Double-blind, randomized, placebo-controlled, Phase II/III trial on the efficacy and tolerability of treatment with budesonide oral suspension vs. placebo in children and adolescents with eosinophilic esophagitis

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The Budesonide oral suspension is a new drug formulation especially developed for the treatment of eosinophile esophagitis in children and adolescents. The purpose of this clinical study is to investigate whether Budesonide oral suspension is...

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

Summary

ID

NL-OMON50028

Source
ToetsingOnline

Brief title
BUU-5/EEA

Condition

- Gastrointestinal inflammatory conditions

Synonym
eosinophilic eosphagitis, eosinophylic gullet 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: Adolescents, Children, EoE

Outcome measures

Primary outcome

• Rate of patients with pathological remission and clinical response at DB week

12 (LOCF) defined as fulfilling both criteria:

- Histological remission, i.e., peak of <16 eos/mm2 hpf at DB week 12 (LOCF),

AND

- Clinical response defined as:

Stratum I: Age 2 to 11 years at DB V1:

>=30% drop in the total score of PEESS® Version 2.0 - parent report for children

and teens (ages 2-18) from baseline to DB week 12 (LOCF),

- Stratum II: Age 12 to <18 years at DB V1:

>=30% drop in the total score of PEESS® Version 2.0 - children and teens report

(ages 8-18) from baseline to DB week 12 (LOCF).

Patients who experience either a food impaction which needs endoscopic

intervention, or who need an endoscopic dilation at any time during the

DB-treatment phase, or who were prematurely withdrawn due to lack of efficacy

after at least 8 weeks of DB treatment and who showed no change or a

deterioration in the Global Assessment Score (ParGA/PatGA) compared to baseline at their last visit in the DB-treatment phase (DB V4 EOT/withdrawal DB), will be assessed as treatment failures, and thus will not fulfill by definition the *pathological remission and clinical response* criterion. These patients still can be treated with verum budesonide in the open label induction phase.

Secondary outcome

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

1. Rate of patients with histological remission, defined as a peak of <16 eos/mm2 hpf at DB week 12 (LOCF),

2. Change in the peak eos/mm2 hpf from screening to DB week 12 (LOCF),

3. Rate of patients with clinico-pathological remission defined as:

• Histological remission, i.e., peak of <16 eos/mm2 hpf at DB week 12 (LOCF), and

o Clinical remission (i.e., no or only minimal problems) defined as clinical response (>=30% drop in the total score of PEESS® Version 2.0 from baseline to DB week 12 [LOCF]) AND

Stratum I: Age 2 to 11 years at DB V1:

PEESS® Version 2.0 - parent report for children and teens (ages 2- 18)

• <=4 points in each of the subdomains GERD/nausea- vomiting/pain, and

• <=7 points in the subdomain dysphagia,

or

• <=5 points in the total score and >=2 subdomains with a drop of at least 50% compared to baseline at DB week 12 (LOCF),

Stratum II: Age 12 to <18 years at DB V1:

PEESS® Version 2.0 - children and teens report (ages 8-18)

• <=4 points in each of the subdomains GERD/nausea- vomiting/pain, and

• <=7 points in the subdomain dysphagia,

or

• <=5 points in the total score and >=2 subdomains with a drop of at least 50%

compared to baseline

at DB week 12 (LOCF),

4. Rate of patients with clinical remission (i.e., no or only minimal problems)

defined as above (clinical remission component of the endpoint

clinico-pathological remission) at DB week 12 (LOCF),

5. Rate of patients with clinical response at DB week 12 (LOCF), defined as

Stratum I: Age 2 to 11 years at DB V1:

>=30% drop in the total score of PEESS® Version 2.0 - parent report for children

and teens (ages 2-18) from baseline to DB week 12 (LOCF), Stratum II: Age 12 to

<18 years at DB V1:

>=30% drop in the total score of PEESS® Version 2.0 - children and teens report

(ages 8-18) from baseline to DB week 12 (LOCF)

6. In the subgroup of patients with >=4 points in NRS for dysphagia on the day

of the baseline visit (only patients of Stratum II: Age 12 to <18 years at DB

V1), the rate of patients with resolution of dysphagia symptom (i.e., no or

only minimal problems). Resolution of dysphagia symptom is defined as

• a severity of <=2 points on 0 to 10-point (0-10) NRS on each day in the week

prior to DB week 12 (LOCF).

