Hybrid Argon Plasma Coagulation (Hybrid-APC) for the treatment of Barrett*s esophagus with Low-Grade, High-Grade Intraepithelial Neoplasia or after Endoscopic Resection for Early Neoplasia

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

Summary

ID

NL-OMON40133

Source
ToetsingOnline

Brief title
Prospective Multicenter study Hybrid-APC Barrett's esophagus neoplasia

Condition

- Malignant and unspecified neoplasms gastrointestinal NEC

Synonym
Barrett dysplasia precancerous

Research involving

Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W,ERBE Elektromedizin Gmbh

Intervention

Keyword: Barrett, Esophagus, Hybrid-APC, neoplasia

Outcome measures

Primary outcome

1. Complete eradication of BE

2. Complete eradication of neoplasia

Secondary outcome

1. Number of Hybrid-APC treatment sessions (resection not considered)

2. Early and late postoperative complications (retrosternal pain, dysphagy, odynophagy, fever bleedings, perforation, stenosis, mortality) and required therapies for the treatment of stenosis (rate of bougie applications, number of dilatations applied to each patient)

3. Recurrence rate of BE and neoplasia within one year follow-up in both groups

4. Predictive factors for treatment success

5. Neoplastic progression under treatment

Study description

Background summary

Barrett*s esophagus (BE) is considered as the most important known risk factor for esophageal carcinoma. In BE, the normal squamous epithelium of the

esophagus has been replaced by intestinal columnar epithelium which is characterized histologically by the presence of goblet cells. Progression into cancer is through the histological stages classified as no dysplasia, low-grade intra-epithelial neoplasia (LGIN) and high-grade intra-epithelial neoplasia (HGIN).
Patients with BE are kept under endoscopic surveillance to detect malignant progression at an early and curable stage. Currently, endoscopic resection (ER) of visible lesions and ablation for eradication of the remaining BE is the standard method of treatment.

Background for Hybrid-APC
The injection of solutions (e.g. 0.9 potassium chlorid solution with or without supplementa-tion of epinephrine, methylcellulose solution, hydroxyethylstarch, hyaluronacid, autologous blood or blood substitute fluids) into the submucosa to limit the depth of thermal injury has been established both in pre-clinical studies for different tissues of the gastrointestinal tract and in the clinical practice for EMR and ESD respectively.We intend to apply fluid cushions prior to the argon plasma coagulation to protect layers below the mucosa, e.g. L. muscularis propria, against thermal damage and perforation.
The hypothesis is that the risk for stenosis and other post procedural complication will be decreased.

Study objective

The aim of the clinical trial is to evaluate Hybrid-APC as a thermal ablation therapy for the treatment of BE following preceded endoscopic resection (ER) or as a primary therapy for neoplasia that are initially not detectable using high resolution endoscopy. To improve eradication of BE and to reduce the number of post treatment complications such as stenosis in comparison to conventional APC, a fluid cushion is injected into the submucosa of the esophagus prior to APC ablation using the Hybrid-APC device.

Study design

A prospective, single arm multicenter clinical trial will be performed to determine the eradication rate of BE after treatment with Hybrid-APC in a patient population with Barrett*s esophagus containing LGIN, HGIN or early cancer. Enrollment is carried out up to a final number of 150 patients at 6 study sites The main study site is located in Germany. Next to the study centres in Germany, the Dutch centres, AMC, Amsterdam and St Antonius, Nieuwegein are involved. All histology slides from biopsies and ER specimens of BE will be read by expert local GI pathologists. Central pathology review is required for all cases who are enrolled without a prior ER and a baseline pathology of HGIN or LGIN. Biopsy slides of recurrences of LGD, HGD or cancer during follow-up will be reviewed by the central pathologist.

