*Original Article*

# Healing Effect of Rebamipide in Addition to Omeprazole for Gastric Ulcer: Preliminary Results of a Randomized, Double-blind, Placebo-controlled Trial

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***Background:*** Rebamipide is a mucoprotective agent which has anti-oxidative and anti-inflammatory effects, as well as the ability to increase mucosal blood flow. From theoretical basis, addition of rebamipide to proton pump inhibitors (PPI) may facilitate the healing of gastric ulcer (GU).

***Objective:*** To compare the GU healing rates between treatment with a combination of rebamipide plus omeprazole and omeprazole monotherapy.

***Materials and Methods:*** This double-blind, randomized, placebo-controlled trial was conducted at Rajavithi Hospital, Bangkok between 2018 to 2019. Patients with GU size 0.5 to 3 cm were randomly assigned into either combination group (omeprazole 20 mg OD + rebamipide 100 mg TID) or PPI monotherapy group (omeprazole 20 mg OD + placebo). Primary endpoint was healed GU after 4 weeks of treatment determined by follow-up esophagogastroduodenoscopy.

***Results:*** A total of 70 patients were randomized and 64 completed the present study. The proportion of patients with non-steroidal anti-inflammatory drugs (NSAIDs) use and *Helicobacter pylori* positive were 42.9% and 68.6% in the combination group, 62.9% and 60% in the PPI group, without statistically significant difference. Overall, healed GU occurred in 77.1% in the combination group, and 60% in the PPI group, as intention-to-treat analysis ($p$ = 0.198). Mean change of size of GU was -0.8 cm (-1, -0.60) in the combination group, and -0.68 cm (-0.81, -0.55) in the PPI group ($p$ = 0.3). In subgroups analysis, patients with the presence of *H. pylori*, atrophic gastritis and/or intestinal metaplasia, NSAIDs use and current smoking have higher rates of healed GU by the combination therapy compared with PPI alone ($p$>0.05). There were no differences in compliance and treatment side effects between the two groups.

***Conclusion:*** Treatment with rebamipide plus PPI has a trend toward improved GU healing, compared with PPI monotherapy, especially in subgroup of patients with features of difficult to heal GU (presence of *H. pylori*, atrophic gastritis, intestinal metaplasia, NSAIDs and smoking).

***Keywords:*** Gastric ulcer, Mucoprotective drug, Omeprazole, Peptic ulcer disease, Proton pump inhibitor, Rebamipide

**J Med Assoc Thai 2020;103(Suppl.8): S7-13**
**Website:** http://www.jmatonline.com

Peptic ulcer disease (PUD) is a common condition that carries significant morbidity and mortality worldwide. Gastric mucosal integrity is maintained by a balance between the aggressive factors (e.g. acid, chemical, *H. pylori* and bile) and the gastric mucosal barrier or defense which include mucus and bicarbonate secreted by surface epithelial cells, prostaglandins, and gastric mucosal blood flow[1-4]. Therefore, both anti-secretory and mucoprotective agents are commonly used in gastric disorders, and sometimes used as a combination due to theoretically synergistic mechanisms[5].

Rebamipide is a broad-spectrum mucoprotective agent mainly acts by stimulating the generation of endogenous prostaglandins in the gastric mucosa, which has been reported to facilitate the healing of chronic gastritis and GU[6]. Beneficial effects of this agent have been demonstrated through several mechanisms including the ability to increase mucosal blood flow, antioxidation and anti-inflammatory effect[7]. The healing effect of rebamipide has been demonstrated previously in randomized controlled studies among patients with *H. pylori* positive GU. In study by Terano et al, which conducted in Japan, 309 patients with *H. pylori* positive GU (after 1 week of eradication therapy) were randomized to receive either rebamipide 300 mg/d or placebo for 7 weeks. The GU healing rate in the rebamipide group was significantly higher than that in the placebo group[8]. In another study by Song et al conducted in Korea and China, 132 patients with *H. pylori* positive GU (after 1 week of eradication therapy) were randomized to receive either rebamipide 300 mg/d or

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**How to cite this article:**
Jiriyasin S, Bunchorntavakul C. Healing Effect of Rebamipide in Addition to Omeprazole for Gastric Ulcer: Preliminary Results of a Randomized, Double-blind, Placebo-controlled Trial. J Med Assoc Thai 2020;103 (Suppl.8): S7-13.
doi.org/10.35755/jmedassocthai.2020.S08.12064

omeprazole 20 mg/d for 7 weeks. The GU healing rates were similar between rebamipide and omeprazole groups[9].

