

Assessment of Burden of Partial Response to Standard Doses of Proton Pump Inhibitors in Patients with Clinically Diagnosed Gastroesophageal Reflux Disease: A Real-World Evidence Study In India

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Yogesh Garje¹, Rajiv Saikia², Sunil Gupta³, Soujanya Peri⁴, Praveen Sharma⁵, Shruti Dharmadhikari⁶, Ashwini Satpathy^{6*}, Chintan Khandhedia⁶, Neeraj Markandeywar⁶, Amey Mane⁶, Suyog Mehta⁶, Sadhna Joglekar⁷

¹Ex-employee, Medical Affairs and Clinical Research, Sun Pharmaceutical Industries Limited, Mumbai, Maharashtra, India

²St. Augustine Hospital, Chapaguri, Bongaigaon, Assam

³Global Gastro & Liver Center, 6 2 Malviya Nagar, Jaipur, Rajasthan

⁴Universal India Hospital, Opp to Oakridge International School, Soucha Marvel 2nd Floor Khajaguda Village, Hyderabad, Telangana

⁵Liver & Gastro Care, G-7 ground floor Shop No. 3 & 4, Model Town IIIrd, New Delhi

⁶Medical Affairs and Clinical Research, Sun Pharma Laboratories Ltd, Mumbai, Maharashtra

⁷Ex-employee Medical Affairs and Clinical Research, Sun Pharmaceutical Industries Limited, Mumbai, India

***Corresponding Author Details:**

Name: Dr Ashwini Satpathy

Address: Senior Manager, Medical Affairs & Clinical Research, Sun Pharma Laboratories Ltd., Mumbai, Maharashtra, India 400063

Email: ashwini.satpathy1@sunpharma.com

ORCID ID: 0000-0001-6425-6134

Supplementary Information

Supplementary Table 1. Details of co-morbidities in GERD patients treated with PPIs (N=5205)

Concurrent illness	Total, n (%)	Pantoprazole, n (%)	Esomeprazole, n (%)	Lansoprazole, n (%)	Omeprazole, n (%)	Rabeprazole, n (%)
Total, n (%)	5205 (100%)	1906 (36.62%)	1097 (21.08%)	74 (1.42%)	149 (2.86%)	1979 (38.02%)
Cardiovascular	2610 (50.14%)	1065 (55.88%)	411 (37.47%)	26 (35.14%)	65 (43.62%)	1043 (52.7%)
Dyslipidemia	1742 (66.74%)	684 (64.23%)	264 (64.23%)	9 (34.62%)	30 (46.15%)	755 (72.39%)
Hypertension	664 (25.44%)	239 (22.44%)	118 (28.71%)	9 (34.62%)	23 (35.38%)	275 (26.37%)
Coronary Artery Disease (CAD)	130 (4.98%)	81 (7.61%)	22 (5.35%)	6 (23.08%)	11 (16.92%)	10 (0.96%)
Ischemic Heart Disease (IHD)	50 (1.92%)	43 (4.04%)	4 (0.97%)	0 (0%)	0 (0%)	3 (0.29%)
Congestive Cardiac Failure (CCF)	11 (0.42%)	8 (0.75%)	0 (0%)	2 (7.69%)	1 (1.54%)	0 (0%)
Dilated Cardiomyopathy (DCTA)	7 (0.27%)	5 (0.47%)	2 (0.49%)	0 (0%)	0 (0%)	0 (0%)
Palpitations	5 (0.19%)	5 (0.47%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Cardiac arrhythmias	1 (0.04%)	0 (0%)	1 (0.24%)	0 (0%)	0 (0%)	0 (0%)
Endocrinological	914 (17.56%)	393 (20.62%)	175 (15.95%)	21 (28.38%)	17 (11.41%)	308 (15.56%)
Diabetes Mellitus						
Type 2 Diabetes Mellitus (T2DM)	488 (53.39%)	224 (57%)	81 (46.29%)	12 (57.14%)	10 (58.82%)	161 (52.27%)
Type 1 Diabetes Mellitus (T1DM)	21 (2.3%)	19 (4.83%)	0 (0%)	0 (0%)	0 (0%)	2 (0.65%)
Impaired Glucose Tolerance (IGT)	4 (0.44%)	4 (1.02%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Thyroid gland disorders						
Hypothyroidism	374 (40.92%)	132 (33.59%)	84 (48%)	9 (42.86%)	7 (41.18%)	142 (46.1%)
Hyperthyroidism	19 (2.08%)	8 (2.04%)	8 (4.57%)	0 (0%)	0 (0%)	3 (0.97%)
Others (Inflammation of the thyroid gland and thyroid disorder)	8 (0.88%)	6 (1.53%)	2 (1.14%)	0 (0%)	0 (0%)	0 (0%)
Neurological	452 (8.68%)	208 (10.91%)	87 (7.93%)	5 (6.76%)	12 (8.05%)	140 (7.07%)
Diabetic Neuropathy	307 (67.92%)	133 (63.94%)	60 (68.97%)	0 (0%)	5 (41.67%)	109 (77.86%)
Vertigo	28 (6.19%)	11 (5.29%)	5 (5.75%)	0 (0%)	0 (0%)	12 (8.57%)
Anxiety	27 (5.97%)	12 (5.77%)	2 (2.3%)	2 (40%)	2 (16.67%)	9 (6.43%)
Stroke	69 (15.27%)	36 (17.31%)	17 (19.54%)	3 (60%)	3 (25%)	10 (7.14%)
Others ^a	21 (4.65%)	16 (7.69%)	3 (3.45%)	0 (0%)	2 (16.67%)	0 (0%)
Gynecological	28 (0.54%)	18 (0.94%)	5 (0.46%)	2 (2.7%)	1 (0.67%)	2 (0.1%)
Oligomenorrhoea	11 (39.29%)	6 (33.33%)	3 (60%)	0 (0%)	1 (100%)	1 (50%)
Metrorrhagia	3 (10.71%)	2 (11.11%)	1 (20%)	0 (0%)	0 (0%)	0 (0%)
PCOD/PCOS	3 (10.71%)	3 (16.67%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Uterine fibroid	3 (10.71%)	1 (5.56%)	0 (0%)	2 (100%)	0 (0%)	0 (0%)
Uterine prolapse	3 (10.71%)	2 (11.11%)	0 (0%)	0 (0%)	0 (0%)	1 (50%)
Others ^b	5 (17.86%)	4 (22.22%)	1 (20%)	0 (0%)	0 (0%)	0 (0%)

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Concurrent illness	Total, n (%)	Pantoprazole, n (%)	Esomeprazole, n (%)	Lansoprazole, n (%)	Omeprazole, n (%)	Rabeprazole, n (%)
Infectious Diseases	55 (1.06%)	18 (0.94%)	21 (1.91%)	1 (1.35%)	7 (4.7%)	8 (0.4%)
Tuberculosis (TB)	31 (56.36%)	17 (94.44%)	2 (9.52%)	0 (0%)	6 (85.71%)	6 (75%)
Throat irritation	18 (32.73%)	0 (0%)	18 (85.71%)	0 (0%)	0 (0%)	0 (0%)
Acute enteritis	3 (5.45%)	0 (0%)	1 (4.76%)	0 (0%)	0 (0%)	2 (25%)
Dengue	3 (5.45%)	1 (5.56%)	0 (0%)	1 (100%)	1 (14.29%)	0 (0%)
Genitourinary	220 (4.23%)	122 (6.4%)	30 (2.73%)	5 (6.76%)	10 (6.71%)	43 (2.17%)
Urinary Tract Infection (UTI)	104 (47.27%)	46 (37.7%)	20 (66.67%)	0 (0%)	2 (20%)	36 (83.72%)
Benign Enlargement of the Prostate (BEP)	39 (17.73%)	29 (23.77%)	3 (10%)	4 (80%)	2 (20%)	1 (2.33%)
Nephropathy	28 (12.73%)	19 (15.57%)	7 (23.33%)	0 (0%)	0 (0%)	2 (4.65%)
Chronic Kidney Disease (CKD)	28 (12.73%)	12 (9.84%)	0 (0%)	0 (0%)	4 (40%)	2 (4.65%)
Renal calculi	13 (5.91%)	10 (8.2%)	0 (0%)	0 (0%)	2 (20%)	1 (2.33%)
Others ^c	8 (3.64%)	6 (4.92%)	0 (0%)	1 (20%)	0 (0%)	1 (2.33%)
Respiratory	158 (3.04%)	63 (3.31%)	35 (3.19%)	11 (14.86%)	6 (4.03%)	43 (2.17%)
Upper Respiratory Tract Infections (URTI)	42 (26.58%)	13 (20.63%)	5 (14.29%)	1 (9.09%)	0 (0%)	23 (53.49%)
Allergy	38 (24.05%)	0 (0%)	21 (60%)	5 (45.45%)	2 (33.33%)	10 (23.26%)
Asthma	29 (18.35%)	18 (28.57%)	5 (14.29%)	2 (18.18%)	2 (33.33%)	2 (4.65%)
COPD	27 (17.09%)	18 (28.57%)	3 (8.57%)	3 (27.27%)	2 (33.33%)	1 (2.33%)
Bronchitis	13 (8.23%)	6 (9.52%)	1 (2.86%)	0 (0%)	0 (0%)	6 (13.95%)
Interstitial Lung Disease (ILD)	5 (3.16%)	4 (6.35%)	0 (0%)	0 (0%)	0 (0%)	1 (2.33%)
Pulmonary aspergillosis	4 (2.53%)	4 (6.35%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Bone and joint diseases	61 (1.17%)	40 (2.1%)	4 (0.36%)	3 (4.05%)	6 (4.03%)	8 (0.4%)
Spondylitis	23 (37.7%)	10 (25%)	4 (100%)	1 (33.33%)	2 (33.33%)	6 (75%)
Osteoporosis	16 (26.23%)	16 (40%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Arthritis (Rheumatoid/Osteo/Gouty)	22 (36.07%)	14 (35%)	0 (0%)	2 (66.67%)	4 (66.67%)	2 (25%)
Gastroenterological disorders	116 (2.23%)	83 (4.35%)	12 (1.09%)	1 (1.35%)	1 (0.67%)	19 (0.96%)
Fatty liver	68 (58.62%)	43 (51.81%)	6 (50%)	0 (0%)	1 (100%)	18 (94.74%)
Cholelithiasis	15 (12.93%)	13 (15.66%)	1 (8.33%)	0 (0%)	0 (0%)	1 (5.26%)
Hepatitis	4 (3.45%)	4 (4.82%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Pancreatitis	29 (25%)	23 (27.71%)	5 (41.67%)	1 (100%)	0 (0%)	0 (0%)
Others	426 (8.18%)	220 (11.54%)	38 (3.46%)	1 (1.35%)	16 (10.74%)	151 (7.63%)
Obesity	331 (77.7%)	186 (84.55%)	35 (92.11%)	1 (100%)	14 (87.5%)	95 (62.91%)
Retinopathy	57 (13.38%)	18 (8.18%)	2 (5.26%)	0 (0%)	0 (0%)	37 (24.5%)
Vitamin deficiency	27 (6.34%)	12 (5.45%)	1 (2.63%)	0 (0%)	2 (12.5%)	12 (7.95%)
Others (Systemic lupus erythematosus, blurred vision, hernia)	11 (2.58%)	4 (1.82%)	0 (0%)	0 (0%)	0 (0%)	7 (4.64%)

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^a Depression, early dementia, hemiplegia, Parkinson's, spastic facial palsy, seizures, tremor, migraine, hemiplegia, numbness, bipolar disorder, tremor

^b Ovarian tumor, Cervical cancer, Cervicitis, Menorrhagia, Vaginitis

^c Prostatism, hyperuricemia, lupus nephritis

Supplementary Table 2. Concomitant medications given to GERD patients under five different PPIs

Drug Class	Pantoprazole, n (%)	Esomeprazole, n (%)	Lansoprazole, n (%)	Omeprazole, n (%)	Rabeprazole, n (%)
Total (N)	1906	1097	74	149	1979
Concomitant medications					
Antidiabetic	692 (36.31)	315 (27.99)	12 (16.22)	37 (24.83)	529 (26.73)
Antihypertensives	512 (26.86)	201 (18.32)	9 (12.16)	34 (22.82)	553 (27.94)
Dietary supplement (Nutrition)	43 (2.26)	5 (0.46)	3 (2.7)	3 (2.01)	24 (1.21)
Prostate relaxant	30 (1.57)	3 (0.27)	4 (5.41)	2 (1.34)	3 (0.15)
Anti-asthmatic	22 (1.15)	4 (0.36)	6 (8.11)	3 (2.01)	2 (0.1)
Thyroid hormone	128 (6.72)	84 (7.66)	4 (5.41)	6 (4.03)	140 (7.07)
Anti-thyroid drugs	10 (0.52)	5 (0.46)	0 (0)	0 (0)	0 (0)
Anti-platelet	21 (1.1)	8 (0.73)	5 (6.76)	12 (8.05)	11 (0.56)
Others	109 (5.72)	42 (3.83)	6 (8.11)	16 (10.74)	29 (1.46)
Expectorant	19 (1)	0 (0)	0 (0)	1 (0.67)	0 (0)
Anti-tuberculosis	15 (0.79)	2 (0.18)	1 (1.35)	6 (4.03)	7 (0.35)
Neuro pain modulating drug + Methionine synthase cofactor	14 (0.73)	1 (0.09)	0 (0)	1 (0.67)	1 (0.05)
Antibiotic	13 (0.68)	36 (3.28)	1 (1.35)	0 (0)	7 (0.35)
Immunosuppressant	12 (0.63)	0 (0)	0 (0)	3 (2.01)	2 (0.1)
Anti-hypertensive + Anti-platelet + Anti-platelet + Anti-hyperlipidemic	11 (0.58)	0 (0)	0 (0)	0 (0)	2 (0.1)
Anti-hyperlipidemic	9 (0.47)	2 (0.18)	4 (5.41)	3 (2.01)	4 (0.2)
Anti-epileptic	8 (0.42)	1 (0.09)	0 (0)	0 (0)	0 (0)
Tricyclic antidepressants	8 (0.42)	0 (0)	0 (0)	2 (1.34)	6 (0.3)

Supplementary Table 3. Proportion of patients (N=231) with GERD symptoms treated with 40 mg Pantoprazole twice daily compared with 80 mg DDR from baseline to the follow-up visits

Dose	Heartburn	Regurgitation	Abdominal pain	Pain on food intake	Nausea	Vomiting	Belching	Bloating	Day and night - symptom	Any other complaints ^a
Baseline										
40 mg BD ^b (N=116), n (%)	86 (74.14)	76 (65.52)	79 (68.10)	69 (59.48)	75 (64.66)	74 (63.79)	79 (68.10)	83 (71.55)	74 (63.79)	26 (22.41)
80 mg DDR ^b (N=115), n (%)	95 (82.61)	76 (66.09)	78 (67.83)	60 (52.17)	62 (53.91)	70 (60.87)	80 (69.57)	98 (85.22)	74 (64.35)	17 (14.78)
<i>p</i> -value (Between doses) ^c	0.118	0.927	0.964	0.263	0.097	0.647	0.810	0.01	0.930	0.136
First Follow-up (4 weeks)										
40 mg BD (N=116), n (%)	28 (24.14)	18 (15.52)	23 (19.83)	17 (14.66)	17 (14.66)	19 (16.38)	25 (21.55)	33 (28.45)	23 (19.83)	24 (20.69)
80 mg DDR (N=115), n (%)	42 (36.21)	29 (25.00)	26 (22.41)	31 (26.72)	34 (29.31)	25 (21.55)	49 (42.24)	56 (48.28)	35 (30.17)	12 (10.34)
<i>p</i> -value (Between doses)	0.041	0.067	0.605	0.021	0.006	0.300	0.001	0.002	0.063	0.032
Second Follow-up (8 weeks)^d										
40 mg BD (N=116), n (%)	29 (25.0)	4 (3.45)	20 (17.24)	5 (4.31)	6 (5.17)	10 (8.62)	7 (6.03)	25 (21.55)	7 (6.03)	22 (18.97)
80 mg DDR (N=115), n (%)	25 (21.55)	18 (15.52)	1 (0.86)	1 (0.86)	1 (0.86)	0 (0.00)	28 (24.14)	29 (25.00)	23 (19.83)	7 (6.03)
<i>p</i> -value (Between doses)	0.558	0.002	<0.001	0.100	0.057	0.001	<0.001	0.510	0.002	0.003

^a Epigastric Pain, Retrosternal Burning, Dysphagia, Burning Abdomen

^b BD – Twice a day, DDR – Dual delayed release

^c *p*-values between treatment groups, pantoprazole 40 mg BD vs. 80mg DDR, by Chi-square test

^d *p*-value <0.001 for all symptoms between Baseline vs. Second Follow-up (8 weeks) in both treatment groups (McNemar test)