Research Protocol

**(GREATER THAN LOW RISK (GTLR) / CLINICAL TRIAL)**

Title: **Safety, Feasibility and Efficacy of Anti-Reflux Ablative Therapy (ARAT) in Patients with GERD after Gastric Sleeve Surgery: A Prospective Cohort**

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|  |  |
| --- | --- |
| **Protocol Number** | **2022/ETH01208** |
| **Coordinating Principal Investigator** | **A/Prof. Payal Saxena** |
| **Signature:** | **Date:** |
|  |  |
| **Protocol Authors (Co-investigators)** | **A/Prof. Arthur Kaffes**  **Dr. Kyung Ho Choi** |
| **Sponsor (if applicable)** | **This study will be sponsored by the local health districts of each participating site and each site will take on all sponsor-related liabilities for their own site.** |
| **Proprietary Notice (if applicable)** | **N/A** |

**Ethics Statement:**

The study will be conducted in accordance with the *National Statement on Ethical Conduct in Human Research* (2018) ([Link to National Statement](https://www.nhmrc.gov.au/about-us/publications/national-statement-ethical-conduct-human-research-2007-updated-2018)) , the *CPMP/ICH Note for Guidance on Good Clinical Practice* ([Link to CPMP/ICH](https://www.tga.gov.au/publication/note-guidance-good-clinical-practice-july-2000) ) and consistent with the principles that have their origin in the Declaration of Helsinki. Compliance with these standards provides assurance that the rights, safety and well-being of trial participants are respected.

|  |  |
| --- | --- |
| **Protocol Title** | Safety, Feasibility and Efficacy of Anti-Reflux Ablative Therapy (ARAT) in Patients with GERD after Gastric Sleeve Surgery: A Prospective Cohort |
| **Objectives** | The primary objective:   * To assess rate of PPI discontinuation post ARAT in patients who have previously undergone sleeve gastrectomy   The secondary objectives are:   * To measure reduction of PPI use * To measure changes in GERDQ score * To measure changes in acid exposure time and DeMeester Scores on 72-hour capsule manometry * To assess adverse events |
| **Study design** | Prospective single arm pilot study |
| **Planned sample size** | 20 |
| **Selection criteria** | **Indications**   1. Persisting reflux symptoms if weaning from medication (PPI dependent) 2. Unacceptable prolonged medication use 3. Intolerance to PPI 4. DeMeester score >14.72 or acid exposure to >6% 5. At least LA Grade A esophagitis   **Inclusion Criteria:**   1. Indication #1 and at least one other indication (#2 OR #3 OR #4 OR #5) 2. Equal or above 18 years of age or below 85 3. Patients who have undergone vertical sleeve gastrectomy   **Exclusion Criteria:**   1. Conditions of primary esophageal dysmotility (i.e Achalasia, Distal esophageal spasm, etc) 2. Conditions causing secondary esophageal disorders (i.e systemic sclerosis, dermatomyositis) 3. Peptic stricture 4. Malignancy of the esophagus 5. Barrett’s esophagus with dysplasia 6. Hill Grade 4 7. Eosinophilic Esophagitis at screening endoscopy 8. Previous gastro-esophageal surgery including surgical fundoplication procedures 9. Portal hypertension and esophageal varices 10. Significant comorbidities (Charleson index score >5 or ASA >2) 11. Coagulation disorders 12. Pregnancy |
| **Study Procedure** | Anti-reflux Ablative Therapy |
| **Statistical considerations** | None |
| **Time Period of Data Collection** | December 2022 to December 2024 |
| **Duration of the Study** | 5 years |
| **Funding** | ERBE Elektromedizin GmbH (Hybrid-APC catheters) |
| **Sponsor** | This study will be sponsored by the local health districts of each participating site and each site will take on all sponsor-related liabilities for their own site. |

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# 1. BACKGROUND AND INTRODUCTION

## 1.1 Disease and proposed intervention background

Gastro-esophageal reflux disease (GERD) is a common gastrointestinal disease with prevalence increasing in the East and West(1, 2). It is a common occurrence after laparoscopic sleeve gastrectomy (LSG) with prevalence of de novo reflux ranging between 9.8 – 30%(3, 4). GERD after LSG should be considered a serious adverse outcome due to worsening quality of life and increased incidence of Barrett’s esophagus after surgery(5).

Surgical intervention with fundoplication is the gold standard of treatment in those with GERD (6-8). However, it is not technically feasible in those who have undergone LSG. A feasible surgical alternative to improve reflux is to convert the LSG to a Roux-en-Y gastric bypass (RYGBP)(9). However, there are those who do not wish to have repeat surgery and higher morbidity may be related to additional surgery and nutritional deficiencies(10-12).

Numerous endoscopic technologies have developed for the treatment of GERD for the general population including Medigus Ultrasonic Surgical Endostapler (MUSE, Medigus Ltd., Israel)(13), transoral incisionless fundoplication (TIF, EsophyX device; EndoGastric Solutions, USA)(14), GERD-X (G-SURG, Germany)(15) and Stretta (Mederi Therapeutics, USA)(16). However, there is no strong consensus for its use in those after LSG. Recently, Anti-reflux mucosectomy (ARMS) was first conceived by a Japanese group after successful mucosal resection in a refractory GRD patient with Barrett’s esophagus and high grade dysplasia, leading to resolution of reflux symptoms(17). Many pilot and feasibility studies have shown clinical efficacy and between 50 – 67% PPI discontinuation rates(18-20). There is a small but not insignificant risk of bleeding and perforation of 1%(21). ARMS also requires meticulous and repetitive motions of submucosal injection followed by hot snare resection in a circumferential pattern at the GOJ in a retroflexed endoscope position. Only one small pilot study exists containing 6 bariatric surgical patients with an endoscopic anti-reflux procedure reporting 100% technical feasibility with 5 of 6 patients reporting clinical response with >50% reduction in gastro-esophageal reflux disease health-related quality of life questionnaire (GERD-HRQL) scores(22).

Ablation may be a superior alternative due to the reduced risk of bleeding and perforation, as well as a more efficient process as shown by Inoue’s group containing 12 patients undergoing anti-reflux mucosal ablation (ARMA) with a mean operating time of 40 minutes (compared to a mean of 55 minutes for ARMS)(21, 23). Anti-reflux therapy (ARAT) using Hybrid APC may be even more efficient as both submucosal lifting and ablation can be performed through the instrument channel without the need for exchange. The first application of Hybrid APC as an anti-reflux procedure in endoscopy was reported in a retrospective study by Mondragón et al. showing cessation of PPI use of 78.6% at 36 months in a non-bariatric population(24).

Preliminary data is summarized in the Tables 1&2.

