**Supplementary Material 1. Study Information**

Study Title:A Prospective, Open-Label, Observational Study to Evaluate the Prediction Factors on Responses of Esomezol and Lifestyle Modification Respectively at 1Month and 3Months among Korean Adults Diagnosed with Laryngopharyngeal Reflux

This study is aimed to evaluate the contribution factors of the treatment response in patients with laryngopharyngeal reflux disease (LPRD). You should read the instructions and consent form carefully before deciding whether to participate in this study or not. It is important that you understand why this research is being done and what it does. The researcher conducting this study will explain to you about the study. This study will be conducted only for those who have voluntarily expressed their intention to participate.

Please read the following carefully before deciding to participate and, if necessary, discuss it with your family and friends. If you have any questions, please fill free to ask and your researcher or associates will explain in detail. Your signature means that you have been informed of details of the study and risks of the study. Your signature on this document means that you (or your legal representative) wish to participate in this study.

**1. Background and purpose of the study**

The purpose of this study is to prospectively evaluate the contributing factors affecting the response to proton pump inhibitor (PPI, Esomezol®, S-omeprazole strontium tetrahydrate 49.3 mg, Hanmi Medical, Seoul, Korea) and lifestyle modification treatment after 1 month and 3 months in Korean adult patients with LPRD. We intend to use the results of this study as basic data for use in patient management related to disease management, medication, and therapeutic lifestyle improvement of patients with LPRD in Korea.

**2. Participants of the study and duration of the study**

About 400 Korean adult patients with LPRD who visit the otorhinolaryngology outpatient clinic will participate in this study, and the study subjects will be asked to participate in this study for 3 months.

**3. Research methods**

If you agree to participate in this study, sign the consent form and content to all the terms and conditions for participating in this study, we will collect data at each of your hospital visits, which will be approximately three times during the 3 months of the study period.

In the initial visit, medical assessment for the diagnosis of LPRD will be performed. After the confirmation of your diagnosis, you will be asked to give us information on Esomezol® and other medications that you had been taken before or are currently taking and needs to be taken during the study period. After thorough medical and medication history taking, you will be assessed as an eligible participant for this study. When this screening process is finished, you will be enrolled as a participant of this study and Esomezol® along with therapeutic lifestyle modification will be prescribed for the treatment of your LPRD. You will be asked to comply with the following instructions as therapeutic lifestyle modification: head elevation during sleep (sleep habit), restriction of late-night meals within 2–3 hours before sleep (diet habit 1), small bites with slow eating (diet habit 2), avoidance of caffeine, carbonated beverages, chocolate, peppermint, tomato, citrus fruits, fats, fried food, and red wines (diet habit 3), avoidance of alcohol and cigarette smoking.

In the following visits, you will be asked to provide information on compliance to medication and therapeutic lifestyle modifications (weight, sleep habits, diet habits, physical activity, abstinence from alcohol, smoking cessation, etc.), and adverse events (adverse reactions) that you have experienced during the study period. Esomezol® will be prescribed to you on each visits, which you will be asked to take until your next visit, at the investigator's discretion.

The information collected at each of your hospital visits and its process are as follows.

1) Initial visit (first visit)

- Introduction to specific study information and documentation of informed consent

- Confirmation of inclusion/exclusion criteria

- Record birth date, participant initial, sex, height, body weight, smoking status, alcohol status, and measure blood pressure and heart rate

- Verification of past and/or current medical history according to the date of LPRD diagnosis

- Review family history of LPRD and verify past medication history within 1 month prior to participating date of this study

- Complete questionnaire for mental health status (Hospital Anxiety and Depression, HAD) and subjective symptoms of LPRD (Reflux Symptom Index, RSI), and conduct laryngoscope (Reflux Finding Score, RFS) and objective laboratory tests which the investigator deems necessary

- Prescription of Esomezol® for 1 month

- Confirm current (baseline) status of each items in therapeutic lifestyle modification (sleeping habit, diet habits, physical activity, smoking status, and alcohol status, etc)

- Verification of concurrent medication history and explanation of the definition and detailed examples of adverse events (adverse reactions)

2) Second visit (1 month from the initial visit) and additional visits (on participants’ request)

- Check body weight, blood pressure, and heart rate

- Complete RSI questionnaire, and conduct laryngoscope for evaluation of RFS and objective laboratory tests which the investigator deems necessary

- Check compliance to medication (Esomezol®) and prescribe Esomezol® for 2 more months

