The use of CryoBalloon Focal Ablation System for residual Barrett's Esophagus Post ablation; a pilot study.

NCT02230410

April 4, 2016

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General Study Information

Principal Investigator: Kenneth Wang MD

Study Title: The use of CryoBalloon Focal Ablation System for residual Barrett's Esophagus Post ablation; a pilot study.

Protocol version number and date: Version 1 June 2014

Purpose

Hypothesis: Radiofrequency ablation (RFA) is a commonly used method for eliminating Barrett's esophagus (BE). RFA is highly effective, yet there is a set of patients who continue to have persistent dysplasia or intestinal metaplasia despite several treatments, thus this population requires follow up endoscopic therapy with a different ablative modality such as cryotherapy.

Aims, purpose, or objectives:
The primary objective of this study is to evaluate the usefulness of the C2 CryoBalloon Focal Ablation (510K cleared K131523, C2 Theraputics, Redwood City CA) in treating patients with persistent Barrett's Esophagus (less than 2 cm) despite 2 or more serial Radio Frequency ablation or endoscopic mucosal resection treatment sessions.

Background (*Include relevant experience, gaps in current knowledge, preliminary data, etc*.):

Barrett's esophagus (BE) is a pre-neoplastic condition formed by the metaplasia of the normal squamous mucosa of the distal esophagus into a specialized intestinal mucosa. Its development is mostly associated with chronic injury from gastroesophageal reflux. BE is widely considered the leading risk factor for the development of esophageal adenocarcinoma (EAC). (1) In 2009 alone, EAC accounted for 14,500 deaths in the U.S.(2) It is one of the fastest growing malignancies which carries a dismal prognosis of less than 15% survival in a 5-year period.(3)

The development of ablative therapy for BE with high grade dysplasia (HGDDYS) aims to prevent neoplastic progression to EAC. Several emerging endoscopic strategies have become attractive to gastroenterologists as standard esophagectomy portends 4% to 12% perioperative mortality with other long term complications.(4) Endoscopic mucosal resection (EMR), in spite of its potential therapeutic and diagnostic advantages, requires further endoscopic skills and procedural time. Radiofrequency ablation (RFA) is another ablative technique. RFA employs bipolar electrodes, which deliver ablative energy to the tissue.(5) The latest results of the AIM Dysplasia Trial 10 at their 2-year follow-up shows 85% and 83% eradication of dysplasia and intestinal metaplasia, respectively, after intention-to-treat analysis.(6)At these rates, there is a set of patients who continue to have persistent dysplasia or intestinal metaplasia despite serial RFA treatments and may benefit from a different ablative modality such as cryotherapy.

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Subject Information – charts, records, images, or specimens are considered 'subjects'

Target accrual: In this pilot study we propose to enroll up to 20 participants. We estimate that due to potential of unforeseen ulcerations, lesions or other abnormalities at the time endoscopy we may need to invite 24 participants to meet our accrual target.

Subject population:
Inclusion Criteria

Eligible patients for enrollment in this study must fulfill all of the following criteria:

a) Age > 18 years old

b) Able to provide informed consent

c) Patients with unifocal or multifocal BE with 2 cm who have failed at least 2 serial RFA or other endoscopic therapy such as Endoscopic Mucosal resection.

4.2 Exclusion Criteria

Exclusion from the study with any of the following:

a) Age younger than 18 years old

b) Presence of esophageal varices

c) Esophageal stricture precluding passage of an endoscope

d) Inability to provide informed consent

e) Esophageal cancer (T2 and above)

f) Coagulopathy with INR > 2.0, thrombocytopenia with platelet counts < 50,000

g) pregnancy (if required a pregnancy test would be performed as part of routine clinical care)

Will a Certificate of Confidentiality be obtained? *No*

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Study Design

Methods: *Describe, in detail, the research activities that will be conducted under this protocol*:

In this pilot study results of treatment response will be documented. During clinically indicated endoscopic procedures, the Barrett's segment length, length and presence of islands or tongues of Barrett's mucosa, mucosa abnormalities (type and size) will be documented. The battery-powered Cryoballoon Focal Ablation System (CbFAS) is a 510K cleared disposable through-the-scope balloon-based catheter made of conformable material obviating the need for sizing. The balloon catheter will place at the area of persistent visible Barrett's mucosa (2 cm. or less) for treatment following standard endoscopic technique. Upon activation by the physician, the balloon probe at the end of the catheter is simultaneously inflated and cooled with nitrous oxide. The balloon probe comes in contact with the wall of the target tissue and ablates unwanted tissue. Nitrous oxide is fully contained within the balloon. The nitrous oxide gas exits the patient through the proximal end of the catheter. The participants will be here for clinically indicated endoscopy and therapy. Patients will return in 3 months for clinically indicated endoscopy and surveillance of Barrett's Esophagus and/or esophageal cancer. At that endoscopy the Barrett's segment length, length and presence of islands or tongues of Barrett's mucosa, mucosa abnormalities (type and size) will again be documented to evaluate results. Results of clinical histological specimens obtained at both endoscopies that have been reviewed by expert GI Pathologists per clinical routine for classification of adenocarcinoma, high-grade dysplasia, low-grade dysplasia, indefinite for dysplasia, non-dysplastic intestinal metaplasia, normal squamous mucosa and normal gastric mucosa as established guidelines will be documented. Patient demographics, Endoscopy and Pathology results will be review in the Electronic Medical record including the GI Endoscopy database, MICS and Synthesis. Patients will be identified for participation from the GI Endoscopy database. Participants may have up to three cryo ablation endoscopic procedures performed.

