Clinical trial to evaluate safety and dose response using the C2 CryoBalloonTM 180 Ablation system for the treatment of dysplastic Barrett*s esophagus

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The objective of this study is to determine the safe and efficacious dose required to eradicate LGD or HGD in BE, or residual BE after endoscopic removal of early cancer (*therapeutic dose*), using the C2 CryoBalloon 180 Ablation System. *Dose* is...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Malignant and unspecified neoplasms gastrointestinal NEC
Study type	Interventional

Summary

ID

NL-OMON48956

Source
ToetsingOnline

Brief title
C2 CryoBalloon 180 Ablation System Dose Response Study

Condition

- Malignant and unspecified neoplasms gastrointestinal NEC
- Gastrointestinal neoplasms malignant and unspecified

Synonym
Barrett's esophagus, esophageal cancer

Research involving
Human

Sponsors and support

Primary sponsor: C2 Therapeutics, contactpersoon Marcia Wachna
Source(s) of monetary or material Support: C2 Therapeutics;Inc.

Intervention

Keyword: Barrett's esophagus, Cryoablation, Cryotherapy, Esophageal neoplasms

Outcome measures

Primary outcome

* Feasibility, defined as the number of procedures with treatment success (all BE treated as intended by the endoscopist)

* Safety will be evaluated by the incidence of Dose-related SAEs. Dose-related SAEs include pain in the treatment area greater than 6 (0-10 VAS score) at 24 hours AND 7 days post-treatment; symptomatic stricture requiring an additional EGD plus endoscopic dilation before first follow-up EGD; symptomatic stricture requiring endoscopic dilation at follow-up EGD; or any stricture (symptomatic or asymptomatic) preventing passage of the diagnostic endoscope at follow-up EGD. Any other serious adverse events within 30 days after treatment will be evaluated by DSMB for relationship to the dose and severity.

* Dose response (efficacy) is defined as eradication percentage of BE confirmed by histological evidence of eradication of BE, after circumferential treatment with the therapeutic dose (phase II). The eradication percentage will be assessed by the EGD-Adjudication Committee (EGD-AC), consisting of three physicians specialized in gastroenterology, by comparing pre-treatment and follow-up digital images of the ablated areas in a systematic and standardized manner.

Secondary outcome

1. Post-procedure pain in the treatment area from the cryoablation treatment (VAS 0-10), described as the median pain scores directly and 1, 7 and 30 days after treatment.

2. Post-procedure dysphagia (0-4 dysphagia score), described as the median dysphagia scores directly, 1, 7 and 30 days after treatment.

3. Incidence of all serious and non-serious adverse events up to 30 days post-treatment

4. Efficacy, defined as the percentage of patients with histopathological confirmed complete eradication of BE and absence of subsquamous intestinal metaplasia.

Study description

Background summary

Barrett's Esophagus (BE) is a premalignant condition, which can lead to esophageal adenocarcinoma. This particular cancer is one of the most rapidly increasing and deadliest cancers in the western world. Patients with BE are up to 40 times more at risk of adenocarcinoma than individuals without BE. Once diagnosed with BE, a patient enters a life-long surveillance program in which upper endoscopies with biopsies are performed to survey the progression of the Barrett's tissue to cancer. For more than 20 years, many technologies have been evaluated for ablation of BE. Elimination of BE and restoration of squamous esophageal lining has been demonstrated through ablation; however, no ablation technology currently provides the necessary attributes for wide-spread adoption. The CryoBalloon 180 Ablation System (System) is designed to address many of the limitations of current ablation technologies. The simplicity of the System allows for many potential benefits to the patient, the physician, and hospital. Potential benefits are a shorter and safer procedure, easier deployment minimizing the need for anesthesiology, smaller inventory requirements and no capital equipment improving capital resource utilization. Additionally, patients may experience less pain after cryoablation compared with other ablation techniques. First, the System has undergone acute and

chronic animal testing. The testing was conducted to study safety, deliverability and performance characteristics of the System. The studies were conducted for the evaluation of the device in a normal pig esophagus at dimensions very similar to a human esophagus. General follow-up time frames were either 4 days or 28 days. Hereafter, three human trials have been performed with the Focal cryoablation system, which evaluated the safety of the Focal system with several doses, the device perfomance status, and the efficacy. The studies showed safe treatment and high efficacy for cryoablation, with 100% eradication of Barrett*s epithelium in the patients treated with the maximal dose (10 sec). Currently, several trials are enrolling patients to further evaluate efficacy of the System. Anyhow, this Focal system is only able to treat relatively little areas of Barrett*s tissue. When ablating larger areas with this focal device an important risk is that certain areas won*t be treated or will be overtreated and, additionally, it can be a very time-consuming procedure. Therefore the Cryoballoon 180 Ablation Sytem was recently introduced by C2 Therapeutics. This device ablates a larger area (50% of the circumference over a length of 3cm) in one ablation, thereby enabling the ablation of larger BE tissue. This system was investigated in animal and human trials, and judged to be safe. Now, we want to evaluate the efficacy of the device in different doses, in order to find the optimal dose with maximal efficacy and minimal burden for the patient.

