Supplementary Table 1 Proportion of Patients without Symptoms in the First 7 Days (Per-Protocol Set)

	Fexuprazan 40 mg (*n* = 107)	Esomeprazole 40 mg (*n* = 111)
Without symptom of heartburn	107	111
Proportion of subjects without symptom of heartburn, *n* (%)	28(26.2)	24(21.6)
95% confidence interval	[17.8, 34.5]	[14.0, 29.3]
Common risk difference (SE), % [1]		5.0(5.9)
95% confidence interval for difference		[-6.6, 16.6]
P-value [2]		0.396
Without symptom of acid regurgitation	107	111
Proportion of subjects without symptom of acid Regurgitation, n (%)	27(25.2)	31(27.9)
95% confidence interval	[17.0, 33.5]	[19.6, 36.3]
Common risk difference (SE), % [1]		-2.3(6.0)
95% confidence interval for difference		[-14.0, 9.4]
P-value [2]		0.705
Without symptom of heartburn/acid regurgitation	107	111

	Fexuprazan 40 mg (n = 107)	Esomeprazole 40 mg (n = 111)
Proportion of subjects without symptom of heartburn/acid regurgitation, n (%)	16(15.0)	13(11.7)
95% confidence interval	[8.2, 21.7]	[5.7, 17.7]
Common risk difference (SE), % [1]		3.3(4.7)
95% confidence interval for difference		[-5.9, 12.4]
P-value [2]		0.482

Abbreviations: SE, standard error; LA, Los-Angeles.

[1] Cochran-Mantel-Haenszel (CMH) weights by baseline LA grade. Wald method using Sato variance estimator is used to estimate the 95% confidence interval of common risk difference.

[2] Testing for difference between treatment groups (Cochran-Mantel-Haenszel (CMH) weights by baseline LA grade).

Note: Denominator of percentage is the number of subjects in each treatment group.

Supplementary Table 2 Proportion of patients without symptoms in 8 weeks (Per-Protocol Set)

	Fexuprazan 40 mg (n = 107)	Esomeprazole 40 mg (n =
Without symptom of heartburn	107	111
Proportion of Subjects without Symptom of Heartburn, n (%)	22(20.6)	19(17.1)
95% Confidence Interval	[12.9, 28.2]	[10.1, 24.1]
Common Risk Difference (SE), % [1]		3.8(5.4)
95% Confidence Interval for Difference		[-6.9, 14.4]
P-value [2]		0.484
Without symptom of acid regurgitation	107	111
Proportion of subjects without symptom of acid Regurgitation, n (%)	23(21.5)	30(27.0)
95% Confidence Interval	[13.7, 29.3]	[18.8, 35.3]
Common Risk Difference (SE), % [1]		-5.2(5.8)
95% Confidence Interval for Difference		[-16.5, 6.1]
P-value [2]		0.373
Without symptom of heartburn/acid regurgitation	107	111

	Fexuprazan 40 mg (*n* = 107)	Esomeprazole 40 mg (*n* =
Proportion of Subjects without Symptom of Heartburn/Acid Regurgitation, *n* (%)	11(10.3)	11(9.9)
95% Confidence Interval	[4.5, 16.0]	[4.4, 15.5]
Common Risk Difference (SE), % [1]		0.3(4.2)
95% Confidence Interval for Difference		[-7.8, 8.5]
P-value [2]		0.933

Abbreviations: SE, standard error; LA, Los-Angeles.

[1] Cochran-Mantel-Haenszel (CMH) weights by baseline LA grade. Wald method using Sato variance estimator is used to estimate the 95% confidence interval of common risk difference.

[2] Testing for difference between treatment groups (Cochran-Mantel-Haenszel (CMH) weights by baseline LA grade).

Note: Denominator of percentage is the number of subjects in each treatment group.

Supplementary Table 3 Proportion of Symptom-Free Day/Night-time in the First 7 Days (Per-Protocol Set)

	Fexuprazan 40 mg (*n* = 107)	Esomeprazole 40 mg (*n* = 111)
Proportion of symptom-free of heartburn		
Mean (SD)	45.39(42.03)	44.14(41.25)
Median	42.86	42.86
Min, Max	0.00, 100.00	0.00, 100.00
LS Mean (SE)	41.60(8.35)	40.35(8.75)
LS Mean Difference		1.25
95% Confidence Interval for Difference		[-9.95, 12.45]
P-value [1]		0.826
Proportion of symptom-free of acid regurgitation		
Mean (SD)	47.00(42.36)	55.21(40.34)
Median	42.86	71.43
Min, Max	0.00, 100.00	0.00, 100.00
LS Mean (SE)	49.21(8.33)	57.70(8.73)
LS Mean Difference		-8.49
95% Confidence Interval for Difference		[-19.67, 2.68]

	Fexuprazan 40 mg (*n* = 107)	Esomeprazole 40 mg (*n* = 111)
P-value [1]		0.136
Proportion of symptom-free of heartburn/acid regurgitation		
Mean (SD)	32.18(38.31)	34.88(38.41)
Median	14.29	14.29
Min, Max	0.00, 100.00	0.00, 100.00
LS Mean (SE)	31.78(7.70)	34.66(8.07)
LS Mean Difference		-2.88
95% Confidence Interval for Difference		[-13.21, 7.45]
P-value [1]		0.583

LS mean, least squares mean; Max, maximum; Min, minimum; SD, standard deviation; SE, standard error; LA, Los-Angeles.

[1] Testing for difference between treatment groups (ANCOVA model with treatment group as a factor and stratification factor (baseline LA grade) as a covariate).

Supplementary Table 4. Proportion of Symptom-Free Day/Night-time in the 8 weeks (Per-Protocol Set)

	Fexuprazan 40 mg (*n* = 107)	Esomeprazole 40 mg (*n* = 111)
Proportion of Symptom-Free of Heartburn		
Mean (SD)	59.95(36.87)	62.38(35.16)
Median	72.00	73.53
Min, Max	0.00, 100.00	0.00, 100.00
LS Mean (SE)	60.35(7.21)	63.04(7.55)
LS Mean Difference		-2.69
95% Confidence Interval for Difference		[-12.36, 6.98]
P-value [1]		0.584
Proportion of Symptom-Free of Acid Regurgitation		
Mean (SD)	63.81(36.88)	69.78(33.93)
Median	80.00	84.00
Min, Max	0.00, 100.00	0.00, 100.00
LS Mean (SE)	64.61(7.14)	70.72(7.48)
LS Mean Difference		-6.12
95% Confidence Interval for Difference		[-15.69, 3.46]

	Fexuprazan 40 mg (*n* = 107)	Esomeprazole 40 mg (*n* = 111)
P-value [1]		0.209
Proportion of Symptom-Free of Heartburn/Acid Regurgitation		
Mean (SD)	49.49(36.70)	54.75(35.92)
Median	53.57	58.18
Min, Max	0.00, 100.00	0.00, 100.00
LS Mean (SE)	52.16(7.30)	57.76(7.65)
LS Mean Difference		-5.61
95% Confidence Interval for Difference		[-15.40, 4.18]
P-value [1]		0.260

LS mean, least squares mean; Max, maximum; Min, minimum; SD, standard deviation; SE, standard error; LA, Los-Angeles.

[1] Testing for difference between treatment groups (ANCOVA model with treatment group as a factor and stratification factor (baseline LA grade) as a covariate).

Supplementary Table 5 Proportion of Subjects without Symptom of Heartburn in the First 3 Days [Moderate/Severe Group] (Per-Protocol Set)

	Fexuprazan 40 mg (n = 58)	Esomeprazole 40 mg (n = 63)
Without Symptom at the Day/Night-time	58	63
Proportion of Subjects without Symptom of Heartburn, n (%)	13(22.4)	5(7.9)
95% Confidence Interval	[11.7, 33.1]	[1.3, 14.6]
Common Risk Difference (SE), % [1]		14.6(6.6)
95% Confidence Interval for Difference		[1.8, 27.5]
P-value [2]		0.026
Without Symptom at the Day-time	58	63
Proportion of Subjects without Symptom of Heartburn, n (%)	17(29.3)	8(12.7)
95% Confidence Interval	[17.6, 41.0]	[4.5, 20.9]
Common Risk Difference (SE), % [1]		15.4(7.4)
95% Confidence Interval for Difference		[0.9, 29.9]
P-value [2]		0.037

	Fexuprazan 40 mg (n = 58)	Esomeprazole 40 mg (n = 63)
Without Symptom at the Night-time	58	63
Proportion of Subjects without Symptom of Heartburn, n (%)	20(34.5)	11(17.5)
95% Confidence Interval	[22.3, 46.7]	[8.1, 26.8]
Common Risk Difference (SE), % [1]		16.7(7.9)
95% Confidence Interval for Difference		[1.3, 32.2]
P-value [2]		0.035

Abbreviations: SE, standard error; LA, Los-Angeles.

