab versus placebo in overall OCS exposure

• To evaluate the effect of tralokinumab versus placebo in the proportion of subjects that have decreased their daily average prescribed, OCS dose

• To evaluate the effect of tralokinumab compared with placebo on asthma exacerbations.

• To evaluate the effect of tralokinumab compared with placebo on lung function

• To evaluate the effect of tralokinumab compared with placebo on asthma symptoms and other asthma control metrics

• To evaluate the effect of tralokinumab compared with placebo with regards to asthma specific health-related quality of life

• To evaluate the effect of tralokinumab compared with placebo with regards to health related quality of life

• To evaluate the effect of tralokinumab compared with placebo with regards to HRU and productivity loss due to asthma

• To evaluate the pharmacokinetics and immunogenicity of tralokinumab

• To evaluate the change from baseline of biomarkers that may be associated with upregulation of IL-13

• To evaluate the relationship between baseline biomarkers and the effect of tralokinumab on OCS dose reduction and clinical efficacy

• To evaluate the impact of OCS optimization on biomarkers

Study design

Randomized, double-blind, parallel group, placebo-controlled phase III study. Approximately 120 subjects will be randomized to tralokinumab or placebo (1:1 ratio). Subjects will be stratified at randomization by the baseline OCS dose (<=10 mg versus >10 mg prednisone or prednisolone) and age group (adults versus adolescents). (NB: only adults in the Netherlands)

- Run-in period (2 weeks)
- OCS optimization period (maximum 8 weeks), except for patients with documented failure of OCS reduction within 6 months prior to visit 1 and only after approval of the study physician.

Once subjects have completed the run-in or run-in/optimization period, subjects will be randomised to receive tralokinumab or placebo over a 40-week treatment

period.

Treatment period consists of 3 phases:
- Induction phase (12 weeks), needed to ensure maximal effect on FEV1
- OCS reduction phase (20 weeks), needed to reach the lowest possible dose based on the titration schedule (CSP table 4)
- Maintenance phase (8 weeks)

Post-treatment safety follow-up visits will be performed at week 44 and week 54.

Subjects will be maintained on their currently prescribed ICS/LABA therapy and any additional asthma controller medications, without changes, from enrollment throughout the run-in/optimization and treatment periods.

Intervention

Subjects will be administered 300 mg tralokinumab (2 x 150mg, 1mL injections) or placebo (2 x 1mL injections) every 2 weeks

Study burden and risks

The subject visits the hospital 28 times maximally. Subjects with documented OCS reduction failure prior to visit 1, visit the hospital 24 times maximally. These visits to the hospital will take 30 minutes up to 4.5 hours each, depending on the assessments per visit.

The following will be done during the hospital visits:
- Physical examination
- Check of vital functions, assessment of length and weight
- ECG
- Collection of blood for clinical chemistry, hematology and exploratory research
- Urinalysis
- Assessment of exhaled nitric oxide (NO)
- Pre- and post-bronchodilator spirometry
- Subject will be asked about health care resource utilization, asthma symptoms, adverse events and medication
- Subject will be asked to complete several questionnaires (ACQ-6, AQLQ(S)+12, WPAI+CIQ, EQ-5D-5L)
- Pregnancy test will be done (women of child baring potential only)
- FSH test done only for female subjects to confirm post-menopausal status in women<50 years who have been ammenorrheic for >12 months
- Test for Hepatitis B and C, and HIV and concentration levels maintenance treatment.

Subjects will be asked to complete an electronic diary (eDiary) every morning

and evening and determine morning and evening peakflow. This will take approximately 10 minutes per day.

In addition, the subject should complete questionnaires several times at home:
- ACQ-6: every 2 weeks from visit 1 till visit 26
- AQLQ(S)+12: every 14 days from visit 1 till 6, from visit 6 every 28 days till visit 26
- WPAI+CIQ: every 2 weeks from visit 6 till visit 26
- EQ-5D-5L: every week from visit 6 till visit 26

Patients using OCS other than prednisone or prednisolone, will be switched to an equivalent dose of prednisone or prednisolone at visit 1. During the optimalization period (visit 2-5) OCS dose will be optimized without loss of asthma control. The treatment period starts at randomization (visit 6) and OCS dose will remain constant for 8 weeks (induction phase, visit 6-11). During the reduction phase (visit 12-21) attempts will be made to reduce OCS dose. During the maintenance phase (visit 22-25) the OCS dose will remain constant again. During the treatment period (visit 6-26) patients will receive tralokinumab or placebo (1:1) every 2 weeks via subcutaneous injections (2 subcutaneous injections each time).

Subjects will continue using their current ICS/LABA and additional asthma controller medication. The costs for this asthma medication will be reimbursed by AstraZeneca.

Contacts

Public
Selecteer

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. Age 12 to 75 years
2. Documented physician-diagnosed asthma.
3. Documented treatment with Inhaled Corticosteroid (ICS) at a total daily dose corresponding to >=500µg fluticasone propionate dry powder formulation equivalents and a LABA.
4. Receiving Oral Corticosteroid (OCS) for the treatment of asthma.
5. Morning pre-BD FEV1 value < 80% of their predicted normal value (PNV).
6. Post-BD reversibility of >=12% in FEV1.

Exclusion criteria

1. Clinically important pulmonary disease other than asthma.
2. History of anaphylaxis following any biologic therapy.
3. Hepatitis B, C or HIV
4. Pregnant or breastfeeding
5. History of cancer
6. Current tobacco smoking or a history of tobacco smoking for >=10 pack-years.
7. Previous receipt of tralokinumab

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel

Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	13-04-2015
Enrollment:	24
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	tralokinumab
Generic name:	tralokinumab

Ethics review

Approved WMO Date:	27-11-2014
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-01-2015
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	04-02-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-07-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC

Approved WMO Date:	02-09-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-09-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	01-04-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	06-04-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	11-04-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-08-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	11-10-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2014-001391-54-NL
CCMO	NL50890.018.14
Other	volgt z.s.m.