Unfortunately, to date, the healing effect of a combination of rebamipide and PPI has never been evaluated in patients with PUD by randomized controlled trial. Nevertheless, several randomized studies and meta-analysis suggested that treatment with rebamipide in addition to PPI is superior to PPI monotherapy for healing of endoscopic submucosal resection (ESD)-derived artificial GU, particularly large ulcers[10-13].

In the present study, we evaluated the efficacy of rebamipide combination with omeprazole in comparison to omeprazole monotherapy for the treatment of GU. Rebamipide may be a choice of treatment to improve efficacy of GU therapy.

## Materials and Methods

### *Study population*

This prospective, randomized, double-blind, placebo-controlled trial was conducted at the Department of Gastroenterology, Rajavithi Hospital, a tertiary care hospital and referral center in Bangkok, Thailand. The protocol of this research was reviewed and approved by the Ethics Committee of Rajavithi Hospital [ID 61195]. Written informed consents were obtained from all patients prior to enrollment. Patients were consecutively recruited from Medical Endoscopic Unit between December 2018 and November 2019; follow-up ended December 2019.

Inclusion criteria were patients underwent esophagogastroduodenoscopy (EGD) with (1) aged between 18 to 70 years old, (2) gastric ulcer size 0.5 to 3 cm (measured by placing the opened biopsy forceps (0.7 cm in length) beside the gastric ulcer)[14], and (3) acceptance to participate in the present study. Exclusion criteria were (1) history of allergy to omeprazole or rebamipide, (2) use of mucoprotective agents such as rebamipide, sucralfate, bismuth, or misoprostol within 2 weeks before enrollment, (3) history of gastric cancer or gastric surgery, (4) severe comorbid diseases, (5) lactating or pregnant women, (6) allergic to omeprazole or rebamipide; or (7) high risk endoscopic stigmata according to Forrest classification: adherent clot, non-bleeding visible vessel, active bleeding.

### *Study design*

The study flow chart was summarized in Figure 1. Patients who fulfilled inclusion and exclusion criteria were enrolled and provided informed consent. Baseline clinical information was collected included age, sex, body mass index (BMI), current smoking and alcohol drinking status, current NSAIDs, anti-platelet, anticoagulant and corticosteroid usage, underlying diseases and indication for EGD. At the 1st visit, patients were assigned randomly to either the combination group or the PPI group by block randomization. The combination group was administered rebamipide (Mucosta®; Thai Otsuka Pharmaceutical Co., Ltd, Bangkok, Thailand) 100 mg TID (300 mg/d) orally and omeprazole (Miracid®;

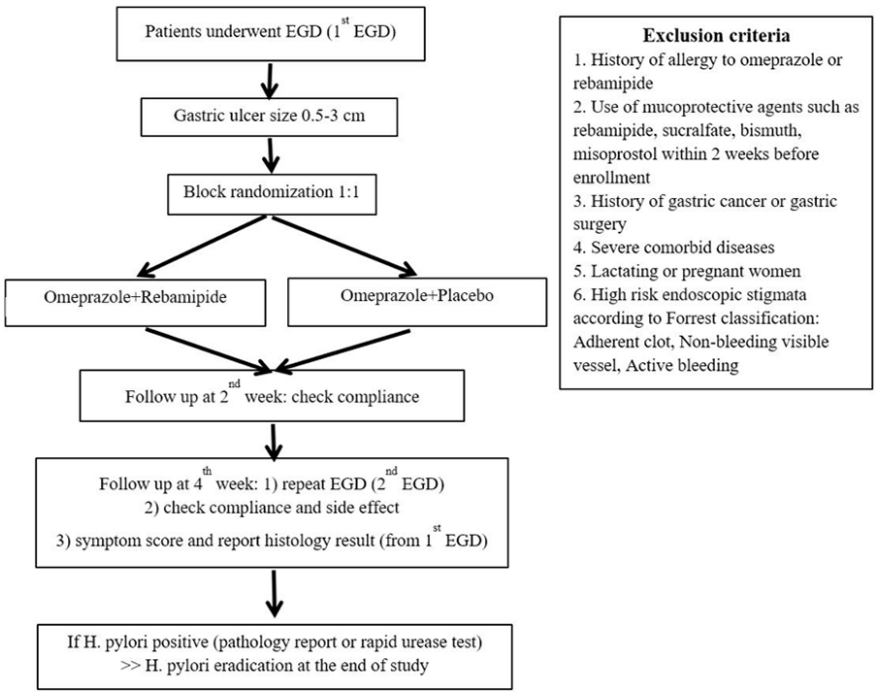


**Figure 1.** Study flow chart.

Berlin Pharmaceutical Industry Co., Ltd., Bangkok, Thailand) 20 mg OD orally, whereas the PPI group was administered omeprazole 20 mg OD orally and placebo (Chulalongkorn University Drug and Health Products Innovation Promotion Center: CU-D-HIP; Faculty of Pharmaceutical Sciences, Chulalongkorn University) 1 tablet TID orally. All subjects were emphasized to the importance and compliance to complete the study drugs in 4 weeks, along with the contraindication: not allowed to take any drug in the group of NSAIDs, other PPI and other mucoprotective agents such as sucralfate, bismuth, or misoprostol during the participation in this study until the next visit of EGD.

At the 2nd visit (after 2 weeks of the 1st visit), subjects will be followed-up and checked for the drug compliance and adverse events. At the 3rd visit (after 4 weeks of the 1st visit), subjects will be examined by EGD to evaluate the ulcer healing at the gastrointestinal endoscopy center, Department of Medicine, Rajavithi Hospital. Symptom score, compliance and side effects of the treatment will also be evaluated. Subjects will be informed the result of endoscopic biopsy (each of 2 specimens from antrum and corpus). If the histology suggests *H. pylori* infection or positive rapid urease test, the subjects will be treated by the first line eradication regimen after the end of study in 4th week. At the completion of study, missing visit subjects will be contacted via telephone for the clinical symptom interview and the reason of absence. If GU do not progress to scar-stage or complete healing after 4 weeks of the 1st visit, the subjects will be received treatment according to standard fashion and will be re-examined by EGD until complete healing or scar-stage.

During the follow-up EGD, ulcer after treatment will be examined by the physician who is blinded for the subject's treatment data. Primary outcome was the rates of healed GU (completely healed ulcer or progressed to scar-stage) in 4 weeks. The ulcer stage and quality of ulcer healing will be classified according to the classification of Sakita and Miwa: Active (A1, A2), Healing (H1, H2) and Scarring (S1, S2)[15]. Secondary outcomes were (1) The mean change in size of GU at baseline and after 4 weeks of treatment; and (2) The change of symptom score at baseline and at 4th week after treatment. Resolution of symptoms defined as 80 to 100% improvement of symptoms after 4 weeks compared with pre-treatment symptom score.

### *Statistical analysis*

We estimated that the improvement rate to scar stage would be approximately 86.7% in the combination group and 59% in the PPI group, based on previous studies of Fujiwara et al[11] and Yeomans et al[16]. The calculated sample size was 42 subjects in each group and assumed that 10% of the patients would not be able to complete study. We calculated that a minimum of 50 subjects per group, and total 100 subjects would be required for the present study.

All statistical analysis was performed using the software program SPSS for Windows version 23.0 (SPSS Inc., Chicago, Illinois, USA). Demographics data and baseline characteristics, including size of GU, *H. pylori* status, presence of atrophic gastritis and/or intestinal metaplasia from histological report and presence of healed GU from second EGD were collected. Categorical data presented as n (%) and continuous data presented as mean $\pm$ SD.

The primary endpoint, the number of patients in each treatment group whose ulcer had progressed to healed ulcer, were analyzed using intention-to-treat and per-protocol analysis. The *p*-value corresponds to independent t-test and Fisher's exact test. Mean change of size of GU presented with 95% CI and were compared using independent t-test and paired t-test. All statistical examinations were two tailed with *p*-value <0.05 defined as statistically significant.

## Results

### *Baseline patient characteristics*

A total of 70 patients who met inclusion and exclusion criteria were enrolled in this study and assigned randomly, 35 patients in each group. Of these, 6 patients (8.57%) (2 patients in the combination group and 4 patients in the PPI group) did not undergo follow-up EGD to complete study (4 patients did not return to the hospital and 2 patients denied the follow-up EGD).

