Focal cryoballonablation for dysphagia in patients with advanced esophageal cancer

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1. To evaluate the feasibility of cryoballoon therapy in patients with incurable esophageal carcinoma and symptoms of dysphagia, defined as technical success rate. In addition, the efficacy and safety will be assessed by looking at the clinical...

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

Summary

ID

NL-OMON56643

Source
ToetsingOnline

Brief title
Focal cryoballoonablation for malignant dysphagia

Condition

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

Synonym
esophageal cancer, esophageal carcinoma

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: Nederlandse vereniging voor gastro-

enterologie, gastrostart,NVGE Gastrostart

Intervention

Keyword: Antitumorresponse, Cryoballoonablation, Dysphagia, Esophageal cancer

Outcome measures

Primary outcome

1. Feasibility: defined as technical success rates of a full cryotherapy procedure. This includes the ability to pass the scope and the completion of a full circle of freezing and thawing, with the number of cycles needed per site as deemed necessary by the endoscopist

2. Efficacy

- Subjective parameters based on clinical success rate at week 2 after last therapy, using the 5 point Likert dysphagia score (0= no dysphagia, 1= dysphagia to solids, 2= dysphagia to semisolids, 3= dysphagia to liquids, 4= dysphagia to saliva). An improvement of one point is considered as clinical success.

- Objective parameters:

- Ability of the diagnostic endoscope to pass

- Percentage of the diameter of the esophageal lumen that is open/ free from tumor, as assessed by the treating endoscopist and two independent assessors, comparing pre- and post-treatment.

3. Safety based on incidence of all serious adverse events up to the end of follow-up

Secondary outcome

Feasibility, efficacy and safety:

• Efficacy based on subjective parameters

o Reported outcomes on dysphagia scores twice weekly, up to two weeks after endoscopy, and thereafter at week 6, 8 and 12.

o General questions, twice weekly, up to two weeks after last treatment:

* How do you experience your symptoms now compared to before treatment (0= symptoms got significantly worse, 1= symptoms got slightly worse, 2= symptoms remained the same, 3, symptoms slightly improved, 4= symptoms significantly improved, 5= symptoms fully disappeared)

* How do you experience your symptoms now compared to yesterday (0= symptoms got significantly worse, 1= symptoms got slightly worse, 2= symptoms remained the same, 3, symptoms slightly improved, 4= symptoms significantly improved)

• Post procedural pain based on twice weekly pain scores up to two weeks after last treatment

o Pain at the area of the esophageal tumor during meals based on a NRS 0-10 (with 0 indicating no pain and 10 indicating unbearable pain)

o Pain at the area of the esophageal tumor when not eating/at rest using the same score as above

• Incidence of AE*s, defined as any undesirable experience occurring to a subject following treatment and/or that are secondary to the treatment. All adverse events reported spontaneously by the subject or observed by the investigator/ staff will be recorded.

• Necessity of receiving any other kind of palliation for dysphagia during follow-up

Immunology:

• (Changes in) Host*s anti-tumor response after cryoballoon ablation compared

to baseline.

Study description

Background summary

Dysphagia is commonly encountered in patients with esophageal carcinoma who are no candidates for treatment with curative intent. It often has a considerable impact on quality of life and can cause malnourishment. Current palliative treatments mainly include esophageal stenting and radiotherapy, but these can be associated with substantial drawbacks such as a high rate of adverse events, fatigue or an untimely/ temporary symptom improvement. Recent studies showed promising results for the use of spray cryotherapy as palliation for dysphagia. Moreover, there are suggestions that cryotherapy has a positive effect on the host*s anti-tumor response. However, no data exists on the feasibility, efficacy, safety for cryoballoon therapy in the esophagus. Secondly, cryo-immunologic data in patients with EC is lacking.