**Table 1 ARMS, ARMA & ARAT study outcomes**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Study** | **Type** | **n** | **Improved reflux symptoms** | **Discontinuation of PPI rate and follow up** | **DMS or AET pH <4.0 (pH study)** | **Adverse event rate** |
| Inoue et al. 2014(18)  Pilot | ARMS | 10 | Yes (DeMeester score 5.1 to 0.8, P < 0.0022) | 100%, follow up duration N/A | AET: 29.1% to 3.1% (P < 0.01) | 20% (2)  2 strictures due to circumferential ARMS |
| Debourdeau et al. 2020(22)  Retrospective | ARMS in bariatric cohort | 6 | Yes (50% reduction in GERDQ in 5/6 patients over 6 months) | N/A | N/A | 2/6 patients (mild) |
| Monino et al. 2020(19)  Retrospective | ARMS | 21 | Yes (GERD-Q score 12.5 to 9.0, P = 0.028, at 6 months) | 50% at 6 months | Not measured | 19% (4)  14.3% (3) Dysphagia  4.8% (1) Haem-etemesis without drop in Hb  4.8% (1) Conversion to surgical fundoplication |
| Inoue et al. 2020(23)  Pilot | ARMA | 12 | Yes (FSSG 25 to 10.5, GERD-Q 0.5 to 12, P = 0.002, at 2 months) | 67% at 2 months | DMS: 33.5 to 2.8 (P = 0.049)  AET: 9% to 0.5% (P 0.068) | 8.3% (1)  Dysphagia due to stricture |
| Yoo et al. 2020(20)  Prospective | ARMS-C | 33 | Yes (GERD-Q 11 to 6, P < 0.001, at 6 months) | 63% at 6 months | DMS: 11.6 to 4 (P < 0.001) | 6% (2)  2 strictures |
| Mondragón et al. 2020(24)  Prospective | ARAT | 108 | Yes | 78.6% at 36 months | AET: 18.8% to 2.8% (P = 0.001) | No Major AE  12.9% (14/108) stricture requiring dilatation |
| Sumi et al. 2021(21)  Retrospective | ARMS | 109 | Yes (FSSG, 25.9 to 11.7, P < 0.01, at 1 year) | 51% at 1 year | AET: 20.8% to 10.4% (P < 0.01)  DMS: 64.4 to 24.9 (P < 0.01) | Major AE:  1.8% (2/109)  1 Post-operative haemorrhage  1 minor perforation  Minor AE:  Regular ARMS  14.4% (13/88) stricture requiring dilatation  Butterfly Method  4.8% (1/21) stricture requiring dilatation |

AE – adverse events, AET - Acid exposure time, ARMS - Anti-reflux mucosectomy, DMS - DeMeester Score, FSSG – Frequency Scale for the Symptoms of GERD, PPI - Proton pump inhibitor,

**Table 2 Outcome data for laparoscopic surgical fundoplication**

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Study** | **n** | **Hospital stay & post-operative morbidity** | **Post-operative dysphagia** | **Recurrent symptoms** | **Percentage of patients on PPI at follow up** | **Esophagitis** | **24-hour manometry** | **Follow up duration** | **Adverse event rate** |
| Spechler et al. 2001(25)  RCT | 37 | Peri-operative complication: 17.2% (10/58)(25) | N/A | GRACI score 82.6 at 9.1 years | 62% (23/37) | Post-surgery: Mean grade 1.8 (n = 20) | Post-surgery AET: Mean pH <4 17.1% (n = 10) | 9.1 years | 81% (increased abdo girth, abdo fullness, inability to belch/vomit, early satiey) |
| Dallemange et al. 2005(6)  Prospective  database | 100 | N/A | 37.2% at 5 years | 10.5% had reflux at 10 years | 10.4% at 5 years and  8.6% at 10 years | N /A | N/A | 10 years | Abdominal distension and flatulence 40% |
| Mehta et al. 2006(8)  RCT | 91 | Median 2 days (1 – 10)  Peri-operative complication: 11% | 4/91 within 3 months | DeMeester score 1.1 at 6.9 years | 19% | N/A | N/A | 6.9 years | 4.4% with dysphagia required endoscopic dilatation |
| Strate et al.  2008(26)  RCT | 100 without motility disorders | Median 5 days (3 – 23)  Morbidity: 3% (infection, bleeding) | 9% at 2 years | 21% had reflux at 2 years | N/A | Pre-surgery: 78%  Post-surgery: 16% | DMS 30.7 🡪 4.6 (p < 0.001) after 2 years  36% (52 / 144 including motility disorder pts) had pathological manometry after surgery | 2 years | Bloating 53% (pre- 50%)  Inability to belch up to 25%  Re-operation:  9.5% (19/200) |
| Galmiche et al. 2011(7)  RCT | 130 | Peri-operative morbidity: 3%(27) | 11% (at 5 years) | 8% heartburn  2% acid regurgitation | N/A | 10% (LA Grade A and above) | Post-surgery AET: Mean pH <4 8.6% | 5 years | 25.4% (33/130) treatment failure requiring additional therapy (mainly PPI)  Bloating 40%  Flatulence 57% |
| Oor et al. 2017(28)  RCT | 111 | Peri-operative complication: 15.5%(29) | 43.2% | 47.5% on-going symptoms | 45.0% at 17 years | N/A | N/A | 17 years | Surgical re-intervention for all causes: 30.6% (34/111)  16% (18/111) re-intervention for GERD or Dysphagia |
| Håkanson et al. 2021(30)  RCT | 456 (PF vs. TF) | 4.6% intra-operative complications  (pneumothorax, parenchymal / splenic lac, intestinal perf) | 1.6 dysphagia episodes per day (unclear how many patients) | GSRS reflux score component 4.5 🡪 0.7 at 5 years | 84% (start) 🡪 23% (3 -year post op) | N/A | PF: AET 15% (baseline) 🡪 2.5% (3 years)  TF: AET 16% (baseline) 🡪 3% (3 years) | 5 years | 2 cases of re-operation |

PF – posterior fundoplication, TF – total fundoplication

## 1.2 Rationale for performing the study

Conversion from LSG to RYGBP is a commonly used invasive method to treat post-operative GERD. However, an endoscopic procedure may provide equal or superior therapeutic effect in patients with reflux disease with long-term remission by a minimally invasive approach. Endoscopic procedures may be more favorable for those who are reluctant to undergo repeat surgery. There is less anaesthetic risk for patients undergoing sedation for endoscopy as opposed to surgery and is thus a safer option for patients with significant comorbidities. Therefore, the aim of this study is to assess the safety, feasibility, and efficacy of ARAT by measuring the reduction in PPI use in patients after LSG.