Treatment protocol:
Hybrid Argon Plasma Coagulation procedure
* The Hybrid-APC probe is introduced into the esophagus through the working channel and under real time visualization.
* Subsequent Injection of a fluid cushion into the submucosa of the Barrett mucosa is per-formed with the Hybrid-APC probe and the ERBEJET2 waterjet system
* Targeted ablation is performed with the APC probe
* The maximum extent of Barrett*s epithelium that can be treated in a single session is as fol-lows : for BEC3:max 50% of the
circumference is allowed.
* Cell debris visible following Hybrid-APC treatment has to be removed carefully using a transparent endoscopy cap
Treatment phase
* The First Hybrid APC treatment will be performed after a baseline endoscopy with biopsies. As a rule the treatments will be done in outpatient's services. Only in case of poor medical condition or long distance travelling admission will be advised in line with general guidelines.
* Subsequent Hybrid APC sessions in 3 month intervals are continued until complete removal of the BE has been achieved upon inspection with high resolution endoscopy and NBI or chromoendoscopy. There is a maximum of 5 treatment sessions allowed, like the allowed number of RFA treatments.
If complete remission of IM (CR-IM) and/or complete remission of intra-epithelial neoplasia will not be achieved by Hybrid APC, an escape treatment with ER may be performed. This will be defined as a failure for Hybrid-APC treatment.

Follow-up phase
Three months after the last treatment procedure, the treatment outcome will be assessed by high resolution endoscopy and NBI or chromoendoscopy and biopsies from the following
locations:

- The area immediately below (i.e. <5mm) the neo-squamocolumnar junction (at least 4 biopsies);
- Any residual Barrett*s mucosa (4QBx/2
cm);

- Neosquamous epithelium (4QBx/2
cm).

Biopsies will be taken with a standard biopsy forceps. These FU endoscopies are the same as the general guidelines.
If residual BE is detected an additional ablation session is allowed. In this case the follow-up of the patient will re-start 3 months later.
Follow-up endoscopies will be scheduled at 3, 6, 12 and 24 months after the final Hybrid APC treatment

Intervention

Eradication of barrett's esophagus

Study burden and risks

For study subjects the participation in the study means that the required therapy of Barrett's esophagus is either carried out as usual with the current "gold standard" method, e.g. the conventional APC without injections or radiofrequency ablation, or the ablation is carried out with the Hybrid-APC method. With Hybrid-APC ablation neither different kind of complications nor increased incidence of known complications are expected.
Treatment with Hybrid-APC might require longer endoscopy time compared to Barrett*s treatment using conventional treatment without submucosal injection. This might involve an increase in the amount of anesthesia for the patient.
The further therapy and post treatment cure is consistent with the established clinical standards in endoscopic Barrett*s mucosa treatment. There are 5 treatment sessions allowed. This number of sessions is the same as with RFA therapy. Control endoscopies after treatment will be performed according to the standard guidelines. There will be one extra control procedure.

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

a) Patients in the age of 18-85 years
b) Residual BE (defined as columnar lined esophagus with intestinal metaplasia) after prior ER (max 3 ER procedures) for HGD or mucosal cancer, irrespective if the residual BE harbors NDBE, LGD or HGD, OR patients with a BE without prior ER and a confirmed histological diagnosis of HGD or LGD.
c) Written informed consent.

Exclusion criteria

a) BE with a C-value <1 or a C-value >10 cm
b) Prior ER for G3/G4; L1; V1; R1 (vertical margin only) or submucosal invasion;
c) Presence of endoscopically visible abnormalities at the time of initial APC treatment (additional ER is allowed);
d) Presence of cancer in random biopsies obtained at the mapping endoscopy, 8-12 weeks before initial APC treatment;
e) Pregnancy
f) Patients in whom complete eradication is not considered a relevant treatment goal or in whom additional treatment is contraindicated;
g) Patients in whom >80% of the BE has been resected by ER;
h) Patients with incomplete wound healing 3 months post-ER despite adequate PPI-medication;
i) Prior ablative therapy in the esophagus;
j) Significant esophageal stenosis prior to initial APC treatment defined as a stenosis that can not be passed by a therapeutic endoscope or a stenosis that has been dilated endoscopically before.
k) Presence of esophageal varices
l) Anticoagulant therapy (apart from aspirin or NSAIDS) that can not be continued prior to APC or hemostatic disorders
m) Life expectancy less than 1 year

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):	09-04-2014
Enrollment:	40
Type:	Actual

Medical products/devices used

Generic name:	Hybrid APC probe and Waterjet device ERBEJET2
Registration:	Yes - CE intended use

Ethics review

Approved WMO

Date:	05-05-2014
Application type:	First submission
Review commission:	METC Amsterdam UMC

Approved WMO

Date:	27-05-2014
Application type:	Amendment
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	NL46608.018.14