[1] Cochran-Mantel-Haenszel (CMH) weights by baseline LA grade. Wald method using Sato variance estimator is used to estimate the 95% confidence interval of common risk difference.

[2] Testing for difference between treatment groups (Cochran-Mantel-Haenszel (CMH) weights by baseline LA grade).

Note: Denominator of percentage is the number of subjects in each treatment group.

Supplementary Table 6 Proportion of Atypical Symptom-Free Days during Day/Nighttime (Per-Protocol Set)

	First 3 Days		First 7 Days		8 Weeks	
	Fexu-prazan 40 mg (*n* = 107)	Esome-prazole 40 mg (*n* = 111)	Fexu-prazan 40 mg (*n* = 107)	Esome-prazole 40 mg (*n* = 111)	Fexu-prazan 40 mg (*n* = 107)	Esome-prazole 40 mg (*n* = 111)
Proportion of Symptom-Free of Chronic Cough						
Mean (SD)	89.10(25.81)	76.88(39.13)	89.32(25.97)	76.71(37.99)	92.44(21.28)	81.94(32.13)
Median	100.00	100.00	100.00	100.00	100.00	100.00
Min, Max	0.00, 100.00	0.00, 100.00	0.00, 100.00	0.00, 100.00	0.00, 100.00	0.00, 100.00
LS Mean (SE)	81.15(6.66)	68.60(6.98)	77.50(6.51)	64.19(6.82)	80.64(5.42)	69.30(5.68)
LS Mean Difference		12.55		13.31		11.34
95% Confidence Interval for Difference		[3.61, 21.49]		[4.58, 22.04]		[4.07, 18.61]
P-value [1]		0.006		0.003		0.002
Proportion of Symptom-Free of Throat Irritation						
Mean (SD)	56.39(45.42)	51.35(44.90)	58.88(43.07)	53.28(44.09)	66.11(39.89)	62.49(39.39)

| | First 3 Days | | First 7 Days | | 8 Weeks | |
	Fexu-prazan 40 mg (n = 107)	Esome-prazole 40 mg (n = 111)	Fexu-prazan 40 mg (n = 107)	Esome-prazole 40 mg (n = 111)	Fexu-prazan 40 mg (n = 107)	Esome-prazole 40 mg (n = 111)
Median	66.67	66.67	71.43	57.14	88.89	80.77
Min, Max	0.00, 100.00	0.00, 100.00	0.00, 100.00	0.00, 100.00	0.00, 100.00	0.00, 100.00
LS Mean (SE)	54.96(9.01)	49.30(9.45)	57.77(8.73)	51.78(9.15)	70.13(7.94)	66.70(8.32)
LS Mean Difference		5.66		5.99		3.43
95% Confidence Interval for Difference		[-6.43, 17.75]		[-5.72, 17.70]		[-7.23, 14.08]
P-value [1]		0.357		0.315		0.527

LS mean, least squares mean; Max, maximum; Min, minimum; SD, standard deviation; SE, standard error; LA, Los-Angeles.

[1] Testing for difference between treatment groups (ANCOVA model with treatment group as a factor and stratification factor (baseline LA grade) as a covariate).

Supplementary Table 7 Incidence of TEAEs by System organ class and Preferred term (Safety Set)

System organ class Preferred term	Fexuprazan 40 mg (*n*=131)	Esomeprazole 40 mg (*n* =131)	Total (*n* = 262)
Patients with TEAEs	22(16.8) [34]	25(19.1) [34]	47(17.9) [68]
Gastrointestinal disorders	13(9.9) [15]	9(6.9) [13]	22(8.4) [28]
Diarrhoea	4(3.1) [4]	2(1.5) [2]	6(2.3) [6]
Chronic gastritis	2(1.5) [2]	1(0.8) [1]	3(1.1) [3]
Gastritis	2(1.5) [2]	1(0.8) [1]	3(1.1) [3]
Nausea	1(0.8) [1]	2(1.5) [2]	3(1.1) [3]
Vomiting	0	2(1.5) [3]	2(0.8) [3]
Dyspepsia	2(1.5) [2]	0	2(0.8) [2]
Hiatus hernia	1(0.8) [1]	1(0.8) [1]	2(0.8) [2]
Abdominal discomfort	1(0.8) [1]	0	1(0.4) [1]
Abdominal distension	0	1(0.8) [1]	1(0.4) [1]
Abdominal pain	0	1(0.8) [1]	1(0.4) [1]
Brunner's gland hyperplasia	1(0.8) [1]	0	1(0.4) [1]
Gastritis erosive	1(0.8) [1]	0	1(0.4) [1]
Gastrooesophageal reflux disease	0	1(0.8) [1]	1(0.4) [1]