Screening will be performed before enrolment into the study to confirm potential participants eligibility and will include:

* Initial PPI screening questionnaire
* Gastroscopy if not performed within 24 months prior to enrolment (clinic visit 1)
* High-resolution Esophageal manometry (HREM) to rule out primary esophageal dysmotility disorders.
* pH measurement with BRAVO Capsule. BRAVO capsule spontaneously migrates after initial placement on an average of 7 to 10 days.

GERDQ, validated GERD scoring system, will be performed at enrolments and at follow up clinical visits with the primary purpose of measuring symptomatic change as a result of medical or surgical therapy. pH-monitoring measured reflux and GERDQ measured symptom severity correlate well with esophagitis and is thus a validated tool to monitor relief of symptoms and assess reversal of mucosal damage(31).

# 2. Hypothesis

Endoscopic therapy using anti-reflux ablation therapy (ARAT) is safe, feasible and efficacious in patients after LSG.

# 3. Study Objectives and Aims

## 3.1 The Primary objective

* To measure the cessation of PPI use after Anti-Reflux Ablative Therapy (ARAT) in patients after LSG.

## 3.2 Secondary objectives

* To measure PPI use reduction pre- and post-procedure quantified from a baseline of twice dose daily, single dose daily, intermittent use and percentage reduction
* To measure changes in GERDQ score
* To measure changes in acid exposure time and DeMeester scores on 72-hour pH-monitoring
* To assess adverse events

# 4. Study Design

## 4.1 Study type

This study is a prospective single arm, multicenter study of safety, feasibility, and efficacy of endoscopic ARAT in patients after LSG.

## 4.2 Expected patient numbers and sample size

20 patients

## 4.3 Time period of study

|  |  |  |
| --- | --- | --- |
| **Task** | **Start Date** | **End Date** |
| **Ethics Submission** | OCT 2022 | NOV 2022 |
| **Ethics Review and Approval** | NOV 2022 | DEC 2022 |
| **Recruitment** | JAN 2023 | JAN 2025 |
| **Conduction of surveys/groups etc (follow up)** | JAN 2023 | JAN 2025 |
| **Collection of data** | JAN 2023 | JAN 2025 |
| **Analysis of Data** | JAN 2023 | JUL 2025 |
| **Preparations of Reports** | AUG 2025 | NOV 2025 |
| **Publication Draft** | DEC 2025 | MAR 2026 |
| **Submission of Publications and Final Reports** | MAR 2026 | OCT 2026 |

## 4.4 Endpoints

Primary endpoint:

* PPI therapy at 12 months post ARAT

Secondary endpoints:

1. PPI dose at 12 months post ARAT
2. GERDQ questionnaire score at baseline (prior to ARAT), 3 month and 12 month.
3. Acid exposure time (AET, % of time pH <4) and DeMeester Score at baseline (prior to ARAT) and at 12 months
4. Major and minor adverse events as per the Lexicon of endoscopic adverse events

## 4.5 Centres

|  |  |
| --- | --- |
| **Site Name/s** | Advanced Endoscopy and Gastroenterology  Suite G10, 100 Carillon Avenue, Newtown NSW 2042 |
| **Site Contact/Investigator** | Associate Professor Payal Saxena |
| **Study Procedures** | Recruitment, consent, clinic review, data collection, data analysis |

|  |  |
| --- | --- |
| **Site Name/s** | Royal Prince Alfred Hospital |
| **Site Contact/Investigator** | Associate Professor Payal Saxena |
| **Study Procedures** | ARAT, data collection, data analysis |

|  |  |
| --- | --- |
| **Site Name/s** | Chris O’Brien Lifehouse |
| **Site Contact/Investigator** | Associate Professor Payal Saxena |
| **Study Procedures** | ARAT, data collection |

# 5. Study participants

**Table 3 Data collections parameters**

|  |  |  |  |
| --- | --- | --- | --- |
| **Demographics** | **Screening** | **Procedure** | **Follow up** |
| Male or Female | Esophagitis (LA Grade) | Procedure duration | Esophagitis (LA Grade) |
| Age | Hiatus hernia (Hill Grade) | Peri-procedural complications | Hiatus hernia (Hill Grade) |
| BMI (Height and weight) | Acid Exposure Time  DeMeester Score | Post-procedural complications | Acid Exposure Time  DeMeester Score |
| Duration of GE RD symptoms (months) | Lower Esophageal Sphincter Pressure |  | Adverse events:   * Dysphagia * Infection * Aspiration pneumonia * Other organ system complications (CVA, MI, Renal failure, etc) * Stricture formation * Bleeding * Perforation * Need for repeat procedure |
| Average duration of PPI use (months)  Dose | Date of laparoscopic sleeve gastrectomy |  | Hospital stay (number; days) |
| Comorbidities (Charleson comorbidity index) or ASA |  |  | Simple Satisfaction score:   * Very satisfied or satisfied * Very unsatisfied or unsatisfied |
|  |  |  | Adverse events using the Lexicon criteria (bleeding, pain and dysphagia) |

## 5.1 Inclusion criteria

Indications confirmed via screening:

1. Persisting reflux symptoms if weaning from medication (PPI dependence)
2. Unacceptable prolonged medication use
3. Intolerance to PPI due to medication related side effects
4. DeMeester score >14.72 or acid exposure to >6% (from 24 hour pH monitoring)
5. LA Grade A esophagitis or more (from previous gastroscopy)

Inclusion Criteria

1. Indication #1 and at least one other indication (#2 OR #3 OR #4 OR #5)
2. Equal to or above 18 years of age or below 85 years of age
3. Patients who have undergone vertical sleeve gastrectomy

## 5.2 Exclusion Criteria

1. Conditions of primary esophageal dysmotility (i.e Achalasia, Distal esophageal spasm, etc)
2. Conditions causing secondary esophageal disorders (i.e systemic sclerosis, dermatomyositis)
3. Peptic stricture
4. Malignancy of the esophagus
5. Barrett’s esophagus with dysplasia
6. Hill Grade 4
7. Eosinophilic Esophagitis at screening endoscopy
8. Previous gastro-esophageal surgery including surgical fundoplication procedures
9. Portal hypertension and esophageal varices
10. Significant comorbidities (Charleson index score >5 or ASA >2)
11. Coagulation disorders
12. Pregnancy

## 5.3 Key elements of recruitment

1. *Who will be recruited?*

Patients who meet the inclusion and exclusion criteria.

1. *How will participants be identified and recruited?*

Participants will be identified from clinical referrals. Initial screening will be performed as a part of standard of care before study enrolment and will include initial PPI screening questionnaire and screening investigations (including gastroscopy if not performed within 24 months before enrolment, HREM, BRAVO pH monitoring).