1. Levine DS, Rubin CE, Reid BJ, Haggitt RC. Specialized metaplastic columnar epithelium in Barrett's esophagus. A comparative transmission electron microscopic study. Lab Invest 1989;60:418-32.

2. Jemal A, Siegel R, Ward E, Hao Y, Xu J, Thun MJ. Cancer statistics, 2009. CA Cancer J Clin 2009;59:225-49.

3. Umar SB, Fleischer DE. Esophageal cancer: epidemiology, pathogenesis and prevention. Nature clinical practice Gastroenterology & hepatology 2008;5:517-26.

4. Swisher SG, Deford L, Merriman KW, et al. Effect of operative volume on morbidity, mortality, and hospital use after esophagectomy for cancer. J Thorac Cardiovasc Surg 2000;119:1126-32.

5. Fleischer DE, Overholt BF, Sharma VK, et al. Endoscopic ablation of Barrett's esophagus: a multicenter study with 2.5-year follow-up. Gastrointest Endosc 2008;68:867-76.

6. Inadomi JM. Time to Burn? Endoscopic Ablation for Barrett's Esophagus. Gastroenterology 2011;141:417-9.

Check all that apply. If none apply, leave blank:

☐ This is a multisite study involving Mayo Clinic and non-Mayo Clinic sites.
When checked, describe the research procedures/activities being conducted **only** at Mayo Clinic:

☐ Mayo Clinic staff will be engaged in research activity at a non-Mayo Clinic site. *When checked, provide the location and a detailed description of the Mayo Clinic research staff involvement*.

☐ This study is to establish and/or maintain an ongoing database or registry for research purposes only.

☒ The research involves contact or interaction with subjects, for example, surveys, questionnaires, observation, blood draw.

☐ The study involves audiotaping or videotaping

Blood Collection

If this study involves prospective blood collection by finger, heel, ear stick or venipuncture, complete the following:

☐ **From healthy, non pregnant, adult subjects who weigh at least 110 pounds**. For a minimal risk application, the amount of blood drawn from these subjects may not exceed 550ml in an 8 week period and collection may not occur more frequently than 2 times per week.

Volume per blood draw: _____ml

Frequency of blood draw (e.g. single draw, time(s) per week, per year, etc.) _____

☐ **From other adults and children considering age, weight, and health of subject.** For a minimal risk application, the amount of blood drawn from these subjects may not exceed the lesser of 50 ml or 3 ml per kg in an 8 week period, and collection may not occur more frequently than 2 times per week.

Volume per blood draw: _____ml

Frequency of blood draw (e.g. single draw, time(s) per week, per year, etc.)_____

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Review of Chart, Images, Specimens

Provide the date range for collection of data and/or specimens that will be included in your research dataset. (*Example: 01/01/2000 to 12/31/2012*)

Date range: From ___/___/_____ to ___/___/_____

Check all that apply:

☐ This study involves only data and/or specimens that exist at the time this application is submitted to the IRB (IRB submission date). No data or specimens will be collected beyond this date.

☐ This study involves only data and/or specimens that will be collected after submission to the IRB.

☐ The study involves data and/or specimens that exist at the time of submission to the IRB **and** data and/or specimens that will be collected after submission to the IRB, for example a study that includes collection of existing data and prospective collection of specimens.

☐ Data and/or specimens used in this study are collected under another IRB protocol. *When checked, provide the IRB number(s) from which the research material will be obtained and check the box below to attest that subjects have provided consent for future use of their data and/or specimens, as described in this protocol*.

IRB Number(s):

□Subjects have provided consent for use of their data and/or specimens, as described in this protocol.

☐ Other data sources will be utilized in this study. When checked, provide all data sources:

Data Confidentiality, HIPAA Subject Identifiers

Review the list of subject identifiers below and, if applicable, check the box next to each subject identifier being recorded at the time you are collecting/abstracting data/specimens for use in this study.

Subject Identifiers: Individually identifiable information, including demographic data, that identifies the individual or for which there is reasonable basis to believe it can be used to identify the individual. NOTE: Identifiers apply to subjects enrolled in your study and to the subject's relatives, household members, employers, etc.

Internal refers to subject identifiers that will be included in the dataset maintained by the study team.
External refers to subject identifiers that will be shared with persons outside of the immediate study team, for example, sent to an external collaborator or shared with a national registry.

SUBJECT IDENTIFIERS Check all that apply	INTERNAL IDENTIFIER	EXTERNAL IDENTIFIER
Name		
Social Security number		
Medical record/patient registration number, lab accession, specimen or radiologic image number	X	
Study number, subject ID, or any other unique identifying number, characteristic or code that can be used to link the identity of the subject to the data	X	
Dates: All elements of dates [month, day, and year] directly related to an individual. Their birth date, date of death, date of diagnosis, etc. **Note:** Recording a year only is not a unique identifier.	X	
Medical device identifiers and serial numbers		
Biometric identifiers, including finger and voice prints, full face photographic images and any comparable images		
Web Universal Resource Locators (URLs), Internet Protocol (IP) address numbers, email address		
Street address, city, county, precinct, zip code, and their equivalent geocodes		
Phone or fax numbers		
Account, member, certificate or professional license numbers, health beneficiary numbers		
Vehicle identifiers and serial numbers, including license plate numbers		
If None of the above identifiers will be recorded or maintained in the dataset and/or sent outside of the study team, please check "None".	☐ None	X None

Statistical Information

Note: Power analyses and study endpoints are not needed for a pilot or feasibility studies.

X No statistical information. *If checked, please explain*: Pilot study, small study numbers.

Statistical Considerations

Power Statement:

Data Analysis Plan:

Endpoints

Primary:

Secondary: