Comparison of the Efficacy and Safety between Generic Intravenous Omeprazole (Zefxon®) and Original Omeprazole (Losec®) in the Adjunct Treatment of Non-Variceal Upper Gastrointestinal Bleeding in Siriraj Hospital

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Background: *Clinical efficacy and safety of generic omeprazole have not been well studied in Thailand.*
Objective: *Determine whether generic omeprazole (Zefxon®) is inferior to original omeprazole (Losec®) in the treatment of non-variceal upper gastrointestinal bleeding (UGIB) in Siriraj Hospital.*
Material and Method: *Medical records of adult patients with the diagnosis of non-variceal UGIB receiving intravenous omeprazole (either Zefxon® or Losec®) in Siriraj Hospital between January 2006 and September 2010 were reviewed. Non-inferiority study was used to investigate whether the generic omeprazole was no more than 10% less effective than the original omeprazole. The primary end points were recurrent bleeding and mortality within seven and 30 days. Surgery, endoscopic retreatment, blood transfusions, length of hospital stay and safety were also analyzed.*
Results: *Of 200 randomly selected patients in each group, there was no difference in age, gender, co-morbidities, severity of UGIB, endoscopic findings and endoscopic intervention between patients receiving generic omeprazole and original omeprazole. Overall rate of recurrent bleeding, mortality, and surgical intervention within 30 days were 12.3%, 5.5% and 2.0%, respectively. The rates of recurrent bleeding, overall mortality, and non-variceal UGIB related mortality within seven and 30 days were not significantly different between the two groups. Neither were the rates of endoscopic retreatment and surgery. The incidence of adverse side effects was 3.5% in each group. Cox regression analysis showed no significant association between type of omeprazole and recurrent bleeding or mortality. Compared to the original omeprazole, the hazard ratio of recurrent bleeding, overall mortality, and non-variceal UGIB related mortality in patients receiving generic omeprazole was 1.44 (95% CI 0.82-2.53; p = 0.21), 2.12 (95% CI 0.90-5.43; p = 0.08) and 1.82 (95% CI 0.53-6.21; p = 0.34), respectively.*
Conclusion: *Although the original omeprazole Losec® tended to have more favorable outcomes in the treatment of non-variceal UGIB in the present study, non-inferiority test showed that the efficacy and safety of the generic omeprazole Zefxon® was not inferior to those of the original omeprazole.*

Keywords: *Upper gastrointestinal bleeding, Gastrointestinal hemorrhage, Rebleeding, Omeprazole, Proton pump inhibitor, Drug efficacy, Generic drug, Original drug*

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Upper gastrointestinal bleeding (UGIB) is one of most common emergency conditions in the gastrointestinal tract. It is associated with the mortality rate of 10 to 15%. Most patients presenting with UGIB require hospitalization and thorough management. Endoscopic intervention and intravenous administration of an antisecretory drug play a crucial role in reducing recurrent bleeding, minimizing the necessity of operative treatment and more importantly, decreasing the overall mortality[1,2].

Omeprazole, one of antisecretory drugs - known as a 'proton pump inhibitor (PPI)', inhibits gastric acid secretion by blocking hydrogen/potassium

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ATPase (proton pump) in the gastric parietal cells, which is the enzyme involved in the final step of acid secretion. PPI is capable of inhibiting acid secretion not only in the resting state, but also in the response to other stimuli. Hence, PPI is more effective in acid reduction than other antisecretory drugs[3]. Omeprazole has been shown that it is safe and effective in the treatment of non-variceal UGIB. According to the clinical practice guideline for the management of UGIB purposed by the Gastroenterological Association of Thailand in 2004[4] and International Consensus UGIB Conference Group in 2010[5], a high-dose intravenous PPI administration is recommended (80 mg bolus followed by either an infusion of 40 mg every 12 hours or an infusion of 8 mg/hour for 72 hours).