Initial approach to the patient will be made by the physicians patients are referred to and who are the study investigators. In the rare cases when the clinicians are not the study investigators, study investigators will be introduced to the potential participants by those potential participants physicians.

1. *Will the potential participants be screened?*

Yes. Screening will include initial PPI screening questionnaire and screening investigations. These include a gastroscopy if not performed within 24 months of enrolment, HREM, and BRAVO pH monitoring).

1. *What is the impact of any relationship between researchers and potential participants on recruitment?*

None, the potential participants will be informed that they do not have to be enrolled in the study to have a treatment for their condition

1. *How will the recruitment strategy facilitate obtaining the consent of participants?*

Patient information sheets will be provided by study investigators who are the potential participants physicians during initial screening clinic visit (week -5) and study related questions answered. To take part in the screening procedures, the patient will be required to sign the study consent form. In case all inclusion and exclusion criteria are met after the screening, participants will be invited for the clinic visit 1 to join the study participation. Patients will be consented via hard-copy consent form, the hard copies will be stored in a locked in private rooms of A/Prof. Payal Saxena at Advanced Endoscopy and Gastroenterology.

1. *How will the recruitment strategy ensure that participants can make an informed decision about participation?*

Patient information sheets will be provided during initial screening clinic visit (Week -5) and there will be sufficient time for the participants to raise questions and have them answered prior screening procedures commence.

1. *Are there any risks associated with the recruitment strategy for potential participants or for the viability of the project?*

No.

## 5.4 Confounders

None

## 5.5 Study Limitations

Small patient numbers

# 6. STUDY PROCEDURES

## 6.1 Study Flowchart showing flow of patient

## 

## 6.2 Investigational plan

**Initial screening (week “- 5”):**

Duration of reflux symptoms and PPI dosing and duration (over the last 2-week period) will be recorded on Initial PPI Screening Questionnaire.

**Screening investigations (Week “- 1 – 4”):**

Patients will be consented via hardcopy prior to screening procedures. The consent will then be stored and locked in a filing cabinet in A/Professor Payal Saxena’s rooms at Advanced Endoscopy and Gastroenterology. These screening procedures are standard of care for the investigation of GERD and oesophageal dysmotility disorders. All patients will be asked to reduce PPI use to alternate day dosage 14 days prior and completely cease H2-antagonists and PPIs 7 days prior to their gastroscopy and BRAVO capsule insertion(32). GERDQ questionnaire will be performed on the day of BRAVO capsule insertion to assess baseline GERDQ Score. If GERD symptoms are unbearable during this weaning process, patients will also be given the choice to use their PPI as needed without affecting their inclusion into the study. However, a note will be made that PPI was used. PPI usage can restart 72 hours after BRAVO insertion until the day of ARAT. High resolution esophageal manometry will also be performed to rule out esophageal disorders.

The Los Angeles classification will be used for grading esophagitis during gastroscopy(33).

Hills classification(34) will be recorded for each patient and are as follows:

* grade I, a thick fold of tissue along the lesser curvature hugging the endoscope;
* grade II, the fold is less prominent with spontaneous openings and closing around the endoscope;
* grade III, the fold is not prominent, and the endoscopy is not tightly gripped with frequent visualization of esophageal squamous mucosa;
* grade IV, no fold is seen, hiatal hernia is always present with a visible diaphragmatic pinch of gastric mucosa and visible esophageal squamous mucosa with complete dissociation between gastroesophageal junction (GEJ) and endoscope shaft.

**Clinic visit 1 (Week 0):**

Patients will have screening results discussed and further arrangements for study procedure are made should the participants to continue in the study if inclusion and exclusion criteria are met.

**The day of the procedure (Week 1):**

*Anti-reflux ablative therapy – ARAT*

An endoscope with 9.8mm outer diameter and a 2.8mm working channel will be used (Olympus). An electrosurgical unit (ERBE VIO-200D, Tübingen, Germany), ErbeJet2 module (ERBE), and an H-APC Catheter (ERBE) will be used along with a mixture of 0.9% saline solution and 0.5% methylene blue. All procedures will be performed with the patient in the left lateral position under deep sedation with Propofol, (+/- midazolam) and fentanyl. Hybrid APC will be performed in a retroflexion view within the esophagus. The steps of the procedure will be the following:

1. Endoscopic evaluation: The GEJ is reviewed and cleaned as necessary in retroflexion view
2. Marking: 2 marking line composed of 5 – 6 dots below the GEJ towards the fundus, using soft coagulation (effect 2, 30 W) with 1.5 - 2.0cm in between the two lines. The distance between the two lines corresponds to the ablation free zone.
3. Elevation: Submucosal bleb will be created with injection of a mixed solution of saline and methylene blue all along the GEJ in retroflexion. The pressure level of injection will be set at 60 with a total amount of fluid used set at 20mls.
4. Ablation: High-power coagulation (Forced coagulation effect 3, 100W) will be applied along the GEJ starting at the z-line down to 3cm below this point in a circumferential manner ablating 270 – 320 degrees of mucosa.

Follow up:

After ARAT, the patient will be observed for 2 hours to monitor and rule out adverse events. Analgesics and antiemetics will be given if required. A liquid diet will be initiated for 48 hours, followed by an additional 72 hours of a soft diet. A normal diet will resume on day 6. To promote healing after ARAT, PPI will be administered at double dose for 4 weeks. This will be followed by 1 week of daily dosage, then 1 week of alternate daily dosage, then PPI’s will be completely ceased. At the end of PPI cessation, this will correlate with Clinic visit 2

**Telehealth (day 1 and day 7 post-ARAT procedure):**

Symptoms and adverse events will be recorded. During these telehealth conferences, participant symptoms will be reviewed, and PPI dosages checked.

**Clinic visit 2 (6 weeks post ARAT):**

Participants will be assessed with the GERDQ questionnaire and for symptoms/adverse events. 2-week PPI diaries will be provided to participants to fill before clinic visit 3 (month 3) and clinic visit 4 (month 12)

**Follow up gastroscopy (month 3 and 12):**

Gastroscopy will be performed on both visits, repeat BRAVO capsule insertion will be done for 72-hour pH monitoring at month 3 and 12 follow up gastroscopy.

**Clinic visit 3 (month 3) and Clinic visit 4 (month 12):**

Visits will be performed for symptom assessment with the GERDQ questionnaire as well as to collect from the participants 2-week PPI diaries. If PPIs were needed due to symptom recurrence, these were allowed and documented. If PPIs were used on 3 occasions or less with total accumulative doses ≤14 over the entire follow-up period, these were counted as remaining off PPI to allow for a trial of PPI use.