Study objective

1. To evaluate the feasibility of cryoballoon therapy in patients with incurable esophageal carcinoma and symptoms of dysphagia, defined as technical success rate. In addition, the efficacy and safety will be assessed by looking at the clinical success rate 2 weeks post-therapy, regression of tumor in the esophageal lumen, and lastly occurrence of serious adverse events (SAE*s).
2. To evaluate the host anti-tumorresponse after cryotherapy on tumor biopsies and in peripheral blood samples

Study design

Multi-center Prospective Uncontrolled Interventional Pilot Study. Patients will be identified during the RAKU (Regionaal Academisch Kankercentrum Utrecht) multi-disciplinary team meeting held at weekly intervals at the University Medical Center Utrecht, or at a multidisciplinary team meeting in the Amsterdam University Medical Center (GIOCA).
Study procedures will be performed in the University Medical Center Utrecht or the Amsterdam University Medical Center. The study procedures differ partly for patients in the UMCU compared to patients in the Amsterdam UMC:
- Patients in both centers will receive a maximum successive of 3 cryoballoon treatments at a two-weekly interval (range between 1 and 3 weeks). Two weeks

after the last treatment session, a follow-up endoscopy is performed.
- Only in patients at the UMC Utrecht peripheral blood samples and tumor biopsies will be taken during every endoscopy session. From these patients, biopsies and blood samples will later be analyzed to evaluate the host*s anti-tumor response.
- For both patients in both treatment centers counts that clinical follow up will be extended until 3 months after the last treatment session.
Our aim is to conduct the study within 6 months.

Intervention

For all treatments the C2 Focal CryoBalloonTM will be used. The intervention consists of 3 subsequent treatments with an interval of 1-3 weeks. During each treatment session, two freeze-thaw cycles of 12 seconds will be performed per treatment site. The number of cycles could be increased depending on the need as assessed by the endoscopist, indubitably also taking into account safety. Next to this, during endoscopy, tumorbiopsies will be taken only in patients at the UMC Utrecht. All treatment procedures will be done by an endoscopist with extensive experience with cryoballoon ablation.

Study burden and risks

Patients are required to visit the hospital three times (range 1-3) for a treatment session and one time for a follow-up endoscopy. These treatment sessions, if showing the expected effect, might replace palliative treatments that patients otherwise would receive. In a subset of patients (patients in the UMCU), peripheral blood samples and tumor biopsies will be taken during each hospital visit for the endoscopy. Furthermore, patients are asked to answer five short questions electronically twice a week. Besides this, patients will be called once, by a research nurse, after every treatment session to evaluate symptoms and adverse events. Cryoballoon therapy has been shown to be safe in previous studies for the treatment of Barrett*s esophagus. We do not anticipate that patients are exposed to a higher risk compared to other patients receiving cryoballoon therapy. Moreover, spray cryotherapy has already shown promising results for the treatment of dysphagia in patients with esophageal cancer and there are indications that cryotherapy has a positive effect on the anti-tumor response. In addition, other palliative options such as stenting and radiotherapy are not free of drawbacks and have potential (serious) side effects, temporary/untimely symptom improvement, and a sometimes even a lower quality of life.

Contacts

Public

Universitair Medisch Centrum Utrecht

Heidelberglaan 100
Utrecht 3584 CX
NL
Scientific
Universitair Medisch Centrum Utrecht

Heidelberglaan 100
Utrecht 3584 CX
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Age >18 years at time of consent Histopathologically-confirmed esophageal / gastroesophageal cancer Patients in the palliative setting (with or without (future) systemic chemotherapy) Dysphagia defined as a score of >=2 (able to swallow only semi-solids) Signed written informed consent

Exclusion criteria

Alternative etiology for dysphagia Inability to pass ultraslim endoscope Severe medical comorbidities precluding endoscopy Uncorrected coagulopathy Prior distal esophagectomy Expected survival <6 weeks Prior radiotherapy for esophageal cancer T4b esophageal cancer

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	24-06-2024
Enrollment:	20
Type:	Actual

Medical products/devices used

Generic name:	C2 Focal Cryoballon Ablation System
Registration:	Yes - CE intended use

Ethics review

Approved WMO

Date:	08-03-2024
Application type:	First submission
Review commission:	METC NedMec

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	NL84764.041.24