In Siriraj Hospital, patients with UGIB were considered for hospitalization especially in those with age over 60 years, co-morbid conditions, hemodynamic instability, drug-related coagulopathy, or having continuous red blood from nasogastric tube after irrigation. The PPI therapy was given to such patients and could continue up to 72 hours, or until the patients underwent endoscopy if available. Endoscopic hemostatic treatment was performed in patients with high-risk stigmata for rebleeding, such as active bleeding and non-bleeding visible vessel in an ulcer bed. Post-endoscopic PPI therapy (oral or intravenous infusion) was used depending on endoscopic findings, patient' severity and physician's judgment. In general, patients with low-risk stigmata, *e.g.* gastritis or clean-based ulcer, did not require the infusion of PPI. On the other hand, patients with high-risk stigmata received post-endoscopic intravenous PPI therapy and switched to oral PPI therapy when appropriate.

Regarding PPI in Thailand, the original brand name omeprazole (Losec® 40mg, AstraZeneca, USA) is listed in the National List of Essential Medicines in 2008 and its market price is approximately 14.00 USD. Meanwhile, the drug directory of Siriraj Hospital includes not only the original omeprazole but also a generic omeprazole (Zefxon® 40 mg, Biopharm Chemical, Thailand). The market price of this generic omeprazole is about 5.00 USD. In an era of financial crisis and healthcare reform, it would be great if physicians were able to decrease the expense on medicine, such as using generic drugs instead of original brand name drugs, without compromising the quality of patients care. The objective of this study was to determine whether the generic omeprazole (Zefxon®) is non-inferior to the original omeprazole (Losec®) in the treatment of non-variceal UGIB in Siriraj Hospital.

Material and Method

After obtaining approval from Siriraj Hospital Ethics Committee (Si 488/2009), medical records of adult hospitalized patients (age of $\geq$ 18 years) with the diagnosis of non-variceal UGIB receiving intravenous omeprazole (either Zefxon® or Losec®) at the Faculty of Medicine Siriraj Hospital between January 2006 and September 2010 were reviewed. Non-inferiority test was used to investigate whether the generic omeprazole-Zefxon® was no more than 10% less effective than the original brand name omeprazole-Losec®. The primary end points were recurrent bleeding and mortality within 7 and 30 days. Surgery, endoscopic re-treatment, blood transfusions, length of hospital stay, and safety were also analyzed. Providing that 90% of patients with non-variceal UGIB treated with intravenous Losec® had no recurrent bleeding at 30 days and the 10% margin of non-inferiority was adopted. Therefore, 195 patients were required per group, with 95% power and type I error of 5% in this non-inferiority study (nQuery Advisor 5.0). Accordingly, 200 medical records in each treatment group were randomly selected by systemic sampling of patient's hospital number.

All analyses were based on the intention-to treat principle. Data were prepared and analyzed using PASW statistics 18.0 (SPSS Inc., Chicago, IL, USA) and Statistical software R version 2.12.0 (R Development Core Team 2010, Austria). Continuous data were expressed as mean and standard deviation, or median and range, as appropriate. Number and percentage were described for categorical data. Unpaired t-test or Mann-Whitney U-test, as appropriate, was used to compare continuous data between groups. Categorical data were compared using Chi-square test or Fisher's exact test. A non-inferiority test was used to compare the efficacy and safety between groups. The rates of recurrent bleeding, overall mortality and non-variceal UGIB within 30 days were estimated using Kaplan-Meier method. The log-rank test was performed to analyze the differences in the rates of recurrent bleeding, overall mortality and non-variceal UGIB within 30 days between the two groups. Cox regression analysis was used to evaluate the effect of type of drug on recurrent bleeding and mortality at 30 days. All tests of significance were two tailed, except for tests of non-inferior for which one-tailed tests are appropriate. A p-value < 0.05 was considered statistically significant.

Table 1. Patient's characteristics. Data were given as mean ± SD, or median (min-max), or number (percentage)

	Generic omeprazole (Zefxon®) n = 200	Original omeprazole (Losec®) n = 200	p-value
Male	128 (64)	138 (69)	0.34
Age (years)	64.6 ± 15.1	63.3 ± 14.8	0.38
Body mass index	23.5 ± 4.6	23.9 ± 4.9	0.50
Inpatient setting	115 (57.5)	90 (45)	0.034*
Presenting symptom			
Hematemesis	42 (21)	35 (17.5)	0.45
Coffee ground	63 (31.5)	55 (27.5)	0.44
Hematochezia	9 (4.5)	6 (3)	0.60
Melena	145 (72.5)	148 (74.0)	0.82
Hematocrit (%)	24.9 ± 8.9	25.6 ± 8.2	0.40
Prothrombin time (seconds)	12.8 (10.3-191.8)	12.9 (10.2-163.6)	0.91
Diabetic mellitus	66 (33)	69 (34.5)	0.83
Hypertension	102 (51)	113 (65.5)	0.32
Smoking	23 (11.5)	31 (15.5)	0.44
Alcohol drinking	34 (17)	45 (22.5)	0.38
Consumption of antiplatelet or anticoagulant or NSAIDs	132 (66)	130 (65)	0.92

* p-value < 0.05

Results

During the study period, 1,125 patients with the diagnosis of non-variceal UGIB received intravenous omeprazole (Losec® 797 cases and Zefxon® 328 cases). Of 200 randomly selected patients in each group (Losec® group and Zefxon® group), there was no difference in age, gender, body mass index, presenting symptoms, co-morbidities and laboratory test between the two groups except patients receiving the generic omeprazole seemed to be inpatient cases (in-hospital UGIB) (p = 0.034) (Table 1). However, inpatient setting was not associated with the primary outcomes (p = 0.11). Based on esophago-gastro-duodenoscopic (EGD) findings, there was no significant difference in the underlying etiology, stigmata of recent hemorrhage, *H. pylori* infection and EGD intervention (adrenaline injection, coagulation probe, hemoclip, argon plasma coagulation, or combined therapy) between patients receiving original omeprazole and generic omeprazole (Table 2).

The severity of UGIB, which predicts the risk of rebleeding and mortality using Batchford score[6], Rockall admission score[7], Rockall post-endoscopy score[7] and clinical risk stratification by the Gastroenterological Association of Thailand[4], was not significantly different between the two groups (Table 3). Of note, almost 40% of patients in each group received a continuous infusion of other intravenous PPI (pantoprazole and esomeprazole) after initial EGD endoscopy. Duration of intravenous omeprazole administration and total length of PPI administration were not different between the two groups: 2.1 ± 3.2 vs. 2.2 ± 5.9 days (p = 0.06) and 3.5 ± 5.2 vs. 3.2 ± 6.6 days (p = 0.10), respectively. Neither was the amount of blood transfusion (3.4 ± 4.8 vs. 2.5 ± 2.2 units; p = 0.29).

The overall rate of recurrent bleeding, mortality, and surgical intervention within 30 days in the present study were 12.3%, 5.5% and 2.0%, respectively. Meanwhile, the rate of recurrent bleeding, overall mortality, non-variceal UGIB related mortality within 7 and 30 days was not significantly different between patient receiving original omeprazole and generic omeprazole (Table 4). The rate of endoscopic retreatment and surgery was also not different between the two groups. However, patients receiving generic omeprazole had a longer hospital stay than the other group (8.4 ± 17.7 vs. 5.8 ± 10.6 days; p = 0.036). The incidence of adverse side effects was 3.5% in each group (mainly are urticaria). Log rank test showed that the survival time of recurrent bleeding, overall mortality and non-variceal UGIB related mortality at 30 days was not significantly different between patient receiving original omeprazole and generic omeprazole (p = 0.21, 0.07 and 0.33, respectively). Fig. 1 shows the recurrent bleeding rates using Kaplan-Meier method. Cox regression analysis showed no association between type of omeprazole and recurrent bleeding or mortality at 30 days. Compared to the original

Table 2. Esophago-gastro-duodenoscopic (EGD) findings and intervention. Data were given as number (percentage)

	Generic omeprazole (Zefxon®) n = 186	Original omeprazole (Losec®) n = 192	p-value
EGD diagnosis			0.45
Gastric ulcer	87 (46.8)	83 (43.2)	
Duodenal ulcer	32 (17.2)	35 (18.2)	
Gastric and duodenal ulcers	20 (10.8)	29 (15.1)	
Erosive gastritis	8 (4.3)	13 (6.8)	
Mallory Weiss tear	7 (3.8)	4 (2.1)	
Esophagitis	4 (2.1)	4 (2.1)	
Dieulafoy's lesion	3 (1.6)	6 (3.1)	
Malignancy	5 (2.7)	3 (1.6)	
Others	20 (10.8)	15 (7.8)	
Stigmata of recent bleeding			0.96
None	39 (21.0)	42 (21.9)	
Clean-based ulcer	68 (36.6)	68 (35.4)	
Dark spot	22 (11.8)	24 (12.5)	
Blood present or oozing	14 (7.5)	12 (6.3)	
Adherent clot	7 (3.8)	6 (3.1)	
Visible vessel	31 (16.7)	31 (16.1)	
Spurting vessel	5 (2.7)	9 (4.7)	
H.pylori infection			0.30
Negative	86 (46.2)	102 (53.1)	
Positive	41 (22.0)	42 (21.9)	
Not done	59 (31.7)	48 (25.0)	
EGD intervention	57 (30.6)	57 (29.7)	0.84

Table 3. Severity and clinical risk stratification of patients with non-variceal UGIB. Data were given as mean $\pm$ SD or number (percentage)

	Generic omeprazole (Zefxon®) n = 200	Original omeprazole (Losec®) n = 200	p-value
Batchford score (0-23)	12.76 $\pm$ 3.10	12.53 $\pm$ 3.23	0.49
Rockall admission score (0-7)	3.72 $\pm$ 1.47	3.46 $\pm$ 1.43	0.07
Rockall postendoscopy score (0-11)	4.73 $\pm$ 1.92	4.44 $\pm$ 1.89	0.15
Other high risk factors			
Age $\geq$ 60 years	129 (64.5)	126 (63.0)	0.84
Major co-morbidity[a]	105 (52.5)	99 (49.5)	0.62
Hemodynamic unstable[b]	124 (62.0)	105 (52.5)	0.07
Coagulopathy (PT > 13)	81 (40.5)	81 (40.5)	1.00
Anemia (Hb < 10g/dl)	48 (24.0)	55 (27.5)	0.49
Need blood transfusion	173 (86.5)	167 (83.5)	0.48

[a] Renal disease, cirrhosis, cardiovascular disease, COPD
[b] Pulse > 100 bpm, systolic blood pressure < 100 mmHg

omeprazole, the hazard ratio of recurrent bleeding, overall mortality, non-variceal UGIB related mortality in patients receiving generic omeprazole was 1.44 (95% CI 0.82-2.53; p = 0.21), 2.12 (95% CI 0.90-5.43; p = 0.08) and 1.82 (95% CI 0.53-6.21; p = 0.34), respectively. Although the original omeprazole Losec® tended to have more favorable outcomes as shown in Table 4 and Fig. 1, the non-inferiority test revealed that the efficacy and safety of generic omeprazole Zefxon® was not inferior to the original omeprazole because the

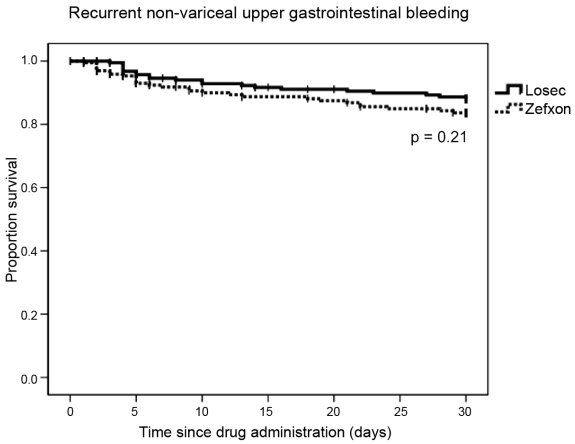

Fig. 1 The recurrent bleeding rates within 30 days of patients receiving generic omeprazole (Zefxon®) and original omeprazole (Losec®)

upper limits of 95% confidence interval of differences of several important clinical outcomes were no more than 10% (Table 4).

Discussion

Generic drugs are increasingly used in many countries[8], including Thailand, owing to their low cost and policy of health care reimbursement in some countries. However, clinical concerns have been raised when generics are used. Indeed, several investigators reported that some generic substitution was associated with poor bioavailability and pharmacokinetics, thereby reducing drug efficacy[9]. Theoretically, clinical efficacy and safety of generic drugs must be similar to those of original drugs, particularly when used in critically ill patients and life-threatening conditions such as UGIB patients. The present study demonstrated that the generic omeprazole exhibited a non-inferior efficacy and safety comparing to the original omeprazole in the treatment of non-variceal UGIB.

Pre-endoscopic PPI therapy in non-variceal UGIB, particularly with high-dose PPI (80 mg bolus followed by either an infusion of 40 mg every 12 hours or an infusion of 8 mg/hour for 72 hours), has been shown to downstage the endoscopic lesion and minimize the requirement of endoscopic intervention[5]. Endoscopic hemostatic therapy must be performed in patients with high-risk stigmata *e.g.* active bleeding, a visible vessel in an ulcer bed, or an ulcer with adherent clot[4,5]. Interestingly, there was clear evidence that continuous infusion of PPI decreased rebleeding and mortality in patients with high-risk stigmata who underwent successful endoscopic therapy[5]. Moreover, discharge prescription in such patients should include a single daily-dose oral PPI for a duration according to the underlying lesion *e.g.* 6 weeks for duodenal ulcer and 8 weeks for gastric ulcer.

Between January 2006 and September 2010, there were 1,125 patients with the principle diagnosis of non-variceal UGIB admitted in Siriraj Hospital (average 210 cases per annum). Peptic ulcer was the most common etiology of non-variceal UGIB and male to female ratio was 2:1. These findings were consistent with those of other large studies[7,10,11]. The overall rate of recurrent bleeding, mortality and surgical intervention within 30 days in the present

Table 4. Outcomes of the treatment (intention to treat analysis within 30 days after drug administration)

	Generic omeprazole (Zefxon®) n = 200	Original omeprazole (Losec®) n = 200	Difference (95%CI)	Chi-square test (p-value)	Non-inferiority test (p-value)
Recurrent bleeding					
Within 7 days	15 (7.5)	10 (5.0)	2.5 (-2.4,7.5)	0.41	<0.001*
Within 30 days	28 (14.0)	21 (10.5)	3.5 (-3.0,10)	0.36	<0.001*
Overall mortality					
Within 7 days	10 (5.0)	4 (2.0)	3.0 (-0.8,7.1)	0.17	<0.001*
Within 30 days	15 (7.5)	7 (3.5)	4.0 (-0.6,8.8)	0.13	<0.001*
UGIB related mortality					
Within 7 days	6 (3.0)	1 (0.5)	2.5 (-0.3,5.9)	0.13	<0.001*
Within 30 days	7 (3.5)	4 (2.0)	1.5 (-2.0,5.3)	0.54	<0.001*
Endoscopic retreatment	15 (7.5)	9 (4.5)	3.0 (-1.8,8.0)	0.29	<0.001*
Surgical intervention	5 (2.5)	3 (1.5)	1.0 (-2.2,4.4)	0.72	<0.001*

* p-value < 0.05

study were 12.3%, 5.5% and 2.0%, respectively. These outcomes were comparable to a recent meta-analysis of PPI therapy in peptic ulcer bleeding (21 randomized controlled trial-2,915 patients), which showed the recurrent bleeding rate of 5.2-19.4%, mortality rate of 2.5-7.0% and surgical intervention rate of 4.5-12.3%[12].

The present study showed that the rates of recurrent bleeding, overall mortality, and non-variceal UGIB related mortality at 30 days were not significantly different between patients receiving original omeprazole and generic omeprazole. Cox regression analysis demonstrated that there was no significant association between types of omeprazole and recurrent bleeding or mortality at 30 days. However, the original omeprazole tended to have more favorable outcomes. Specifically, recurrent bleeding rate within 30 days of the generic omeprazole was 14% whereas that of the original omeprazole was 10.5%; equivalent to 3.5% difference (95%CI -3.0, 10.0: p = 0.36). Since the hypothesis of the present study was that the generic omeprazole was no more than 10% less effective than the original omeprazole, non-inferiority test indicated no significant difference of the outcomes between the two drugs.

Limitations of the present study should be addressed. Firstly, of overall 400 patients in the present study, 22 (5.5%) did not receive EGD endoscopy. Due to the inherent limitation of retrospective study, it was unclear why these patients did not receive endoscopic evaluation and intervention, which may affect patients' outcomes. Secondly, 40% of patients in each group received an infusion of another intravenous PPI after EGD endoscopy. Therefore, randomized controlled trials of both omeprazoles only are required before a definite conclusion on the efficacy of these drugs *per se* can be given. Thirdly, there was no gastric pH monitoring after drug administration in this retrospective review. It has been evident that high pH and longer duration of pH above 6 was strongly associated with less recurrent bleeding and were dependent on drug treatment[13]. The gastric pH information might help monitor the drug efficacy and could be an important factor in patients with recurrent bleeding. Finally, cost-effectiveness analysis should be performed to provide a rigorous evidence base for the PPI therapy in non-variceal UGIB patients. Nevertheless, physicians should be as economical as possible in terms of quality, efficacy and safety of their healthcare provided. Generic drugs could play an important role in saving hospital expenditures as well as in efficiently allocating available funds for patient's management.

Conclusion

In the present study, the generic omeprazole exhibited a non-inferior efficacy and safety comparing to the original omeprazole in the treatment of non-variceal UGIB although the original omeprazole tended to have more favorable outcomes.

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Potential conflict of interest

None.

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การเปรียบเทียบประสิทธิผลและความปลอดภัยของยาสามัญ omeprazole ชนิดฉีดเข้าหลอดเลือดดำในการรักษาผู้ป่วยเลือดออกในทางเดินอาหารส่วนต้นที่รับไว้รักษาที่โรงพยาบาลศิริราช

ดรินทร์ โล่ห์สิริวัฒน์, รติกร แซ่จ้อง, วรุตม์ โล่ห์สิริวัฒน์, ศศิมา ทองสาย, วิษณุ ธรรมลิขิตกุล

วัตถุประสงค์: *เพื่อเปรียบเทียบประสิทธิผลและความปลอดภัยของยาสามัญ omeprazole ชนิดฉีดเข้าหลอดเลือดดำ (Zefxon®) กับยา omeprazole ต้นแบบ (Losec®) ในการรักษาผู้ป่วยเลือดออกในทางเดินอาหารส่วนต้นที่รับไว้รักษาที่โรงพยาบาลศิริราช*