Table 4 Study schedule and procedures:

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Interventions | Initial screening clinic visit | Screening investigations | Clinic visit 1 (Enrolment) | ARAT | Telehealth day 1 and day 7 | Clinic visit 2 Week 8 | Follow up gastroscopy Month 3 | Clinic visit 3 Month 3 | Follow up gastroscopy  Month 12 | Clinic visit 4 month 12 |
| Timeline  (weeks) | - 5 | - 4 - 1 | 0 | 1 | 1 and 2 | 8 | 16 | 18 | 52 | 54 |
| Participant Information and Consent Form provided | ✓ |  |  |  |  |  |  |  |  |  |
| Participant Consent |  | ✓\* |  |  |  |  |  |  |  |  |
| Initial PPI screening questionnaire | ✓ |  |  |  |  |  |  |  |  |  |
| PPI weaning plan |  | ✓\*\* |  | ✓ |  |  |  |  |  |  |
| 2-week PPI intake diary |  |  |  |  |  |  |  | ✓ |  | ✓ |
| Inclusion / Exclusion criteria |  |  | ✓ |  |  |  |  |  |  |  |
| Physical examination | ✓ |  |  |  |  |  |  |  |  |  |
| GERDQ questionnaire |  | ✓\*\*\* |  |  |  | ✓ |  | ✓ |  | ✓ |
| Gastroscopy |  |  |  |  |  |  | ✓ |  | ✓ |  |
| High Resolution Manometry |  | ✓ |  |  |  |  |  |  |  |  |
| Gastroscopy + BRAVO capsule |  | ✓ |  |  |  |  | ✓ |  | ✓ |  |
| ARAT |  |  |  | ✓ |  |  |  |  |  |  |
| Symptom and adverse event assessment |  |  |  |  | ✓ | ✓ |  | ✓ |  | ✓ |

\* Participant consent is to be signed prior screening procedures commence

\*\* PPI weaning plan 2 weeks prior to BRAVO insertion

\*\*\* GERDQ performed on the day of BRAVO insertion

## 6.3 Study Procedure Risks

The only adverse event recorded for ARAT was described a prospective study containing 108 patients, whereby 12.9% (14) experienced stricture formation which was managed endoscopically with dilatation. Other risks described by similar procedures such as anti-reflux mucosectomy (ARMS) and anti-reflux mucosal ablation (ARMA) are described in the Table 1.

Dysphagia will be graded from (0 = no dysphagia, 1 = some solids, 2 = semi-solids, 3 = liquids, 4 = aphagia) using the Dakkak and Bennett score. Patients reporting dysphagia will have a gastroscopy within 2 weeks of reporting symptoms and endoscopic balloon dilatation performed if feasible. If dilatation is performed, patients will then return to routine screening clinic follow up and gastroscopy.

## 6.4 Participant recruitment and screening

|  |  |
| --- | --- |
| **Will participants be screened?** | YES |
| **If yes, what data will be collected? (NB, if participant is not eligible, will data collected be destroyed or kept?) This should be mentioned in PIS/CF)** | Yes, please refer to table 3. |
| **Who will make initial contact with participants?** | Study investigators who are physicians who patients referred to. These physicians are therefore part of the patient’s treating team. |
| **Who will perform the consent process? How will this be carried out?** | Study investigators who are physicians.  Consent process will occur prior to any screening procedures. Hard copy consent on Clinic Visit 1 (week 0) |
| **Will participants be consented verbally/explicitly/using eConsent?**  [SLHD Research Forms Link](https://www.slhd.nsw.gov.au/rpa/Research/forms.html) | No |
| **Will participants be given a specific time period to consider participating?** | Yes, sufficient time before screening procedures commence. |
| **Review of existing databases or databanks (please identify the database/databank and the custodian)** | No |
| **Review of clinic files (please include who will be reviewing these files, for example a research coordinator).** | Yes (study investigators) |
| **Advertisements (please include where the advertisement will be placed for example, in a newspaper, poster in a clinic or hospital foyer, radio announcements, website etc.)** | No |
| **Information Letter to Medical practitioners** | No |
| **Explain how potential participants will be screened for the study** | Participants will be identified from clinical referrals. Initial screening will be performed as a part of standard of care before study enrolment and will include initial PPI screening questionnaire and screening investigations (Gastroscopy if not performed within 24 months, HREM, BRAVO pH monitoring) |
| **Any other potential recruitment methods.** | No |

## 6.5 Randomization procedure

None.

## 

## 6.6 Participant enrolment

Patient information sheets will be provided during initial screening clinic visit and questions answered. During screening investigations, potential participant will have opportunities to ask further questions and decide whether they would like to participate or not. Once all inclusion and exclusion criteria have been met, the potential participants will be invited to return to clinic visit 1 (corresponding to week 0) for consent.

## 6.7 Information and consent

Information of the study, procedure and potential risks will be explained during initial screening clinic visit (Week -5). Patient information and consent form (PICF) will be provided on this day. Consent will be signed before screening investigations are performed and at least 24 hours after the PICF is provided to potential participant for consideration. Hard copies will be collected and stored in a locked room in Advanced Endoscopy and Gastroenterology, Suite G10, 100 Carillon Avenue, Newtown.

## 6.8 Waiver of consent

No waiver of consent is requested for this study.

## 6.9 End of study treatment/withdrawal procedure

Patients will have the option of withdrawing themselves from the study pre- or post-ARAT procedure if they wish. However, we will continue to monitor and follow up patients as per study timeline to ensure patient care is maintained. If a patient is withdrawn, study data will not be automatically deleted for study data purposes. Patient records in clinic will not be automatically deleted for on-going follow up and patient management.

The study will end at 12 month follow up.

1. *when and how to withdraw participants from the investigational product/trial treatment;*

At any point after the participants sign the Consent, they are free to call or email study investigators and inform them of their decision to withdraw from the study. We will re-iterate and inform the patient that the protocol does not refrain PPI use to control their symptoms. If patients still wish to withdraw from the study to pursue another treatment modality (such as surgical fundoplication or a transoral incisionless fundoplication procedure) they will be free to do so. Follow up will be arranged at regular intervals (3 and 12 months) to monitor for any adverse events.

1. *the type and timing of the data to be collected for withdrawn participant(s);*

Data will only be collected up to the point of study withdrawal. Data will be deleted at patient request only. The only data points collected for withdrawn participants will be the total number of participants initially enrolled (signed consent), followed and reason for withdrawal.

1. *whether and how participants are to be replaced; and*

Patients will not be replaced.

1. *the follow-up for participants withdrawn from the investigational product/trial treatment.*

Follow up will continue at 3 and 12 months, participants will be informed that the visits should be performed for safety reasons, however the data will not be collected. Patients will also be given a phone number to contact for any urgent issues.