The median age was 56.9 years in the combination group and 55.8 years in the PPI group. The number of male subjects was predominant in both groups: 24 (68.6%) male and 11 (31.4%) female in the combination group and 20 (57.1%) male and 15 (42.9%) female in the PPI group. Mean BMI was 24.6 kg and 23.7 kg in the combination and PPI group, respectively. Patients were smoking 9 patients (25.7%) in the combination group and 11 patients (31.4%) in the PPI group. Number of patients who currently alcohol drinking was 12 (34.3%), 15 (2.9%) in the combination and PPI group, respectively. Currently NSAID using (all of patients used conventional NSAID) were 15 (42.9%) in the combination group and 22 (62.9%) in the PPI group. Currently anti-platelet using were 6 (17.1%) and 8 (22.9%) in the combination and PPI group, respectively. One patient in the PPI group used ASA and ticagrelor, the remainder of patients used ASA alone. Overall of patients used NSAID and ASA 19 (54.3%) in the combination group and 26 (74.3%) in the PPI group. One of patients used warfarin in the PPI group, no one used the other anticoagulant in this study. Number of patients who were using corticosteroid were 2 (5.7%) in the combination group and 5 (14.3%) in the PPI group.

Underlying of cirrhosis was documented in 12 patients (34.4%) and 9 patients (25.7%) in the combination and PPI group, respectively. The most common indications for EGD in this study were upper gastrointestinal hemorrhage (UGIB) 26 (74.3%) and 23 (65.7%), esophageal varices (EV) surveillance 6 (17.1%) and 8 (22.9%) in the combination and PPI group, respectively. Number of patients who presence of *H. pylori* infection from rapid urease test or histology

**Table 1.** Baseline patient characteristics

| Variables | PPI + Rebamipide (n = 35) | PPI + Placebo (n = 35) | *p*-value |
|---|---|---|---|
| Age (years), mean (SD) | 56.9 (12.9) | 55.8 (10.1) | 0.681 |
| Male | 24 (68.6) | 20 (57.1) | 0.458 |
| BMI (kg/mm$^2$) | 24.6 (6) | 23.7 (3.8) | 0.434 |
| Smoking | 9 (25.7) | 11 (31.4) | 0.792 |
| Alcohol drinking | 12 (34.3) | 15 (42.9) | 0.624 |
| NSAIDs use | 15 (42.9) | 22 (62.9) | 0.150 |
| Conventional NSAIDs | 15 (100) | 22 (100) | N/A |
| COX-2 inhibitor | 0 | 0 | N/A |
| Antiplatelets | 6 (17.1) | 8 (22.9) | 0.766 |
| ASA | 6 (100) | 7 (87.5) | >0.999 |
| Clopidogrel | 0 | 0 | N/A |
| ASA + clopidogrel | 0 | 1 (12.5) | >0.999 |
| NSAIDs and ASA | 19 (54.3) | 26 (74.3) | 0.134 |
| Warfarin | 0 | 1 (2.9) | >0.999 |
| Corticosteroids | 2 (5.7) | 5 (14.3) | 0.428 |
| Underlying cirrhosis | 12 (34.3) | 9 (25.7) | 0.603 |
| Indications for EGD | | | |
| Upper gastrointestinal bleeding | 26 (74.3) | 23 (65.7) | 0.603 |
| Dyspepsia | 1 (2.9) | 0 | >0.999 |
| EV surveillance | 6 (17.1) | 8 (22.9) | 0.766 |
| Iron deficiency anemia | 2 (5.7) | 3 (8.6) | >0.999 |
| Others | 0 | 1 (2.9) | >0.999 |
| *H. pylori* infection | 24 (68.6) | 21 (60) | 0.618 |
| Size of GU, mean (SD) | 0.94 (0.53) | 0.89 (0.49) | 0.691 |
| Small ulcer (<1 cm) | 22 (62.9) | 21 (60) | >0.999 |
| Large ulcer (1.5 cm) | 3 (8.6) | 2 (5.7) | >0.999 |
| Stage of GU | | | |
| A1 | 22 (62.9) | 26 (74.3) | 0.440 |
| A2 | 13 (37.1) | 9 (25.7) | 0.440 |
| Presence of atrophic gastritis or IM | 5 (14.3) | 9 (25.7) | 0.371 |
| Atrophic | 0 | 2 (5.7) | 0.493 |
| IM | 4 (11.4) | 2 (5.7) | 0.673 |
| Both | 1 (2.9) | 5 (14.3) | 0.198 |

Data are expressed as number (%) unless specified
ASA = aspirin; BMI = body mass index; COX = cyclooxygenase; EGD = esophagogastroduodenoscopy; EV = esophageal varices; GU = gastric ulcer; IM = intestinal metaplasia; NSAIDs = non-steroidal anti-inflammatory drugs; SD = standard deviation

were 24 (68.6%) in the combination group and 21 (60%) in the PPI group. Mean size of GU in 1$^{st}$ EGD was 0.94 (±0.53) cm and 0.89 (±0.49) cm, stage of GU was predominant in A1 22 (62.9%) and 26 (74.3%) in the combination and the PPI group, respectively. The presence of atrophic gastritis or intestinal metaplasia (IM) was 5 (14.3%) in the combination group and 9 (25.7%) in the PPI group. There were no significant differences in baseline patient characteristics of the two groups, as summarized in Table 1.

### *Primary and secondary outcomes*

In the intention-to-treat analysis, the rates of healed GU were 77.1% (27/35) in the combination group and 60% (21/35) in the PPI group ($p = 0.198$). In the per-protocol analysis, the rates of healed GU were 81.8% (27/33) in the combination group and 67.7% (21/31) in the PPI group ($p =$

0.252) (Figure 2).

The mean change in size of GU was -0.8 cm (-1, -0.60) in the combination group, and -0.68 cm (-0.81, -0.55) in the PPI group ($p$ = 0.3). The mean change in size of GU and the stage of GU at the follow-up EGD were summarized in Table 2. According to the subjective assessment of the treatment at 4 weeks, all patients reported improvement in their symptoms of persistent dyspepsia, nausea and vomiting or bloating. Resolution of symptoms was reported in 28 of 35 patients (84.8%) in each group ($p$>0.999 between the two groups).

In subgroup analysis, we classified patients with difficult-to-heal features (1) presence of *H. pylori*, (2) exposure to NSAIDs and/ or ASA, (3) atrophic gastritis and/or intestinal metaplasia, (4) current smoking, (5) larger size of GU and (6) underlying of cirrhosis. The results were analyzed in the intention-to-treat and per-protocol analysis (Table 3 and 4). There were no statistical differences between the two groups ($p$>0.05) in all subgroups.

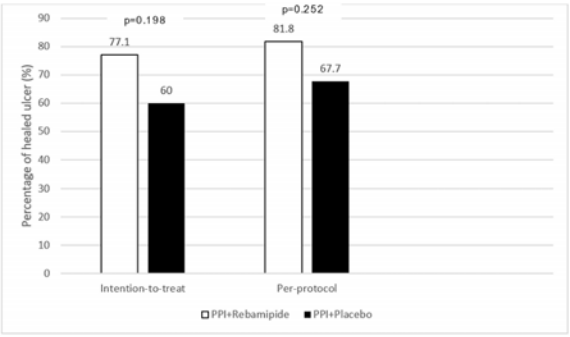


**Figure 2.** The percentage of patients in each treatment group whose ulcer had progressed to healed ulcer after 4 weeks.

### *Compliance and side effects*

Good drug compliance was defined by regular drugs administration of more than 90% of the assigned doses as evaluated by pill count measurement at each visit. Good drug compliance's patients were 32 (91.4%) and 30 (88.2%) in the combination and PPI group, respectively ($p$ = 0.071). Patients who did not undergo 2nd EGD to complete study, we counted as poor compliance.

No serious adverse events occurred in both groups. In the combination group, one patient reported bloating, one patient reported constipation and two patients reported diarrhea. In the PPI group, one patient reported diarrhea. All side effects were self-limited, and the patients were able to complete treatments without interruption.