Study objective

The objective of this study is to determine the safe and efficacious dose required to eradicate LGD or HGD in BE, or residual BE after endoscopic removal of early cancer (*therapeutic dose*), using the C2 CryoBalloon 180 Ablation System. *Dose* is defined as the rate at which the diffuser traverses the length of the Balloon (in millimeters per second) while emitting cryogen.

Study design

Multi-center, prospective, single arm, phase 1 safety study.

Intervention

Endoscopic balloon based cryoablation. The C2 Cryoballoon 180 Ablation system has three main components: a delivery catheter with a spray-hole covered by a balloon probe, a controller and a cartridge containing the cryogenic fluid. The catheter can be inserted into the working channel of a therapeutic endoscope. Once deployed, the balloon is simultaneously inflated and cooled with cryogenic fluid from the cartridge. The BE cells of the esophagus will be ablated if they come into contact with the cooled balloon. In the Cryoballoon 180 ablation system, the spray hole of the catheter will automatically be pulled back during ablation. In this way, an area of 3 cm length covering about 50% of the circumference will be treated. The dosing will be expressed in the speed (in

mm/sec) whereby the catheter will be pulled back during the ablation (lower speeds means a higher dose). Patients will undergo two Swipes, to treat the esophageal circumferentially.

Study burden and risks

Patients will undergo 2 endoscopies in this study, which would have been performed for regular medical care as well. The difference compared to regular treatment is that during the first endoscopy patients will be treated with the Cryoballoon 180 Ablation system instead of regular radiofrequency ablation treatment. During follow-up endoscopy a thorough inspection of the esophagus, and biopsies as well, will be performed. If necessary, additional treatment will be performed with RFA. Patients need to adhere to a liquid diet after the cryoablation (not different from standard care with RFA). Furthermore patients will be contacted by telephone 1, 7 and 30 days after the cryoablation to ask for dysphagia and pain. Finally, patients may experience temporary limited pain, which can be treated with analgesics (paracetamol for example).

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

Patients must meet ALL of the following criteria to be eligible for participation in the study:
1. Flat- type BE esophagus, with an indication for ablation therapy, defined as:
a. Diagnosis of LGD or HGD in BE (confirmed by baseline histopathological analysis), OR
b. Residual BE with any grade of dysplasia after endoscopic resection (EMR or ESD) to treat non-flat BE, *6 weeks prior to enrolling the patient to this study. The ER pathology should indicate endoscopic treatment (i.e. only mucosal invasion or limited submucosal invasion (SM1), no lymphovascular infiltration, free vertical resection margins and not poorly differentiated)
2. Prague Classification Score C*3 and *M1
3. Patients should be ablation-naïve, meaning they have not undergone any previous ablation therapy of the esophagus
4. Older than 18 years of age at time of consent
5. Operable per institution*s standards
6. Provides written informed consent on the IRB-approved informed consent form
7. Willing and able to comply with follow-up requirements

Exclusion criteria

1. Esophageal stenosis preventing advancement of a therapeutic endoscope.
2. Any endoscopically visualized lesion such as ulcers, masses or nodules. Neoplastic nodules must first be treated with ER >6 weeks prior to planned treatment under this protocol.
3. Prior ER of more than 2cm in length or >50% of the esophageal lumen circumference
4. History of locally advanced (>SM1) esophageal cancer
5. History of esophageal varices
6. Prior distal esophagectomy
7. Active esophagitis LA grade B or higher
8. Severe medical comorbidities precluding endoscopy
9. Uncontrolled coagulopathy
10. Pregnant or planning to become pregnant during period of study
11. Patient refuses or is unable to provide written informed consent
12. Participation in another study with investigational drug within the 30 days preceding or during the present study, interfering with participation in the

current study
13. General poor health, multiple co-morbidities placing the patient at risk or otherwise unsuitable for trial participation

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	16-01-2018
Enrollment:	25
Type:	Actual

Medical products/devices used

Generic name:	C2 Cryoballoon 180 Ablation system
Registration:	Yes - CE intended use

Ethics review

Approved WMO

Date:	24-11-2017
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Approved WMO

Date:	23-07-2018
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United

	(Nieuwegein)
Approved WMO Date:	26-06-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

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	NL62738.100.17