Study description

Background summary

Recent studies suggest that swallowing budesonide is effective in the treatment of EoE, and can bring the disease in remission, and possbly maintians this for a longer period of time, while it might not be associated with the toxicities of long term use of systemic corticosteroids.

Study objective

The Budesonide oral suspension is a new drug formulation especially developed for the treatment of eosinophile esophagitis in children and adolescents. The purpose of this clinical study is to investigate whether Budesonide oral suspension is effective for induction of remission in children and adolescents with active EoE. Also see protocol paragraph 2.

Study design

This is a double-blind, randomized, multicenter, placebo-controlled, comparative, Phase II/III clinical trial in children and adolescents with EoE, >=2 to <18 years of age.

Intervention

The trial will be conducted with three treatment groups in the form of a parallel group comparison and will primarily serve to compare a 12-week oral treatment with different daily doses of budesonide oral suspension vs. placebo for the treatment of active EoE in a double-blind manner. The up to 4-week screening period will be followed by a 12-week double-blind (DB) treatment period, an optional 12-week open-label induction (OLI) treatment for eligible patients, an optional 24-week open-label extension (OLE) treatment with budesonide oral suspension for eligible patients, a 3-week tapering phase, and a 4-week follow-up period after the patient*s last end of treatment visit. Study treatments (test drug and/or placebo) will be administered orally twice daily during the respective treatment phase, once in the morning after breakfast and once in the evening after the meal (except for the OLE phase where once or twice daily dosing is given based on the decision of the investigator, and except for the tapering phase with only one dose per day).

Study burden and risks

physical examiniation 4 times, inclusive review of pubertal stage and measurement of head circumference (in chlidren up to 5 years)
endoscopy of the esophagus with biopsies 2-3 times; under deep sedation (from 10 years onwards) or narcosis (up to and including 9 years)
questionnaires related to complaints and disease: 4 questionnaires, per questionnaire a variable frequuency
completion of a diary., daily in screening, OLI and DB phase
blood examination 6-12 times
urine examiniation 11 times

The adverse events are characteristic for steroid medication, and can occur depending on the dosage, treatment 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
Adolescents (12-15 years)
Adolescents (16-17 years)

Children (2-11 years)

Inclusion criteria

Inclusion criteria for DB-treatment phase:
- Signed informed consent
- Male or female patients, >=2 to <18 years of age
- Confirmed clinico-pathological diagnosis of EoE according to established diagnostic criteria
- Clinically and histologically active EoE
- Negative pregnancy test in female patients of childbearing potential

Exclusion criteria

Exclusion criteria for DB treatment phase:
- Erosive gastroesophageal reflux disease (GERD)
- 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 untreated or inadequately treated fungal infection [candida esophagitis])
- Any known relevant infectious diseases (e.g., AIDS defining disease, active tuberculosis, hepatitis B, or hepatitis C)
- Diabetes mellitus
- If careful medical monitoring is not ensured: cardiovascular disease, hypertension, osteoporosis, active peptic ulcer disease, glaucoma, cataract, or infection
- History of cancer in the last five years
- History of esophageal surgery at any time or of esophageal dilation procedures within the last 4 weeks prior to screening endoscopy, or need for an immediate endoscopic intervention due to a stricture
- Upper gastrointestinal bleeding within 8 weeks prior to screening endoscopy
- Existing or intended pregnancy or breast-feeding

Study design

Design

Study phase:	2
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):	01-10-2020
Enrollment:	9
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Jorveza
Generic name:	Budesonide
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	09-04-2019
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO Date:	01-04-2020
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO Date:	01-05-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO Date:	25-05-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	02-09-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	16-09-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	08-09-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	20-12-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	13-04-2022
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	08-06-2022
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	16-02-2023
Application type:	Amendment

Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	20-02-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	EUCTR2017-003737-29-NL
CCMO	NL68447.078.19