## Discussion

To our knowledge, the present study is the first randomized, double-blind, placebo-controlled trial evaluating a combination of rebamipide and omeprazole compared to omeprazole monotherapy for the treatment of traditional *H. pylori*- and NSAIDs-associated GU. In this study, healed GU occurred in 77.1% in the combination group, and 60% in the PPI group. Although there was a trend towards better healing effects with a combination therapy, however the difference was not statistically significant. Yet the significant beneficial effect of add-on rabamipide was not demonstrated in this study and this can be largely explained by the limited number of patients as this is a preliminary result reporting 70 patients from the pre-calculated sample size of 100 patients.

As discussed above, a combination of PPI plus rebamipide has shown to be superior to PPI alone for the healing of ESD-derived artificial GU in previous randomized studies. It should be noted that most ESD procedures are

**Table 2.** Stage of GU and the mean change in size after 4 weeks of treatment

| Characteristic of GU | PPI + Rebamipide (n = 33) | PPI + Placebo (n = 31) | *p*-value |
|---|---|---|---|
| Stage of GU (2nd EGD), n (%) | | | |
| A1 | 0 | 0 | N/A |
| A2 | 2 (6.1) | 0 | 0.493 |
| H1 | 1 (3) | 2 (6.5) | >0.999 |
| H2 | 3 (9.1) | 8 (25.8) | 0.188 |
| S1 | 14 (42.4) | 10 (32.3) | 0.450 |
| S2 | 13 (39.4) | 11 (35.5) | 0.802 |
| Size of GU (cm), mean (SD) | | | |
| First EGD | 0.94 (0.53) | 0.89 (0.49) | 0.691 |
| Second EGD | 0.12 (0.3) | 0.16 (0.27) | 0.578 |
| Mean change (95% CI) | -0.8 (-1, -0.60) | -0.68 (-0.81, -0.55) | 0.3 |

EGD = esophagogastroduodenoscopy; GU = gastric ulcer; SD = standard deviation

**Table 3.** Ratio of patients whose ulcer progress to completely healed or scar-stage after 4 weeks of treatment in subgroups analysis (Intention-to-treat)

| Subgroups, n (%) | PPI + Rebamipide | PPI + Placebo | *p*-value |
|---|---|---|---|
| *H. pylori* positive | 19/24 (79.2) | 13/21 (61.9) | 0.323 |
| Exposure of NSAID and/or ASA | 14/19 (73.7) | 13/26 (50) | 0.134 |
| Presence of atrophic gastritis and/or IM | 4/5 (80) | 4/9 (44.4) | 0.301 |
| Current smoking | 7/9 (77.8) | 7/11 (63.6) | 0.642 |
| Size of GU (1st EGD) | | | |
| ≥1 cm | 10/13 (76.9) | 6/14 (42.9) | 0.120 |
| ≥1.5 cm | 2/3 (66.7) | 0/2 | 0.400 |
| Underlying of cirrhosis | 8/12 (66.7) | 7/9 (77.8) | 0.659 |

ASA = aspirin; EGD = esophagogastroduodenoscopy; GU = gastric ulcer; IM = intestinal metaplasia; NSAIDs = non-steroidal anti-inflammatory drugs

**Table 4.** Ratio of patients whose ulcer progress to completely healed or scar-stage after 4 weeks of treatment in subgroups analysis (per-protocol)

| Subgroups, n (%) | PPI + Rebamipide | PPI + Placebo | *p*-value |
|---|---|---|---|
| *H. pylori* positive | 19/24 (79.2) | 13/20 (65) | 0.329 |
| Exposure of NSAID and/or ASA | 14/18 (77.8) | 13/23 (56.5) | 0.196 |
| Presence of atrophic gastritis and/or IM | 4/4 (100) | 4/8 (50) | 0.208 |
| Current smoking | 7/8 (87.5) | 7/10 (70) | 0.588 |
| Size of GU (1st EGD) | | | |
| ≥1 cm | 10/12 (83.3) | 6/11 (54.5) | 0.193 |
| ≥1.5 cm | 2/3 (66.7) | 0/1 | >0.999 |
| Underlying of cirrhosis | 8/12 (66.7) | 7/9 (77.8) | 0.659 |

