Local clinical and immunological responses in eosinophilic esophagitis (EoE) patients, role of mucosal barrier function and type II inflammation**

Published: 24-03-2025
Last updated: 19-04-2025

Primary objective: To investigate the effects of fully inhibiting type 2 inflammation on esophageal mucosal barrier function and inflammation in adult EoE patients. Secondary objective: To evaluate the effect of type 2 inflammation and the IL4 /…

Ethical review	Approved WMO
Status	Pending
Health condition type	Gastrointestinal motility and defaecation conditions
Study type	Observational invasive

Summary

ID

NL-OMON57371

Source
ToetsingOnline

Brief title
Sinfonia

Condition

- Gastrointestinal motility and defaecation conditions

Synonym
allergic esophagitis, EoE

Research involving
Human

Sponsors and support

Primary sponsor: Amsterdam UMC

Source(s) of monetary or material Support: De Universiteit Utrecht heeft een subsidie ontvangen van Sanofi voor het uitvoeren van een groter project op het vlak van de pathofysiologie van EoE;het huidige voorstel is hier 1 onderdeel van. Er is een contract afgesloten tussen de Universiteit Utrecht en het Amsterdam UMC voor deze huidige studie (SINFONIA) en de kosten zullen door de Universiteit Utrecht betaald worden uit het grotere geheel. De vergoeding die het Amsterdam UMC ontvangt voor dit onderzoek komt dus indirect uit een subsidie van de industrie. ,Sanofi-aventis,Universiteit Utrecht

Intervention

Keyword: Barrier function, eosinophilic esophagitis (EoE), Inflammation

Outcome measures

Primary outcome

To investigate the effects of fully inhibiting type 2 inflammation on

esophageal mucosal barrier function and inflammation in adult EoE patients.

Secondary outcome

To evaluate the effect of type 2 inflammation and the IL4 / IL13 pathway in

particular on food-induced immune responses in esophageal biopsy specimens

exposed to different food allergens ex vivo.

Study description

Background summary

Eosinophilic esophagitis (EoE) is an allergic inflammation of the esophagus. If not treated properly, inflammation and narrowing of the esophagus can occur. This can eventually lead to food impaction.

Food allergens play an important role in the pathogenesis of EoE, as demonstrated by endoscopic and clinical resolution of EoE once the causative food is removed from the diet and exacerbation when the same food is reintroduced Similarly, amino acid-based elemental diets are effective in both adults and children with EoE. However, the exact mechanism by which food allergens can initiate inflammation in EoE is still unknown, as there are limited data on the early local esophageal immune response after challenge with a specific food trigger.

Previous research has shown that this can be treated with antacids (PPI) and corticosteroids. This reduces the permeability of the esophagus (which is increased in EoE), but not to the level of healthy individuals. Most likely this is due to a mild underlying allergic inflammation that persists under treatment with the above agents. The idea is that dupilumab inhibits this type II inflammation, which will further reduce the permeability.

In addition, the effect of food allergens on esophageal biopsies from both EoE patients and healthy patients will be examined. This will then be compared to the biopsies taken after the use of dupilumab.

Study objective

Primary objective:
To investigate the effects of fully inhibiting type 2 inflammation on esophageal mucosal barrier function and inflammation in adult EoE patients.

Secondary objective:
To evaluate the effect of type 2 inflammation and the IL4 / IL13 pathway in particular on food-induced immune responses in esophageal biopsy specimens exposed to different food allergens ex vivo.

Study design

Prospective observation study clarifying pathophysiology of EoE, in which the effects of the type 2 inflammatory pathway are studied in patients that in regular patient care receive a treatment that completely inhibits this pathway. Esophageal permeability and inflammation in EoE patients will be compared with measurements in 10 non-EoE controls and with the EoE patients themselves during IL4/IL13 blockade.

Furthermore, we would like to take biopsies in another 20 EoE subjects with active disease for our further ex vivo experiments in which response of the esophageal tissue with food allergens is studied.

Intervention

A resistance measurement is done and 16 additional biopsies are taken during the stomach examination (gastroscopy). The gastroscopy would anyway already a potential, potential of patient participates in the study. In addition, blood will be earned and the patient is asked to fill out a questionnaire.

Study burden and risks

None

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

EoE patient group with dupilumab
• Previous diagnosis of active EoE confirmed by histopathology e.g. presence of >15 eosinophilic granulocytes per hpf in mid or proximal oesophageal biopsies
• Scheduled to start with dupilumab as regular care
• 18 to 75 years of age
• Written informed consent must be obtained and documented
EoE patient group with active EoE
• Previous diagnosis of active EoE confirmed by histopathology e.g. presence of >15 eosinophilic granulocytes per hpf in mid or proximal esophageal biopsies
• Scheduled for an upper endoscopy
• 18 to 75 years of age
• Written informed consent must be obtained and documented

Non-EoE control group
• Scheduled for a upper endoscopy for other, non-EoE related, symptoms
• 18 to 75 years of age
• Written informed consent must be obtained and documented

Exclusion criteria

EoE patient group
• Use of oral or systemic antihistaminics, oral cromoglicates, systemic corticoster-oids, leukotriene inhibitors, or monoclonal antibodies, in the month preceding the study
• Proven gastroesophageal reflux disease or other cause for esophageal eosinophil-ia
• History of peptic ulcer disease
• History of Barrett*s esophagus
• History of GI cancer
• ASA class III, IV or V

Non-EoE control group
• Symptoms suggestive of esophageal disease
• Personal history of atopic, skin or systemic diseases

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Basic science

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-03-2025
Enrollment:	40
Type:	Anticipated

Ethics review

Approved WMO Date:	24-03-2025
Application type:	First submission
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
CCMO	NL87737.018.24