1. *terminating the study if sponsor stops the study*

This study will be sponsored by the local health districts of each participating site and each site will take on all sponsor-related liabilities for their own site.

1. *will withdrawn participants be replaced?*

As point ( c )

## 6.10. Patient withdrawal

Participants may withdraw from the study for the following reasons: participant has chosen to withdraw from the study and protocol violation. The participant is free to call or email study investigators and inform them of their decision to withdraw from the study at any point during the work up.

After ARAT, patients will also be given the freedom to withdraw from the study at any point. We will re-iterate and inform the patient that the protocol does not refrain PPI use to control their symptoms. If patients still wish to withdraw from the study to pursue another treatment modality (such as surgical fundoplication or a transoral incisionless fundoplication procedure) they will be free to do so. Follow up will be arranged at month 3 and to monitor for any adverse events. These follow up periods will only be for clinic purposes and will not be entered into the REDcap database.

Data will only be collected up to the point of study withdrawal and subsequently deleted should that be requested by the withdrawn participant. The only data points collected for withdrawn participants will be the total number of participants initially enrolled (signed consent), followed by reason for withdrawal. Remaining collected datasets will be removed from the REDcap database.

# 7. OUTCOMES

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## 7.1. Definition of outcomes

**Primary outcome:**

* PPI cessation: No PPI therapy at month 3 and 12 follow up (allowing for brief trials of PPI use on less than or equal to 3 occasions during the entire follow up period).

**Secondary outcomes:**

* PPI Reduction (assessed at month 3 and 12 follow up)
* Partial response
* Double daily dose requirements reduced to single daily dose.
* Single daily dose requirements reduced to intermittent dosing.
* >50% reduction of overall PPI usage (taken from Initial screening, month 3 and 12 month follow up)
* Minimal or no response
* Reduction of PPI dose not fitting partial response criteria
* <50% reduction of overall PPI usage (taken from Initial screening, month 3 and 12 follow up)
* GERDQ improvement: A score of 0 – 75 recorded for each patient prior to ARAT (after 2 weeks of PPI cessation therapy) and at month 3 and 12 follow up. A total score of <12 with response to each individual question not exceeding 2 indicates symptom elimination.
* Reduction in acid exposure time (AET) and improvement of DeMeester score. Total reflux episodes determined by impedance will be classified as acidic (pH <4) and non-acidic (pH >4) based on pH monitoring. Both AET and DeMeester scores will be calculated from the BRAVO capsule studies and compared between screening investigation results and 12-month time points.
* Adverse events: Noted if occur at day 1, day 7, month 1, 3 and 12 follow up as described by the Lexicon of endoscopic adverse events(35).

8. **MEDICAL DEVICES**

### 8.1. Name of devices

* Olympus endoscope - Already purchased by the hospital, used routinely for endoscopies, TGA approved.
* Electrosurgical unit (ERBE VIO-200D, Tübingen, Germany) – Already purchased by the hospital, used routinely for endoscopies, TGA approved.
* ErbeJet2 module (ERBE) – Already purchased by the hospital, used routinely for endoscopies, TGA approved.
* H-APC Catheter (ERBE) – In use through regular purchase at the hospital, to be provided by ERBE for the study patients, TGA approved
* Medtronic BRAVO capsules – Will be purchased from the research trust fund. The capsules are TGA approved.

### 8.2 Involvement of the device manufacturer in the trial

The company [ERBE](https://de.erbe-med.com/de-en/) are going to supply the Hybrid-APC catheters free of charge.  Publication based on the study results will be the advantage for ERBE and the reason they will provide the catheters free of charge. ERBE does not impose any publication policy for the study results**.**

# 9. DATA COLLECTION

## 9.1. Participant registration

Potential participants who were provided PICF will be recorded on a screening log.

Once participants sign Consent form - name, date of birth, MRN will be recorded on Master coder sheet and unique study number will be assigned to each participant.

## 9.2. Forms and procedure for collecting data

1. Initial PPI screening questionnaire for clinician (please see section 18. Appendices)
2. GERDQ questionnaire attached to appendix (please see section 18. Appendices) and submitted as a separate document
3. PPI and H2-antagonist weaning plan prior to BRAVO insertion (pH monitoring system)
4. PPI intake diaries (please see Appendices) and submitted as a separate document

## 9.3. Case report forms and schedule for completion

All patient details, demographics and datapoints will be directly entered into the REDcap master code sheet (identifiable) and REDCap database (coded).

## 9.4. Data flow

After enrolment in the study, each participant will be assigned a unique study code that will be recorded on the master code sheet on REDCap along with the identifiable information. Relevant medical information will be collected from the participant and hospital records as detailed in the Table 3 Data collections parameters and Table 4 Study schedule and procedures directly into the REDCap data management system; a secure, encrypted database that stores and regularly backs up data within the SLHD ICT services environment. Only personnel involved in the study will be allowed access to the data. Only coded information will be recorded in the research database on REDCap. In accordance with GCP, data will be updated as part of day-to-day management of the study. Information and documentation will be accessible, clearly ordered, and comprehensible.

Endoscopy reports containing images are part of the patient’s medical records and will be stored on the hospital’s electronic medical record (as is standard practice).

Once participants have completed the study, investigators will review the data for any discrepancies requiring further follow-up. Data will be de-identified for research purposes.

## 9.5. Data analysis

Data will be analysed descriptively. Baseline characteristics of the patient population, BE characteristics, technical details, and procedure outcomes will be summarised as a mean (SD) or median (with interquartile range [IQR] and range) for continuous data, and as frequencies and proportions for categorical data. All statistical analysis will be performed using SAS 9.4 (SAS Institute Inc., Cary, NC).

# 10. QUALITY CONTROL AND ASSURANCE

## 10.1. Control of data consistency

Data collection form is developed with pre-defined multiple choice options where possible to insure consistency of the data being collected.

## 

## 10.2. Audits

REDcap database will be reviewed throughout the study by 3 separate study investigators (KC, AK, PS)

## 10.3. Protocol amendments

Should protocol amendments be introduced, the updated protocol will be submitted for the Ethics Committee review and will be implemented only after appropriate approval by the Ethics Committee and authorisation by the Research Governance Office.

# 11. ETHICS

## 11.1. Investigator authorisation procedure

The Principal Investigator and site Investigators are responsible for submitting this protocol and all supporting documents to the relevant Human Research Ethics Committee (HREC). HREC approval followed by Research Governance Office authorisation will be obtained before the study can be commenced.

The investigators PS, KC & AK are also responsible for overseeing the research project and ensuring that protocol is maintained. Any adverse events or changes to protocol will be reported to the Ethics Committee. Participants undergoing the study will have received information on the study and have signed an informed consent form.