System organ class Preferred term	Fexuprazan 40 mg (*n*=131)	Esomeprazole 40 mg (*n* =131)	Total (*n* = 262)
Nervous system disorders	3(2.3) [3]	5(3.8) [6]	8(3.1) [9]
Dizziness	1(0.8) [1]	3(2.3) [3]	4(1.5) [4]
Headache	1(0.8) [1]	1(0.8) [2]	2(0.8) [3]
Carpal tunnel syndrome	0	1(0.8) [1]	1(0.4) [1]
Dysgeusia	1(0.8) [1]	0	1(0.4) [1]
Infections and infestations	4(3.1) [4]	3(2.3) [3]	7(2.7) [7]
Nasopharyngitis	0	2(1.5) [2]	2(0.8) [2]
Bronchitis	1(0.8) [1]	0	1(0.4) [1]
Cystitis	0	1(0.8) [1]	1(0.4) [1]
Influenza	1(0.8) [1]	0	1(0.4) [1]
Periodontitis	1(0.8) [1]	0	1(0.4) [1]
Vaginal infection	1(0.8) [1]	0	1(0.4) [1]
Skin and subcutaneous tissue disorders	4(3.1) [4]	1(0.8) [1]	5(1.9) [5]
Dermatitis contact	1(0.8) [1]	0	1(0.4) [1]
Pruritus	1(0.8) [1]	0	1(0.4) [1]
Pruritus generalized	1(0.8) [1]	0	1(0.4) [1]

System organ class Preferred term	Fexuprazan 40 mg (*n*=131)	Esomeprazole 40 mg (*n* =131)	Total (*n* = 262)
Swelling face	1(0.8) [1]	0	1(0.4) [1]
Urticaria	0	1(0.8) [1]	1(0.4) [1]
Eye disorders	2(1.5) [3]	1(0.8) [1]	3(1.1) [4]
Cataract	1(0.8) [1]	0	1(0.4) [1]
Conjunctival hemorrhage	1(0.8) [1]	0	1(0.4) [1]
Dry eye	0	1(0.8) [1]	1(0.4) [1]
Retinal tear	1(0.8) [1]	0	1(0.4) [1]
General disorders and administration site conditions	2(1.5) [2]	1(0.8) [1]	3(1.1) [3]
Chest discomfort	1(0.8) [1]	0	1(0.4) [1]
Pain	1(0.8) [1]	0	1(0.4) [1]
Sensation of foreign body	0	1(0.8) [1]	1(0.4) [1]
Blood and lymphatic system disorders	0	2(1.5) [2]	2(0.8) [2]
Leukopenia	0	1(0.8) [1]	1(0.4) [1]
Neutropenia	0	1(0.8) [1]	1(0.4) [1]
Ear and labyrinth disorders	1(0.8) [1]	1(0.8) [1]	2(0.8) [2]
Ear discomfort	1(0.8) [1]	0	1(0.4) [1]

System organ class Preferred term	Fexuprazan 40 mg (*n*=131)	Esomeprazole 40 mg (*n* =131)	Total (*n* = 262)
Meniere's disease	0	1(0.8) [1]	1(0.4) [1]
Respiratory, thoracic and mediastinal disorders	1(0.8) [1]	1(0.8) [1]	2(0.8) [2]
Cough	0	1(0.8) [1]	1(0.4) [1]
Rhinorrhea	1(0.8) [1]	0	1(0.4) [1]
Renal and urinary disorders	0	1(0.8) [2]	1(0.4) [2]
Renal cyst	0	1(0.8) [1]	1(0.4) [1]
Ureterolithiasis	0	1(0.8) [1]	1(0.4) [1]
Investigations	0	1(0.8) [1]	1(0.4) [1]
White blood cells urine positive	0	1(0.8) [1]	1(0.4) [1]
Musculoskeletal and connective tissue disorders	1(0.8) [1]	0	1(0.4) [1]
Back pain	1(0.8) [1]	0	1(0.4) [1]
Psychiatric disorders	0	1(0.8) [1]	1(0.4) [1]
Depression	0	1(0.8) [1]	1(0.4) [1]
Reproductive system and breast disorders	0	1(0.8) [1]	1(0.4) [1]
Uterine cervical erosion	0	1(0.8) [1]	1(0.4) [1]