PLEASE NOTE: *This trial has been registered retrospectively.*

Trial Description

Title

Hybrid APC Argon-Plasma-Coagulation Technique for the Therapy of Barrett's Esophagus With Low-grade and High-grade Neoplasia or After Primary Endoscopical Resection of Premature Neoplasia

Trial Acronym

Hybrid-APC

URL of the trial

http://none

Brief Summary in Lay Language

Few patients with longstanding reflux of acid from the stomach into the distal esophagus, manifested by heartburn, develop mucosal changes called Barrett esophagus which develops into cancer in a few cases via precursor lesions such as dysplasia. These changes and early cancer stages limited to the mucosa can be treated endoscopically if found early enough, e.g. during surveillance. Endoscopic therapy consists of resection of visible early tumors and is followed by removal of the remaining, less severely damaged Barrett mucosa by less aggressive methods, usually thermal. Among these thermal methods, radiofrequency ablation (RFA) is currently the most popular due to its high initial success rate while more recent studies have suggested recurrences in up to 30%. On contrast, argon plasma coagulation (APC) has been afflicted with limited efficacy. The decreasing success rates of RFA recently reported and the modification of the APC method by submucosal fluid injection, called Hybrid APC, make a reassessment of APC worthwile.
This study is set up to confirm feasibility and safety of Hybrid APC shown in a study from one hospital now involving multiple centers. Main hypothesis is that the ablation of neoplastic Barrett's esophagus is successful in 90%, either primarily or secondarily after endoscopic resection of visible lesions and /or mucosal carcinoma. The results of this study will serve as a basis for a later randomized comparative study of Hybrid APC with RFA which may provide final scientific evidence.

Main study hypothesis: Ablation of Barrett esophagus either primarily or secodarily after endoscopic resection of visible tumors using Hybrid APC is 90% successful.

Brief Summary in Scientific Language

For neoplastic Barrett's esophagus, a combination of resective and ablative therapies is state-of-the-art-treatment for tumors limited to the mucosa including precancerous dysplastic lesions. Visible neoplastic lesions are removed by

endoscopic resection methods (normally by endoscopic mucosal resection EMR). Subsequently, residual Barrett's mucosa without visual lesions and/or cancer from biopsy is ablated by thermal methods provided bioptic histology does not show more advanced stages than high grade intraepithelial neoplasia (HGIN). Primary BE ablation is performed if no visible lesions can be detected with and biopsies showing only low- or high grade neoplasia (LGIN/HGIN). Radiofrequency ablation (RFA) is currently considered as state-of-the-art treatment due to several randomised studies.
Other thermal methods such as argon plasma coagulation (APC) are mostly used to ablade smaller remaining areas, but could not be established as the sole thermal method after resection due to mixed results from older studies. On the other hand, recent long-term follow-up studies for RFA showed significant relapse rates of Barrett's mucosa and a 5% rate of recurrent BE cancer. The new treatment of Hybrid APC was designed to accomplish a more precise ablation of Barrett's mucosa by prior submucosal injection of saline. It was tested in an single-center pilot study and showed promising results concerning complete ablation of Barrett's mucosa in a three-month follow-up. The Hybrid APC method is based on a modification of the conventional APC therapy combined with an injection probe (probe is certified by Certificat Européenne (CE)).The concept is that the fluid injected into the submucosa can be used as mechanical protection from perforation or injury of deeper tissues, i.e. muscularis layer, limiting the electrosurgical to the surface area, aiming at improved APC effectiveness without increased stricture rate.
The therapeutic algorithm for this clinical trial is similar to multimodal endotherapy of BE consisting of resection and subsequent ablation following a detailed pre-therapeutic endoscopic-bioptic assessment. Patients with BE of 5 cm maximum length (=C5, tongues allowed up to 2 cm=M7, Prague classification) with visible neoplastic lesions (LGIN/HGIN/ presumed mucosal cancer) and/or bioptic diagnosis of cancer will undergo resection of these lesions followed by Hybrid-APC ablation of the remaining mucosa with a maximum extent of half circumferential epr session. Maximum number of ablation sessions is 5. The interval between sessions should be at least 6, but rather 8-12 weeks. Patients without visible lesions and bioptic histology of LGIN/HGIN (confirmed by second opinion histopathology) can be primarily treated by Hybrid APC without resection. Main outcome is the percentage of patients with complete removal of all BE epithelium including neoplasia as shown by one endoscopic-bioptic follow-up.