ASA = aspirin; EGD = esophagogastroduodenoscopy; GU = gastric ulcer; IM = intestinal metaplasia; NSAIDs = non-steroidal anti-inflammatory drugs

performed for the treatment of early gastric cancer which often creates large mucosal defects (>3 to 4 cm ulcer size). In addition, early gastric cancer typically develops on the background of chronic gastritis, particularly with severe atrophic changes and IM. Taken together these factors, ESD-derived GU are considered difficult-to-heal GU and appeared to be more resistant to PPI therapy as compared with traditional GU from *H. pylori* and NSAIDs. In addition, the effect of add-on rebamipide to PPI has shown to be more pronounced in patients with documented features of difficult-to-heal ulcers such as large ulcer and those with a background of atrophic gastritis[10,11]. In the present study of Fujiwara et al, treatment with rebamipide plus rabeprazole improved ESD-induced GU healing rate at 8 weeks compared with rabeprazole alone (86.7% vs. 54.8%, $p = 0.006$). Among those patients with severe atrophic gastritis, rebamipide combination were more effective to improve healing (92.9% vs. 30.0%, $p = 0.0023$)[11]. In line with previous studies, our preliminary results showed a trend toward improved GU healing in the combination group with more differences in the rates of healed GU in the subgroups of patients with difficult-to-heal features. Apart from the limited number of patients (70% of the calculated sample size), several other reasons may also explain the non-statistically significant difference of the outcomes of the present study. It should be noted that the characteristics of ESD-derived GU and traditional GU in the present study were largely different. Firstly, the size of ESD-derived GU (mean size 4 cm) was much larger than the size of GU in the present study (mean size 9 mm). Secondly only small proportion (<10%) of GU in this study occurred on the background atrophic gastritis and/or IM. Taken together these factors, traditional *H. pylori*- and NSAIDs-associated GU in the present study are somewhat considered easy-to-heal GU in which PPI monotherapy may provide adequate healing effect. However, the advantage to improve the quality of

ulcer healing in clinical practice was still in doubt and need further research to explore. Other limitations of the present study included single center, 9% lost to follow-up rate, and relatively short follow-up (as we did not evaluate the rates of GU healing after 8 weeks). Nevertheless, our study population would be a good representative for GU in clinical practice in Asia and the full results of the study are eagerly awaited.

## Conclusion

Treatment with rebamipide plus PPI has a trend toward improved GU healing, compared with PPI monotherapy, especially in patients with features of difficult-to-heal GU (presence of *H. pylori*, atrophic gastritis, intestinal metaplasia, exposure to NSAIDs, current smoking and larger size of GU).

## What is already known on this topic?

Rebamipide is a mucoprotective agent which has the ability to increase mucosal blood flow, anti-oxidative and anti-inflammatory effects. Multiple clinical trials have demonstrated the effect of rebamipide on healing of *H. pylori* and/or NSAIDs induced peptic ulcers.

## What this study adds?

Rebamipide plus PPI has has a trend toward improved GU healing, compared with PPI monotherapy, especially in patients with features of difficult-to-heal GU.


## Acknowledgement

We would like to thank the Gastroenterological Association of Thailand (GAT) and Rajavithi Hospital for the funding support and Thai Otsuka Pharmaceutical Co., Ltd for the support of study drug without involving the study design, conduct and analysis.


## Conflicts of interest

The authors declare no conflict of interest.

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## การศึกษาเปรียบเทียบการหายของแผลในกระเพาะอาหารโดยใช้ยารีบามีไพด์ ร่วมกับโอมีพราโซล เทียบกับการใช้ยาโอมีพราโซลร่วมกับยาหลอก

สาวินี จิริยะสิน, เฉลิมรัฐ บัญชรเทวกุล

***ภูมิหลัง:*** รีบามีไพด์เป็นยาในกลุ่มที่ออกฤทธิ์ปกป้องผนังทางเดินอาหาร โดยทางทฤษฎีการใช้ รีบามีไพด์ร่วมกับยายับยั้งโปรตอนปั๊ม อาจช่วยเร่งการหายของแผลในกระเพาะอาหารได้

***วัตถุประสงค์:*** เพื่อเปรียบเทียบอัตราการหายของแผลในกระเพาะอาหารระหว่างกลุ่มที่ได้รับการรักษาด้วยรีบามีไพด์ร่วมกับโอมีพราโซล และโอมีพราโซลเพียงอย่างเดียว

