Ziverel for refractory reflux symptoms

No registrations found.

Ethical review	Positive opinion
Status	Pending
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON25733

Source
Nationaal Trial Register

Brief title
Ziverel

Health condition

Achalasia

Sponsors and support

Primary sponsor: Amsterdam UMC, location AMC
Source(s) of monetary or material Support: Amsterdam UMC, location AMC
Norgine

Intervention

Outcome measures

Primary outcome

Acid perfusion sensitivity score (acid perfusion test).

Secondary outcome

- Symptom score improvement based on the RDQ Questionnaire score
- Esophageal barrier function measured with Ussing chamber experiments and electrical

tissue impedance spectroscopy during endoscopy.

Study description

Background summary

Rationale: Approximately one third of the patients with gastroesophageal reflux disease (GERD) has refractory symptoms despite daily proton pump inhibitor (PPI) use. Several studies have suggested that an impaired mucosal barrier function might underlie symptom perception and esophageal acid sensitivity, and thus contributes to PPI-resistant symptoms. Therefore, impaired mucosal barrier function is considered a potential therapeutic target in reflux disease. Ziverel is a medical device that consists of hyaluronic acid and chondroitin sulphate. It is a bio-adhesive formulation with tissue regenerating abilities that coats the esophageal wall and thereby acts as a mechanical barrier against the noxious components of refluxate. One ex vivo study model in pigs demonstrated that Ziverel prevents acid perfusion-induced mucosal barrier damage in the esophagus, but these effects still have to be confirmed in humans. It has been demonstrated in prior studies that Ziverel combined with PPIs indeed provided superior control of reflux symptoms in GERD patients compared to placebo. However to date, this only has been investigated in a limited number of studies and the underlying working mechanism in humans has not been elucidated yet. Hence, more information on efficacy and mechanisms of action is warranted.

Objective: To assess the effect of Ziverel on esophageal sensitivity to acid, mucosal barrier function and reflux symptoms in patients with PPI-refractory reflux symptoms.

Study design: A prospective CE-marked medical device study with a double blind placebo-controlled, randomized cross-over design.

Study population: 22 Patients (age ≥ 18 years) with refractory reflux symptoms under PPI will be selected and invited for participation.

Intervention: Patients will receive the first period either a placebo or Ziverel four times daily for 14 days, followed by a second period in which they will receive the other study medication. There will be a washout period (at least 14 days) in between the two treatment periods. At the end of the two 14-day treatment periods questionnaires are filled in, patients will undergo an upper endoscopy with electrical tissue impedance spectroscopy and biopsy sampling for ex vivo Ussing chamber experiments and an esophageal acid sensitivity test (modified Bernstein test) will be performed. Patients will continue 2 times daily standard dose of PPI for the entire duration of the study.

Main study parameters/endpoints The main study parameter is the perfusion sensitivity score (acid perfusion test). Secondary endpoints are (1) symptom score improvement based on the RDQ Questionnaire score, and (2) esophageal barrier function measured with Ussing chamber experiments and electrical tissue impedance spectroscopy during endoscopy.

Study objective

It is hypothesized that Ziverel tackles esophageal hypersensitivity by protecting the mucosal barrier function.

Study design

14 days, after placebo and Ziverel

Intervention

Patients will receive the first period either a placebo or Ziverel four times daily for 14 days, followed by a second period in which they will receive the other study medication. There will be a washout period (at least 14 days) in between the two treatment periods. At the end of the two 14-day treatment periods questionnaires are filled in, patients will undergo an upper endoscopy with electrical tissue impedance spectroscopy and biopsy sampling for ex vivo Ussing chamber experiments and an esophageal acid sensitivity test (modified Bernstein test) will be performed. Patients will continue 2 times daily standard dose of PPI for the entire duration of the study.

Contacts

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Eligibility criteria

Inclusion criteria

In order to be eligible to participate in this study, a subject must meet all of the following criteria:
- Written informed consent
- Both male and female patients will be included

- Age above 18 years
- Symptoms of heartburn and/or acid regurgitation under PPI treatment for at least 3 months.
- A total reflux symptom score (measured through the Reflux Disease Questionnaire , RDQ) above 8 (24).
- Use of proton pump inhibitors at a standard two times daily dose for at least 4 weeks prior to inclusion, same dosage should be maintained during the entire study period.

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:
- Previous gastric or major gastrointestinal surgery other than appendectomy or cholecystectomy.
- Use of any other medication than proton pump inhibitors with a potential effect on gastrointestinal motility, secretion or sensitivity that cannot be stopped for the duration of the study (e.g. H2-blockers, antidepressants, prokinetics, antacids)
- Known Barrett’s esophagus
- History of gastrointestinal cancer
- Known allergy to one of the ingredients of Ziverel
- Severe and clinically unstable concomitant disease (e.g. liver, cardiovascular or lung disease, neurological or psychiatric disorders, cancer or AIDS and other endocrine disorders)
- Pregnant, lactating or fertile women (without contraception)

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-06-2019
Enrollment:	22

Type:	Anticipated

IPD sharing statement

Plan to share IPD: No

Ethics review

Positive opinion Date:	16-04-2019
Application type:	First submission

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
NTR-new	NL7670
Other	METC Amsterdam UMC : METC66698

Study results