Organizational Data

- DRKS-ID: **DRKS00006114**
- Date of Registration in DRKS: **2014/05/16**
- Date of Registration in Partner Registry or other Primary Registry: **[---]***
- Investigator Sponsored/Initiated Trial (IST/IIT): **yes**
- Ethics Approval/Approval of the Ethics Committee: **Approved**
- (leading) Ethics Committee Nr.: **PV4583 , Ethik-Kommission der Ärztekammer Hamburg**

Secondary IDs

Health condition or Problem studied

- ICD10: **K22.7 - Barrett oesophagus**

Interventions/Observational Groups

- Arm 1: **Hybrid-APC treatment**
  ablation of Barrett's dysplasia as well as Low-Grade intraepithelial neoplasia (LGIN), and High-Grade intraepithelial neoplasia (HGIN) by administration of Argon-plasma-coagulation with prior submucosal injection of liquid

Characteristics

- Study Type: **Interventional**
- Study Type Non-Interventional: **[---]***
- Allocation: **Single arm study**
- Blinding: **[---]***
- Who is blinded: **[---]***
- Control: **Uncontrolled/Single arm**
- Purpose: **Treatment**
- Assignment: **Single (group)**
- Phase: **N/A**
- Off-label use (Zulassungsüberschreitende Anwendung eines Arzneimittels): **N/A**

Primary Outcome

Rate of complete eradication of Barrett's mucosa or neoplasia, proven by a negative follow-up endoscopy with bioptic controls

Secondary Outcome

-number of ablative sessions
-complications, postoperative initial and long-term
-success of therapy in relation to patient characteristics
-recurrence rates 12 and 24 months after treatment
-rate of neoplastic progression

Countries of recruitment

- DE **Germany**
- NL **Netherlands**

Locations of Recruitment

- Medical Center **Sana-Klinikum, Offenbach am Main**
- University Medical Center **Universitätsklinikum Hamburg-Eppendorf, Hamburg**
- Medical Center **Horst-Schmidt-Kliniken, Wiesbaden**
- Medical Center **Evangelisches Krankenhaus, Düsseldorf**
- Medical Center **Krankenhaus Barmherzige Brüder, Regensburg**
- University Medical Center **Academisch Medisch Centrum , Amsterdam**
- Medical Center **San Antonius-Hospital, Nieuwegein**
- Medical Center **Asklepios Klinik Barmbek, Hamburg**
- Medical Center **Vivantes Wenckebach-Klinikum, Berlin**

Recruitment

- Planned/Actual: **Actual**
- (Anticipated or Actual) Date of First Enrollment: **2014/03/26**
- Target Sample Size: **150**
- Monocenter/Multicenter trial: **Multicenter trial**
- National/International: **International**

Inclusion Criteria

- Gender: **Both, male and female**
- Minimum Age: **18 Years**
- Maximum Age: **85 Years**

Additional Inclusion Criteria

•Patients with secondary neoplastic Barrett's esophagus after successful EMR of visual lesions/ carcinoma whose endotherapy shall be continued. Histologically maximum high grade intraepithelial neoplasia with Barrett's length of ≥ 1 cm und ≤ 10 cm (Prague classification) without visual neoplasia. Any Patient with EMR not longer ago than 6 month and no ablative theray may be included
•Patients without visual lesions, thoroughly endoscoped (HD-endoscopy, acetic acid staining) and by second look approved low grade intraepithelial neoplasia (LGIN), who are supposed to get Hybrid APC as primary therapy
•Patients without visual lesions, thoroughly endoscoped (HD-endoscopy, acetic acid staining) and by second look approved high grade intraepithelial neoplasia (HGIN), who are supposed to get Hybrid APC as primary therapy according to discretion of examiner
•signed Informed Consent

Exclusion criteria

•proof of Adenocarcinoma with submucosal Infiltration in EMR supplement
•no total ablation of Barrett's mucosa planned
•Patients who are planned to have a total or more than 80% of the Barrett's extension EMR once or more often
•insufficient previous therapy outcome after 3 EMR procedures, e.g. insufficient ER with required re-EMR
•missing re-epithelisation after initial EMR as a sign of disrupted healing process
•status post any ablative therapy, e.g. APC, RFA
•Barrett's esophagus without proven neoplasia or dysplasia
•length of Barrett's esophagus >10 cm (Prague-classification, C-measurement)
•therapy-resistant stenosis (not passable with therapeutic endoscope) after EMR
•Any not curatively treated or not treatable secondary tumors
•Patients with severe general diseases (resisting American Society of Anesthesiologists Classification (ASA) III/IV, dialysis) who will prognostically not profit by the therapy, expectancy of life < 1 year
•Patients with known coagulopathy or anticoagulants other than acetylsalicylic acid
•esophageal varicosis
•pregnancy
•missing Informed Consent

Addresses

■ **Primary Sponsor**

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■ **Institutional budget, no external funding (budget of sponsor/PI)**

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Status

- Recruitment Status: **Recruiting complete, follow-up continuing**
- Study Closing (LPLV): **[---]***

Trial Publications, Results and other documents

- Approval of ethics comm. (mandatory for transfer to Studybox) **Ethikkommisssion Hamburg zustimmendes Votum**
- trial protocol (mandatory for transfer to Studybox) **Prüfprotokoll Hybrid-APC**
- Background literature **Abstract of Pilot Study**

** This entry means the parameter is not applicable or has not been set.*

**** This entry means that data is not displayed due to insufficient data privacy clearing.*