- Check compliance to each items in therapeutic lifestyle modification (sleeping habit, diet habits, physical activity, smoking cessation, and abstinence from alcohol, etc)

- Verification of concurrent medication history and identification of adverse events (adverse reactions) associated with taking Esomezol®

3) Final visit (3 months from the initial visit)

- Check body weight, blood pressure, and heart rate

- Complete RSI questionnaire, and conduct laryngoscope for evaluation of RFS and objective laboratory tests which the investigator deems necessary

- Check compliance to medication (Esomezol®)

- Check compliance to each items in therapeutic lifestyle modification (sleeping habit, diet habits, physical activity, smoking cessation, and abstinence from alcohol, etc)

- Verification of concurrent medication history and identification of adverse events (adverse reactions) associated with taking Esomezol®

**4. Drop out of study participation**

After you have agreed to participate in this study, you may withdraw your agreement at any time. If you wish to stop participating in this study, please fill free to notify the researcher or principal investigator at any time of the study period.

**5. Side effects or risk factors for adverse events (adverse reactions)**

The precautions (side effects or risk factors for adverse events) written in the product description of the research drug Esomezol® that you will be taking are as follows. For more information, please refer to the product manual enclosed in your prescribed drug.

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| (In capsule form)1. **Do not administer this drug** to the following patients.
2. Patients with hypersensitivity to this drug, its components, or benzimidazoles and benzimidazole class compounds, and a history of such hypersensitivity reactions
3. Patients with hypersensitivity to penicillin antibiotics (when combined with amoxicillin to eradicate Helicobacter pylori)
4. Patients with hypersensitivity to macrolide antibiotics (limited to when combined with clarithromycin to eradicate Helicobacter pylori)
5. Patients receiving terfenadine, cisaprid, pimozide, or astemizole (limited to co-administration with clarithromycin for the eradication of Helicobacter pylori) (Please refer to drug-drug interactions)
6. Patients taking atazanavir and nelfinavir (Please refer to drug-drug interactions)
7. Breast-feeding women
8. **Side effects or adverse events (adverse reactions)**
9. The following adverse reactions were confirmed or suspected in clinical trials and post-marketing investigations. There was no dose correlation. Adverse events were classified according to frequency (frequently > 1/100, < 1/10 ; occasionally > 1/1,000, < 1/100 ; rarely > 1/10,000, < 1/1,000 ; very rarely < 1/10,000).
* Blood and lymphatic system: rarely leukopenia, thrombocytopenia, very rarely agranulocytosis, pancytopenia
* Immune system: rarely hypersensitivity reactions such as fever, angioedema, anaphylactic reaction/shock, etc
* Metabolism/Nutrition: occasionally peripheral edema, rarely hyponatremia, very rarely hypomagnesemia
* Psychiatric: sometimes insomnia, rarely agitation, mental confusion, depression, very rarely aggression, hallucinations
* Nervous system: frequent headache, occasionally dizziness, paresthesia, drowsiness, rarely taste disorders
* Vision: rarely blurred vision
* Auditory and labyrinth: sometimes vertigo
* Respiratory system: rarely bronchospasm
* Gastrointestinal system: pancreatitis, frequent abdominal pain, constipation, diarrhea, bloating, nausea/vomiting, sometimes dry mouth, rarely stomatitis, gastrointestinal candidiasis, very rarely microscopic colitis
* Hepatobiliary system: sometimes increased liver enzymes, rarely hepatitis with or without jaundice, very rarely hepatic insufficiency, encephalopathy in patients with pre-existing liver disease
* Skin and subcutaneous tissue: occasionally dermatitis, itching, rash, urticaria, rarely hair loss, photosensitivity, very rarely erythema multiforme, mucosal eye syndrome (Stevens-Johnson syndrome), toxic epidermal necrolysis (Riel syndrome)
* Musculoskeletal system: fractures, rarely joint pain, myalgia, very rarely muscle weakness
* Renal and urinary system: very rarely interstitial nephritis
* Reproductive system: very rarely gynecomastia
* Systemic and administration site: rarely asthenia, increased sweating
* Infection: Clostridium difficile diarrhea (frequency unknown)
1. In addition, the following adverse reactions were reported to be related to, or possibly related to Esomezol® with an incidence of less than 1%.
* Whole body: abdominal distension, allergic reaction, back pain, chest pain, substernal chest pain, facial edema, facial flushing, fatigue, fever, influenza-like disorder, general edema, leg edema, malaise, pain, stiffness, asthenia, peripheral edema
* Cardiovascular system: flushing, hypertension, tachycardia
* Endocrine system: thyroid adenoma
* Digestive system: large intestine hypersensitivity, worsening of constipation, dyspepsia, dysphagia, gastrointestinal dysplasia, epigastric pain, belching, esophageal disorder, frequent defecation, gastroenteritis, gastrointestinal bleeding, hiccups, melanosis, oral disorders, pharyngeal disorders, rectal disorders, gastrointestinal symptoms, increased blood gastrin, tongue disorders, tongue edema, ulcerative stomatitis, vomiting
* Hearing: otalgia, tinnitus
* Blood system: anemia, hypochromic anemia, cervical lymphadenopathy, nosebleeds, leukocytosis, leukopenia, thrombocytopenia
* Liver: bilirubinemia, liver dysfunction, ALT increase, AST increase
* Metabolism/Nutrition: diabetes mellitus, hyperuricemia, hyponatremia, ALP increase, dry mouth, vitamin B12 deficiency, weight gain, weight loss
* Musculoskeletal system: arthritis exacerbation, arthropathy, convulsions, fibromyalgia syndrome, hernia, polymyalgia rheumatica, arthralgia
* Psychiatric and mental nervous system: anorexia, apathy, increased appetite, confusion, exacerbation of depression, hypertonia, agitation, hypoesthesia, erectile dysfunction, insomnia, migraine, aggravated migraine, sleep disturbance, tremor, dizziness, vertigo, visual field loss, paresthesia, drowsiness
* Reproductive system: dysmenorrhea, menstrual disorder, vaginitis
* Respiratory system: asthma exacerbation, cough, dyspnea, laryngeal edema, pharyngitis, rhinitis, sinusitis
* Skin/Attached Organs: acne, itchy anus, rash, erythematous rash, rash maculopapular, angioedema, dermatitis, itchiness, urticaria, increased sweating
* Special sensory organs: otitis media, abnormal sense of smell, loss of taste, confusion of taste
* Genital and urinary system: urinary abnormality, albuminuria, cystitis, dysuria, fungal infection, hematuria, urinary frequency, candidiasis, genital candidiasis, polyuria
* Visual: conjunctivitis, visual abnormality
* Adverse reactions detected on endoscopy: duodenitis, esophagitis, esophageal stricture, esophageal ulcer, esophageal varices, gastric ulcer, gastritis, benign polyps or nodules, Barrett's esophagus, mucosal discoloration, hernia
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**6. Benefits of participating in this research**

