**Appendix 1 Trial registration-dataset**

| **Data category** | ChiCTR2000038409 |
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| Primary registry and trial identifying number | http://www.chictr.org.cn/showproj.aspx?proj=56358 |
| Date of registration in follow-up registry | 5 November 2021 |
| Source(s) of monetary or material support | The trial was supported by the National Natural Science Foundation of China (31720103911) and Jiangzhong Pharmaceutical Company Limited to Heping Zhang. |
| Primary sponsor | Jiangzhong Pharmaceutical Co., Ltd. |
| Contact for public queries | SE, MD, MPH [email address] |
| Contact for scientific queries | SE, MD, MPHBernhard Nocht Institute for Tropical Medicine, Hamburg, Germany |
| Public title | Effect of probiotics on gut microbiota in patients with gastroesophageal reflux treated with rabeprazole |
| Scientific title | *Effect of probiotics on gut microbiota in patients with gastroesophageal reflux treated with rabeprazole* |
| Countries of recruitment | China |
| Health condition(s) or problem(s) studied | Probiotics; Proton pump inhibitors; Gut microbiome |
| Intervention(s) | ***Probiotics group:*** *Initial Treatment Period (Weeks 1-8): Multiple probiotics+ rabeprazole. Maintenance Treatment Period (Weeks 9-12): Multiple probiotics.**Multiple probiotics containing strains such as Lactobacillus casei Zhang, Bifidobacterium lactis V9, and Lactobacillus plantarum P9, 2 g/bar, each containing active probiotics (≥ 50 billion CFU), were obtained from Jiangzhong Pharmaceutical Company Limited (China). Rabeprazole dosage: 10 mg/tablet, twice a day, before meals.****Placebo group****: Initial Treatment Period (Weeks 1-8): Probiotic placebo + rabeprazole. Maintenance Treatment Period (Weeks 9-12): Probiotic placebo.**The Probiotic placebo ingredients are maltodextrin, orange powder, and maltitol, and there are no active ingredients. The appearance, packaging, storage method, and dosing were the same as those of the* *Multiple probiotics from Jiangzhong Pharmaceutical Company Limited (China).* |
| Key inclusion and exclusion criteria | **Inclusion criteria:** (1) One of the following criteria must be met:1) In the past 3 months, gastroscopy performed at domestic tertiary hospitals showed oesophagitis (LA-A, LA-B or LA-C);2) In the past 3 months, gastroscopy performed at domestic tertiary hospitals did not reveal oesophagitis, but symptoms such as heartburn, acid reflux, and poststernal burning pain are present; in addition, the RDQ score is ≥ 12;(2) The subject is aged 18-65 years (inclusive) and is male or female;(3) The subject has signed an informed consent form. |
| **Exclusion criteria:** (1) Used GERD-related drugs, such as acid inhibitors, antacids, prokinetics, gastric mucosal protectors, and herbs (see Appendix 3), or probiotics and probiotic-related preparations in the last 2 weeks;(2) Any of the following conditions:a. Liver insufficiency, defined as alanine aminotransferase (ALT) or aspartate aminotransferase (AST) > 2 × upper limit of normal (ULN);b. Renal insufficiency, defined as serum creatinine (Scr) > 1 x ULN;c. Heart failure or electrocardiogram (ECG) abnormalities;(3) Peptic ulcer and bleeding, oesophageal gastric varices, or upper gastrointestinal malignancies confirmed by endoscopy at tertiary hospitals in China in the last 3 months;(4) Myocardial infarction, stroke, or malignant tumour;(5) History of gastro-oesophageal or duodenal surgery;(6) Plans to become pregnant or father a child in the near future, or pregnancy or breastfeeding inwomen.(7) Inability to cooperate, such as an inability to understand the informed consent form or unwillingness to provide personal information;(8) Allergies to the study drug (rabeprazole) or probiotics;(9) Oesophagitis caused by gastric retention and pyloric obstruction. |
| Study type | Interventional |
| Allocation: randomized intervention model. Parallel assignment masking: double blind (subject, caregiver, investigator, outcomes assessor) |
| Primary purpose: prevention |
| **Date of first enrolment** | **September 2020** |
| Target sample size | 120 |
| Recruitment status | Recruiting |
| Primary outcome(s) | The primary measure is the change in gut microbiome. |
| Key secondary outcomes | The secondary measures are the Reflux Disease Questionnaire score, Gastrointestinal Symptom Rating Scale score, faecal metabolome, body mass index and Los Angeles grade of oesophagitis. |