Ziverel for refractory reflux symptoms

Gepubliceerd: 16-04-2019 Laatst bijgewerkt: 18-08-2022

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

Ethische beoordeling	Positief advies
Status	Werving nog niet gestart
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON25733

Bron
Nationaal Trial Register

Verkorte titel
Ziverel

Aandoening

Achalasia

Ondersteuning

Primaire sponsor: Amsterdam UMC, location AMC
Overige ondersteuning: Amsterdam UMC, location AMC
Norgine

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

Acid perfusion sensitivity score (acid perfusion test).

Toelichting onderzoek

Achtergrond van het onderzoek

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.

Doel van het onderzoek

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

barrier function.

Onderzoeksopzet

14 days, after placebo and Ziverel

Onderzoeksproduct en/of interventie

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.

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

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.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

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)

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Cross-over
Toewijzing:	Gerandomiseerd
Blindering:	Dubbelblind
Controle:	Placebo

Deelname

Nederland
Status: Werving nog niet gestart

(Verwachte) startdatum:	01-06-2019
Aantal proefpersonen:	22
Type:	Verwachte startdatum

Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

Wordt de data na het onderzoek gedeeld: Nee

Ethische beoordeling

Positief advies

Datum:	16-04-2019
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL7670
Ander register	METC Amsterdam UMC : METC66698

Resultaten