วัสดุและวิธีการ: *เป็นการศึกษาย้อนหลังจากเวชระเบียนของผู้ป่วยที่ได้รับการวินิจฉัยหลักว่ามีเลือดออกในทางเดินอาหารส่วนต้นที่โรงพยาบาลศิริราช โดยการสุ่มเลือกผู้ป่วยที่ได้รับยาต้นแบบ คือ Losec® หรือยาสามัญ คือ Zefxon® ระหว่างปี พ.ศ. 2549 ถึง 2553 จำนวนกลุ่มละ 200 คน, และศึกษาวิเคราะห์ชนิด non-inferiority เพื่อเปรียบเทียบประสิทธิผลของยาได้แก่ อัตราการเกิดเลือดออกซ้ำ อัตราตายรวม อัตราตายจากภาวะเลือดออกในทางเดินอาหารส่วนต้น อัตราการได้รับการรักษาโดยการส่องกล้องซ้ำ อัตราการรับการรักษาโดยการผ่าตัด โดยวิเคราะห์ผลที่ 7 วัน และ 30 วันหลังได้รับยาทั้งสอง โดยกำหนดความสำคัญทางคลินิกว่ายาสามัญน่าจะมีประสิทธิผลไม่ด้อยกว่ายาต้นแบบเกินร้อยละ 10*

ผลการศึกษา: *ข้อมูลพื้นฐานทั่วไปของผู้ป่วยที่ได้รับยาสามัญ omeprazole และยาต้นแบบไม่มีความแตกต่างกันทั้งในด้านอายุ เพศ โรครวม ความรุนแรงของภาวะเลือดออกทางเดินอาหารส่วนต้น สิ่งที่ตรวจพบและการรักษาโดยการส่องกล้องตรวจทางเดินอาหารส่วนต้น, โดยภาพรวมผลการรักษาภาวะเลือดออกทางเดินอาหารส่วนต้นที่ 30 วัน พบอัตราการเกิดเลือดออกซ้ำร้อยละ 12.3 อัตราการตายร้อยละ 5.5 และอัตราการผ่าตัดร้อยละ 2.0, ไม่พบความแตกต่างอย่างมีนัยสำคัญทางสถิติ ของอัตราการเกิดเลือดออกซ้ำ อัตราการตาย อัตราการส่องกล้องตรวจทางเดินอาหารส่วนต้นซ้ำหรือการผ่าตัด ระหว่างผู้ป่วยที่ได้รับยาสามัญ omeprazole และยาต้นแบบ, ทั้งสองกลุ่มพบอุบัติการณ์ของอาการไม่พึงประสงค์หลังได้รับยาร้อยละ 3.5, การวิเคราะห์โดย Cox regression พบว่าการเกิดเลือดออกซ้ำไม่มีความสัมพันธ์กับชนิดของยาที่ใช้ (p = 0.21) ผู้ป่วยที่ได้รับยาสามัญมีโอกาสเสี่ยงต่อการเกิดเลือดออกซ้ำภายใน 30 วัน ไม่แตกต่างจากผู้ป่วยที่ได้รับยาต้นแบบ (HR = 1.44, 95%CI: 0.82-2.53), อัตราการตายไม่มีความสัมพันธ์กับชนิดของยาที่ใช้ (p = 0.08) ผู้ป่วยที่ได้รับยาสามัญมีโอกาสเสี่ยงต่อการตายรวมไม่แตกต่างจากผู้ป่วยที่ได้รับยาต้นแบบ (HR = 2.21, 95%CI 0.90-5.43), อัตราการตายจากเลือดออกจากทางเดินอาหารไม่มีความสัมพันธ์กับชนิดของยาที่ใช้ (p = 0.34) ผู้ป่วยที่ได้รับยาสามัญมีโอกาสเสี่ยงต่อการตายจากเลือดออกจากทางเดินอาหาร ไม่แตกต่าง จากผู้ป่วยที่ได้รับยาต้นแบบ (HR = 1.82, 95%CI: 0.53-6.21)*

สรุป: *ประสิทธิผลและความปลอดภัยในการรักษาผู้ป่วยภาวะเลือดออกทางเดินอาหารส่วนต้นของยาสามัญ omeprazole (Zefxon®) เปรียบเทียบยาต้นแบบ (Losec®) ไม่พบความแตกต่างกันอย่างมีนัยสำคัญทางสถิติ แม้ว่าผู้ป่วยกลุ่มที่ได้รับยาต้นแบบมีแนวโน้มว่ามีผลการรักษาที่ดีกว่า*