## 11.2. Patient protection

The responsible investigator/s will ensure that the study is completed in accordance with the guidelines set out in the [National Statement on Ethical Conduct in Human Research](http://www.nhmrc.gov.au/guidelines/publications/e72) (2018) (the National Statement) and the [CPMP/ICH Note for Guidance on Good Clinical Practice](http://www.tga.gov.au/industry/clinical-trials-note-ich13595.htm) and any other relevant legislation/guidelines.

## 11.3 Partnering with consumers

Consumer consultations were not performed for the initial conceptualisation the study.

However, consumer(s) will be invited to provide feedback on any aspects of the study. This may include but is not limited to; evaluation of trial processes, evaluation of patient-facing documentation and feedback relevant to the design or delivery of the study.

‘The Consumer Involvement and Engagement Toolkit (the Toolkit)’ from the Australian Clinical Trials Alliance (ACTA) and Health Consumers NSW will be utilised to guide this process.

# 12. SAFETY

## 12.1. Adverse event reporting

All adverse events will be reported as per ‘A Lexicon for endoscopic Adverse Events: report of ASGE workshop’(35) Please refer to tables 1 and 2 below.

Graphical user interface, application, table

Description automatically generated

Graphical user interface, text, application, email

Description automatically generated  
Text, application

Description automatically generated

## 12.2. Serious adverse event reporting

All serious adverse events will be reported to the research Governance Office as per SLHD Research Ethics and Governance Office (RPAH Zone) requirements. The reports will be followed by a detailed written report. Follow-up reports will identify the participant(s) unique code (rather than by name).

## 12.3. Data safety and monitoring board (DSMB)

Dr Charbel Sandroussi and Dr David Yeo have been nominated as the members of the study DSMB. The study data will be reviewed by the DSMB after the initial 5 patients and quarterly thereafter.

The DSMB report will contain:

* Relevant data regarding the status of the study including enrollment and patient disposition (study completions, withdrawals and discontinuations)
* ARAT procedure details
* A summary of major protocol violations (if applicable)
* Adverse event documentation delineated in the Protocol section 12.1

As a result, the DSMB will produce recommendation:

[ ] Continuation of the trial per the protocol

[ ] Continuation of the trial with specified modifications

[ ] Suspension of the trial pending additional data

[ ] Discontinuation of the entire study

## 12.4. Early termination

Termination of the study may occur if most subjects (3 of 5) have a serious adverse event (i.e perforation, ICU admission, death). Outcomes will be reported to HREC, each with a detailed case report. All participants will be informed either over telehealth or in person. Dr. Kyung Ho Choi will be responsible for the entire termination process.

# 13. BLINDING AND UNBLINDING

N/A

# 14. CONFIDENTIALITY AND STORAGE AND ARCHIVING OF STUDY DATA

Research Data Management Plan (RDMP) is included with the submission.

No data will be stored in Excel or Word. SLHD software licence for REDCap (Research Electronic Data Capture) will be used to capture and store research data as this is a secure web-based data management tool designed for research purposes. Master Code Sheet Project Template within REDCap will be used for storage of identifiable patient data which will auto generate a de-identified record within a separate research data project in the REDCap system using a “Record ID” as a participant identifier.

The data will be kept confidentially throughout the study and for archiving and storage. Paper copies of the consents will be scanned into the REDCap project and then destroyed. Responses of paper copies of the questionnaires will be entered into REDCap project and then destroyed.

The data may be used in the future to build a larger scale trial. The data will be kept for 15 years upon study results publication.

Data collection is the responsibility of the research staff listed on the protocol under the supervision of the Principal Investigator. The Principal Investigator is responsible for ensuring the accuracy, completeness, legibility, and timeliness of the data reported.

ARAT procedures will be performed at Royal Prince Alfred Hospital and Chris O’Brien Lifehouse where all procedural data will be entered in the electronic medical records and directly into REDCap as per Data Collection.

# 15. TRIAL SPONSORSHIP AND FINANCING

This study will be sponsored by the local health districts of each participating site and each site will take on all sponsor-related liabilities for their own site.

ERBE will be covering the costs for consumables related to (Hybrid-APC catheters).

# 16. INDEMNITY

This study is insured by the NSW Health Treasury Managed Fund (TMF).

If a participant suffers any injuries or complications as a result of the research project, they will be advised to contact the study team and will be assisted with arranging appropriate medical treatment. If participants are eligible for Medicare, they can receive any medical treatment required to treat the injury or complication, free of charge, as a public patient in any Australian public hospital.

In addition, patients may have a right to take legal action to obtain compensation for any injuries or complications resulting from the study. Compensation may be available if their injury or complication is sufficiently serious and is caused by unsafe drugs or equipment, or by the negligence of one of the parties involved in the study (for example, the researcher, the hospital, or the treating doctor). Patients do not give up any legal rights to compensation by participating in this study.

# 17. TRAINING

All listed investigators must complete Good Clinical Practice (GCP) Training prior to commencement of the study, if they have not completed it within the last 3 years. Training of all study personnel in the protocol must be undertaken prior to commencement of the study .  All trial-related duties delegated by the Coordinating Principal Investigator or Principal Investigator(s) and trial-related personnel must only be delegated to those that are qualified by experience and training.

# 18. CONFLICTS OF INTEREST

There are no conflict of interest to be declared for the study.

# 19. COMPLAINTS RECEIVED FROM PARTICIPANTS ENROLLED IN A CLINICAL TRIAL

Participants should be provided with information on what to do if they have a concern or complaint about a trial. Contact details for the reviewing HREC must be included on the Participant Information and Consent Form (PICF). Any participant complaints or concerns received by the investigator or researcher directly must be notified to the reviewing HREC within 24 hours of receiving the complaint.

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# 21. ABBREVIATIONS AND DEFINITIONS

AE - adverse events

AET - Acid exposure time

ARAT - Anti-reflux therapy

ARMA - anti-reflux mucosal ablation

ARMS - Anti-reflux mucosectomy

DMS - DeMeester Score

FSSG – Frequency Scale for the Symptoms of GERD

GEJ - between gastroesophageal junction

GERD - Gastro-esophageal reflux disease

GERDQ - Gastro-esophageal reflux disease questionnaire

HREM - High-resolution Esophageal manometry

Hybrid-APC - hybrid Argon plasma coagulation

LSG - Laparoscopic sleeve gastrectomy

MUSE - Medigus Ultrasonic Surgical Endostapler

PICF - Participant Information and Consent Form

PPI - Proton pump inhibitor

RCT - Randomised controlled trials

RYGBP - Roux-en-Y gastric bypass

TIF - transoral incisionless fundoplication

# 22. APPENDICES

**Initial PPI screening questionnaire** (for clinician)

1. Date of Sleeve Gastrectomy?
2. How long has the patient had reflux symptoms in months? (estimate)
3. Total duration of PPI use (months)? (estimate)
4. PPI use Categories:

Twice per day 🗌

Once daily 🗌

Intermittent use 🗌

1. Total number of PPI doses over the last 14 days (maximum = 28 doses)
2. What type and dose of proton pump inhibitor is the patient taking?