***วัสดุและวิธีการ:*** การศึกษานี้เป็นการทดลองทางคลินิกแบบสุ่มควบคุมด้วยยาหลอกดำเนินงานวิจัยที่โรงพยาบาลราชวิถี กรุงเทพมหานคร ระหว่างปี พ.ศ. 2561 ถึง 2562 ผู้ป่วยที่มีแผลในกระเพาะอาหารขนาด 0.5 ถึง 3 ซม. จะถูกสุ่มเป็น 2 กลุ่ม โดยกลุ่มแรกเป็นยาโอมีพราโซล 20 มก. วันละ 1 ครั้ง ร่วมกับรีบามีไพด์ 100 มก. วันละ 3 ครั้ง ส่วนกลุ่มที่ 2 เป็นยาโอมีพราโซล 20 มก. วันละ 1 ครั้ง ร่วมกับยาหลอก โดยประเมินผลลัพธ์หลักจากการหายของแผลในกระเพาะอาหารภายหลังการรักษาที่ 4 สัปดาห์

***ผลการศึกษา:*** รวบรวมผู้ป่วยได้ 70 ราย โดยมีผู้ป่วยที่เข้ารับการติดตามจนสิ้นสุดการศึกษาจำนวน 64 ราย สัดส่วนของผู้ป่วยที่ใช้ยาต้านอักเสบชนิดไม่ใช่สเตียรอยด์และผู้ป่วยที่ติดเชื้อเฮลิโคแบคเตอร์ ไพโลไร มีร้อยละ 42.9 และ ร้อยละ 68.6 ในผุ้ป่วยที่ได้รับการรักษาด้วยยากลุ่มแรก และร้อยละ 62.9 และ 60 ในผู้ป่วยที่ได้รับการรักษาด้วยยากลุ่มที่ 2 โดยไม่พบความแตกต่างอย่างมีนัยสำคัญทางสถิติ การหายของแผลในกระเพาะอาหารโดยการวิเคราะห์แบบ Intention-to-treat พบร้อยละ 77.1 ในกลุ่มที่ 1 และร้อยละ 60 ในกลุ่มที่ 2 (ค่าพีเท่ากับ 0.198) การเปลี่ยนแปลงขนาดของแผลโดยเฉลี่ย -0.8 ซม. (-1, -0.6) ในกลุ่มที่ 1 และ -0.68 ซม. (-0.81, -0.55) ในกลุ่มที่ 2 (ค่าพีเท่ากับ 0.3) การวิเคราะห์กลุ่มย่อย พบว่าผู้ป่วยที่มีการติดเชื้อเฮลิโคแบคเตอร์ ไพโลไร ภาวะกระเพาะอาหารอักเสบชนิด atrophy และ/หรือมีการเปลี่ยนแปลงของเยื่อบุกระเพาะอาหารไปเป็นเยื่อบุลำไส้ ใช้ยาต้านอักเสบชนิดไม่ใช่สเตียรอยด์ และผู้ป่วยที่สูบบุหรี่ จะมีอัตราการหายของแผลในกระเพาะอาหารที่สูงกว่าในผู้ป่วยที่ได้รับการรักษาด้วยยากลุ่มแรก (ค่าพีมากกว่า 0.05) นอกจากนี้ไม่พบความแตกต่างในด้านวินัยในการรับประทานยาหรือผลข้างเคียงในทั้งสองกลุ่ม

***สรุป:*** การรักษาด้วยรีบามีไพด์ร่วมกับโอมีพราโซลมีแนวโน้มในการเพิ่มอัตราการหายของแผลในกระเพาะอาหารเมื่อเปรียบเทียบกับการใช้โอมีพราโซลแต่เพียงอย่างเดียว โดยเฉพาะกลุ่มผู้ป่วยที่มีลักษณะของแผลที่หายยากกว่าปกติ (ผู้ป่วยที่มีการติดเชื้อเฮลิโคแบคเตอร์ ไพโลไร ภาวะกระเพาะอาหารอักเสบชนิดฝ่อเหี่ยวและ/หรือมีการเปลี่ยนแปลงของเยื่อบุกระเพาะอาหารไปเป็นเยื่อบุลำไส้ ใช้ยาต้านอักเสบชนิดไม่ใช่สเตียรอยด์ และผู้ป่วยที่สูบบุหรี่) โดยไม่พบความแตกต่างอย่างมีนัยสำคัญทางสถิติ