There is no direct benefit from your participation in this study, and no monetary compensation is provided. However, the information you provide will help us to better understand the treatment of patients with LPRD. Even if you do not consent to participate in this research or share information for this research, there will be no discrimination nor disadvantages in the course of your treatment and prescription of drugs.

**7. Disadvantages for not participating in this research**

You are free to not participate in this study. Also, there will be no disadvantage to you even if you choose not to participate in this study, and your decision will not affect your future access to care.

**8. Privacy and confidentiality**

Personal information collected from you through your participation in this study is as follows: 1) personally identifiable information, 2) clinical information, 3) epidemiological information.

This information is used for about 3 years for research, and the collected information is appropriately managed in accordance with the Personal Information Protection Act of Korea. We will do our best to ensure the confidentiality of all personal information obtained through research.

Your name and other personal information will not be used when the personal information obtained from this research is disclosed in a scientific journal or conference. However, if required by the law, your personal information may be provided.

In addition, monitor agents, inspectors, and the Medical Research Ethics Review Committee of Seoul National University Hospital may directly view the research results in order to audit whether the Declaration of Helsinki is followed during the entire research period, and to verify the reliability of the procedures and data of this research within the range stipulated by the relevant regulations without infringing on the confidentiality of the research participants.

By signing this consent form, you will be deemed to have been informed of and consent to these matters.

After the end of the study, the research-related data will be kept for 3 years and then disposed of in an appropriate way.

**9. Research inquiry**

If you have any questions about this study or if you have any problems during the study, please feel free to contact the following research staff:

Name: Seong Keun Kwon

Associate professor

Department of Otorhinolaryngology-Head and Neck Surgery, Seoul National University Hospital

Telephone number: 82-2-2XX2-XXXX

If you have any questions on your rights as a research participant at any time, please contact the Medical Research Ethics Review Committee of Seoul National University Hospital.

Medical Research Ethics Review Committee of Seoul National University Hospital

Telephone number: 82-2-2XX2-XXXX

e-mail: sXXXXXb@XXXXX.com