**PPI and H2-antagonist weaning plan to start 2 weeks before BRAVO insertion (pH monitoring system)**

**Participant study ID\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_**

BRAVO capsule insertion date: \_\_\_\_\_\_\_\_\_\_\_\_\_

PPI wean plan

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Week 1, Day** | **-14** | **-13** | **-12** | **-11** | **-10** | **-9** | **-8** |
| **Date** |  |  |  |  |  |  |  |
| *AM* |  | x |  | x |  | x |  |
| *PM* |  | x |  | x |  | x |  |
| **Week 2, Day** | **-7** | **-6** | **-5** | **-4** | **-3** | **-2** | **-1** |
| **Date** |  |  |  |  |  |  |  |
| *AM* | x | x | x | x | x | x | x |
| *PM* | x | x | x | x | x | x | x |

Instructions:

* Please carry out this weaning plan if you are on a proton pump inhibitor (PPI)
* You should NOT take your PPI on the days marked with an ‘x’
* The stomach acid measuring system will be inaccurate if you do not follow this weaning schedule
* If your symptoms are unbearable, you are allowed to take your medication even on the days marked with an ‘x’
* If you DO take your PPI on a day marked with an ‘x’, please circle the ‘x’
* Return this form to your doctor

H2-Antagonist wean plan

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Week 1, Day** | **-14** | **-13** | **-12** | **-11** | **-10** | **-9** | **-8** |
| **Date** |  |  |  |  |  |  |  |
| *AM* |  | x |  | x |  | x |  |
| *PM* |  | x |  | x |  | x |  |
| **Week 2, Day** | **-7** | **-6** | **-5** | **-4** | **-3** | **-2** | **-1** |
| **Date** |  |  |  |  |  |  |  |
| *AM* | x | x | x | x | x | x | x |
| *PM* | x | x | x | x | x | x | x |

Instructions:

* Please carry out this weaning plan if you are on a H2-antagonist
* You should NOT take your H2-antagonist on the days marked with an ‘x’
* The stomach acid measuring system will be inaccurate if you do not follow this weaning schedule
* If your symptoms are unbearable, you are allowed to take your medication even on the days marked with an ‘x’
* If you DO take your H2-antagonist on a day marked with an ‘x’, please circle the ‘x’
* Return this form to your doctor

**PPI and H2-antagonist weaning plan to start 2 weeks before clinic visit 2**

**Participant study ID\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_**

Clinic visit 2 date: \_\_\_\_\_\_\_\_\_\_\_\_\_

PPI wean plan

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Week 1, Day** | **-14** | **-13** | **-12** | **-11** | **-10** | **-9** | **-8** |
| **Date** |  |  |  |  |  |  |  |
| *AM* |  | x |  | x |  | x |  |
| *PM* |  | x |  | x |  | x |  |
| **Week 2, Day** | **-7** | **-6** | **-5** | **-4** | **-3** | **-2** | **-1** |
| **Date** |  |  |  |  |  |  |  |
| *AM* | x | x | x | x | x | x | x |
| *PM* | x | x | x | x | x | x | x |

Instructions:

* Please carry out this weaning plan if you are on a proton pump inhibitor (PPI)
* You should NOT take your PPI on the days marked with an ‘x’
* The stomach acid measuring system will be inaccurate if you do not follow this weaning schedule
* If your symptoms are unbearable, you are allowed to take your medication even on the days marked with an ‘x’
* If you DO take your PPI on a day marked with an ‘x’, please circle the ‘x’
* Return this form to your doctor

H2-Antagonist wean plan

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Week 1, Day** | **-14** | **-13** | **-12** | **-11** | **-10** | **-9** | **-8** |
| **Date** |  |  |  |  |  |  |  |
| *AM* |  | x |  | x |  | x |  |
| *PM* |  | x |  | x |  | x |  |
| **Week 2, Day** | **-7** | **-6** | **-5** | **-4** | **-3** | **-2** | **-1** |
| **Date** |  |  |  |  |  |  |  |
| *AM* | x | x | x | x | X | x | x |
| *PM* | x | x | x | x | X | x | x |

Instructions:

* Please carry out this weaning plan if you are on a H2-antagonist
* You should NOT take your H2-antagonist on the days marked with an ‘x’
* The stomach acid measuring system will be inaccurate if you do not follow this weaning schedule
* If your symptoms are unbearable, you are allowed to take your medication even on the days marked with an ‘x’
* If you DO take your H2-antagonist on a day marked with an ‘x’, please circle the ‘x’
* Return this form to your doctor

**PPI Diary (Clinic visit 3 and Clinic visit 4)**

**Participant study ID\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Week 1** | | | | | | | |
| **Day** | **1** | **2** | **3** | **4** | **5** | **6** | **7** |
| **Date** |  |  |  |  |  |  |  |
| *AM* |  |  |  |  |  |  |  |
| *PM* |  |  |  |  |  |  |  |
| **Week 2** | | | | | | | |
| **Day** | **8** | **9** | **10** | **11** | **12** | **13** | **14** |
| **Date** |  |  |  |  |  |  |  |
| *AM* |  |  |  |  |  |  |  |
| *PM* |  |  |  |  |  |  |  |

Instructions

* Please tick the box corresponding to the morning (AM) or afternoon/evening (PM) (or both) when you take your PPI

**GerdQ Questionnaire**

**Participant study ID\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_** Date: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Questions | Frequency score (points for symptom) | | | |
| 0 day | 1 day | 2-3 days | 4-7days |
| How often did you have a burning feeling behind your breastbone (heartburn)? | 0 | 1 | 2 | 3 |
| How often did you have stomach contents (liquid of food) moving upwards to your throat or mouth (regurgitation)? | 0 | 1 | 2 | 3 |
| How often did you have pain in the centre of the upper stomach? | 3 | 2 | 1 | 0 |
| How often did you have nausea? | 3 | 2 | 1 | 0 |
| How often did you have difficulty getting a good night’s sleep because of your heartburn and/or regurgitation? | 0 | 1 | 2 | 3 |
| How often did you take additional medication for your heartburn and/or regurgitation, other than what the physician told you to take (such as Mylanta, Pink Lady)? | 0 | 1 | 2 | 3 |

DOCTOR USE ONLY

Total score: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_