Double-blind, randomized, placebo-controlled, phase III trial on the efficacy and tolerability of a 6-week treatment with budesonide effervescent tablets vs. placebo for induction of clinico-pathological remission in adult patients with active eosinophilic esophagitis

Published: 12-10-2015
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Primary:* To assess the efficacy of 2 x 1 mg/d budesonide effervescent tablets vs. placebo for the induction of clinico-pathological remission in adult patients with active eosinophilic esophagitis (EoE).Secondary:* To study safety and tolerability...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Gastrointestinal infections
Study type	Interventional

Summary

ID

NL-OMON42672

Source
ToetsingOnline

Brief title
Induction of remission with budesonide vs. placebo in EoE.

Condition

- Gastrointestinal infections

Synonym
oesophageal inflammation

Research involving
Human

Sponsors and support

Primary sponsor: Dr. Falk Pharma GmbH
Source(s) of monetary or material Support: Dr. Falk Pharma GmbH

Intervention

Keyword: EoE, eosiniphilic, oesophagitis, remission

Outcome measures

Primary outcome

Rate of patients with clinico-pathological remission at week 6 (LOCF) defined

as fulfilling both criteria:

- Histological remission, i.e., peak of <16 eos/mm2 hpf at week 6 (LOCF), AND

- Resolution of symptoms (i.e., no or only minimal problems) defined as a

severity of *2 points on 0 to 10-point (0-10) NRS for dysphagia AND

a severity of *2 points on 0-10 NRS for pain during swallowing on

each day in the week prior to week 6 (LOCF).

Secondary outcome

A priori ordered key secondary endpoints (DB-phase):

1. Rate of patients with histological remission, defined as a peak of <16

eos/mm2 hpf at week 6 (LOCF),

2. Change in the peak eos/mm2 hpf from baseline to week 6 (LOCF),

3. Rate of patients with resolution of symptoms (i.e., no or only minimal

problems) defined as a severity of *2 points on 0-10 NRS for dysphagia AND a

severity of *2 points on 0-10 NRS for pain during swallowing on each day in the

week prior to week 6 (LOCF),

4. Rate of patients with total weekly Eosinophilic Esophagitis Activity Index *

Patient-Reported Outcome (EEsAI-PRO) score of *20 at week 6 (LOCF),

5. Rate of patients with an improvement from baseline to week 6 (LOCF) in the

weekly Visual Dysphagia Question (VDQ) score,

6. Rate of patients with an improvement from baseline to week 6 (LOCF) in the

weekly *Avoidance, Modification, and Slow-eating (AMS) score.

Study description

Background summary

Recent studies suggest that swallowing of budesonide is highly effective in the treatment of EoE, and might not be associated with the toxicities of long term use of systemic corticosteroids.

Study objective

Primary:
* To assess the efficacy of 2 x 1 mg/d budesonide effervescent tablets vs. placebo for the induction of clinico-pathological remission in adult patients with active eosinophilic esophagitis (EoE).
Secondary:
* To study safety and tolerability in the form of adverse events and laboratory parameters,
* To assess patients* quality of life.

Study design

This is a double-blind, randomized, multicenter, placebo-controlled, compara-tive, confirmatory Phase III clinical trial.

Intervention

The trial will be conducted with two treatment groups in the form of a parallel group comparison and will serve to compare oral treatment with 2 x 1 mg/d budesonide effervescent tablets vs. placebo for the treatment of active EoE. The up to 6-week screening period will be followed by a 6-week double-blind (DB) treatment period and an optional 6-week open-label induction (OLI) treatment with 2 x 1 mg/d budesonide effervescent tablets in patients eligible

for OLI-treatment (e.g., clinico-pathological non-remitters), and a 4-week follow-up period (if the patient will not further continue in the program).

Study burden and risks

physical examination 3-6x
endoscopy of the oesophagus 2-3x
questionnaire related to complaints and disease: 8 questionnaires, per questionnaire variable 6-10x
blood sampling 4-7x
urine sampling 5-8 x
in total 6-10 visits.

The adverse events are characteristic for steroid medication, and can occur depending on the dosage, treatement period, whether the subject is or has been taking other corticosteroid preparations, and the individual sensitivity.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Signed informed consent,
- Male or female patients, 18 to 75 years of age,
- Confirmed clinico-pathological diagnosis of EoE according to established diagnostic criteria ,
- Active symptomatic and histological EoE,
- A documented trial with proton pump inhibitors (PPIs) in order to rule out PPI-responsive esophageal eosinophilia,
- Negative pregnancy test in females of childbearing potential at baseline visit

Exclusion criteria

- Clinical signs (i.e., acid regurgitation and/or heart burn) and endoscopic signs (at least Los Angeles Classification of Esophagitis Grade A) of gastroesophageal reflux disease (GERD),
- History of abnormal results in case of an optionally performed pH monitoring of the distal esophagus,
- Patients with PPI-responsive esophageal eosinophilia
- Achalasia, scleroderma esophagus, or systemic sclerosis,
- Other clinically evident causes than EoE for esophageal eosinophilia,
- Any concomitant esophageal disease and relevant gastro-intestinal disease (celiac disease, inflammatory bowel disease, oropharyngeal or esophageal bacterial, viral, or fungal infection [candida esophagitis]),
- Any relevant systemic disease (e.g., AIDS, active tuberculosis),
- If careful medical monitoring is not ensured: cardiovascular disease, diabetes mellitus, osteoporosis, active peptic ulcer disease, glaucoma, cataract, or infection,
- Liver cirrhosis or portal hypertension,
- History of cancer in the last five years,
- History of esophageal surgery at any time or of esophageal dilation procedures within the last 8 weeks prior to screening visit,
- Upper gastrointestinal bleeding within 8 weeks prior to screening visit,
- Existing or intended pregnancy or breast-feeding.

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):	18-04-2016
Enrollment:	18
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Budenofalk
Generic name:	budesonide
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	12-10-2015
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	23-12-2015
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	22-09-2016
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

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	EUCTR2014-001484-12-NL
ClinicalTrials.gov	NCT02434029
CCMO	NL54155.041.15