up to 6 months without treatment allowing for a relapse of GERD. Rates of patients suffering from GERD, FD, or IBS according to the diagnostic Rome criteria were determined at baseline (V0), and at the last visits of treatment (VTr) and observational phase (VOb), respectively, and compared by Fisher's Exact Test. **RESULTS:** The rates of patients with erosive GERD according to endoscopy as well as concomitantly with GERD, FD, or IBS according to symptomatic Rome-criteria were each significantly lower after pantoprazole treatment (VTr). While the rate of patients with reflux signs or symptoms increased again in the observational phase (VOb), the rate of FD or IBS showed a trend to further decrease after cessation of medication. **CONCLUSION:** Pantoprazole is efficacious in the treatment of erosive GERD and in patients suffering from symptoms suggesting an overlap of GERD, FD and/or IBS. Erosive esophagitis and GERD symptomatology significantly decreased during treatment and reappeared thereafter in two-thirds and one-third of responders, respectively. Unexpectedly, also FD and IBS symptomatology improved significantly but slower during treatment and maintained after treatment on this level during the observational phase. The mechanisms underlying the beneficial effects of improvement in erosive GERD on symptoms suggestive of FD or IBS still need to be determined. **REFERENCE(S):** [1] Talley NJ, Rev Gastroenterol Disord 2006; 6(2): 72-8.

Table 1: Rates of patients (%) with GI disorders (N = 626)

	V0	VTr	p-value [1]	VOb	p-value [2]	p-value [3]
Erosive GERD #	100.0 (N=626)	25.0 (N=154)	<0.0001	65.2 (N=302)	<0.0001	<0.0001
GERD +	90.7 (N=568)	16.4 (N=101)	<0.0001	35.9 (N=166)	<0.0001	<0.0001
FD +	64.7 (N=405)	22.4 (N=138)	<0.0001	16.6 (N=77)	0.6327	<0.0001
IBS +	13.6 (N=85)	4.7 (N=29)	<0.0001	2.8 (N=13)	0.4191	<0.0001

N: number of patients 100% = V0: 626, VTr: 617, VOb: 463 patients [1] p-values comparing patient rates of V0 vs VTr, [2] VTr vs VOb, [3] V0 vs VOb; α-level of $\leq$ 5 % was considered statistically significant # according to LA + according to Rome-II criteria

T1264

The Effect of 4 Weeks of Treatment with Pinaverium Bromide (PB) + Symethicone (S) On Symptom Intensity in IBS-ROME III Patients. a Report of the Mexican IBS Working Group

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Recently we showed that 4 weeks of treatment with PB+S improved abdominal pain, stool consistency and HRQOL among all IBS subgroups. Neurogastroenterol.Motil. 2008;20(Suppl.1):72, 91. Therefore, in the current study we analyzed the effect on symptom intensity. Methods: In a nationwide study in Mexico, 2203 IBS-Rome III patients (Age: 39±11 yrs, BMI: 27±9) classified as [N(Female%)]: IBS-C: 965(82), IBS-D: 125(57), IBS-M: 1113(76), IBS-U: 67(73), were studied. Based on weekly interviews, physicians recorded the patients gastrointestinal (GI) and extraintestinal (EI) symptoms intensity from the week before entering the trial until the last week of treatment by using 5-point Likert scales (none to very severe). MANOVA for repeated measurements was used adjusting for age, gender, BMI and IBS subgroup. Results: Intensity of the following symptoms improved significantly after treatment without any differences according to the IBS subgroups: bloating, gas, meteorism, mucus in stools, proctalgya, encopresis, nausea, headache, dyspareunia. However, some differences remained such as higher intensity scores for belching (IBS-C: 0.71±0.03a, IBS-D: 0.64±0.08a,b, IBS-M: 0.82±0.03b; letters show homogenous groups by Scheffe's post-hoc), halitosis (0.42±0.03a, 0.35±0.07a, 0.57±0.03b), early satiety (0.76±0.03a, 0.7±0.08a, 0.88±0.03b), anal pruritus (0.34±0.03a, 0.35±0.06a,b, 0.42±0.02b) and pelvic pain (0.62±0.03a, 0.58±0.08a,b, 0.72±0.03b) in IBS-M. Higher intensity for straining (1.2±0.03a, 0.83±0.08b, 1.04±0.3c) and sensation of incomplete evacuation (1.14±0.07a, 0.9±0.07b, 1.1±0.03a) in IBS-C; while urgency (0.70±0.03a, 1.31±0.07b, 0.97±0.03c) and incontinence (0.06±0.01a, 0.17±0.03b, 0.12±0.01b) in IBS-D. An independent effect of BMI was found on incontinence, postprandial fullness, anal pruritus and urgency. While an age effect was found on postprandial fullness. Conclusions: P+S improved gas related symptoms in IBS and some EI manifestations. However, when groups were compared, intensity scores remained higher for upper GI symptoms in IBS-M, outlet symptoms in IBS-C and urgency/incontinence in IBS-D. This suggests that those symptoms characterize the IBS subgroups and research is needed to elucidate whether they can predict severity among them.

T1265

Cardiovascular Safety of Prucalopride in Healthy Subjects: Results from Two Randomized, Double-Blind, Placebo-Controlled, Cross-Over Trials

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Objective: To determine the effects of prucalopride (PRU) on safety, in particular cardiovascular safety (CV) in healthy volunteers. Methods: Phase I, double-blind, placebo (PLA)-controlled, 2-way cross-over trials in 32 (GBR-9) and 24 (GBR-10) healthy subjects. Subjects were randomized to start with either PRU or PLA. In the first trial (GBR-9), the PRU dose was escalated in daily steps of 2 mg o.d., from 2 mg (recommended dose) to 10 mg from day 1-5, followed by 3 days on 10 mg. In the second trial (GBR-10) the PRU dose was escalated to 20 mg from day 1-10, followed by 3 days on 20 mg. Sessions were separated by a washout period of 14 to 21 days to avoid carry-over effects. Electrocardiogram (ECG), blood pressure (BP) and heart rate (HR) were measured and 24-h Holter monitoring was performed. Full 24 hours CV assessments were done at baseline and steady state, predose and C_{max} assessment were performed on the other days of treatment. Results: There were no clinically relevant differences in BP between treatment groups. A small and transient increase in mean HR and associated decrease in PQ and QT was observed after PRU (Table). The within subject differences between PRU and PLA were not clinically relevant. Due to the small increased HR observed and the known overcorrection of QTcB at higher HR, the use of QTcF was considered the most appropriate. No differences were found in mean QTcF values between PRU and PLA. No QTcF >500 ms or increased >60 ms were demonstrated during the treatment sessions. Increases of 30 to 60 ms were observed with a similar frequency during both treatment periods. Holter monitoring did not reveal clinically relevant findings. In addition, no correlation was found between shifts in ECG parameters from PLA vs. PRU (HR, QT, QTc) and the corresponding PRU plasma concentrations, indicating that PRU at concentrations up to 10 times the therapeutic dose did not have an effect on QTc interval. Headache, diarrhoea, nausea, and abdominal pain were the most common AEs and reported more frequently with PRU treatment than with PLA. Conclusions: From a cardiovascular perspective, PRU is safe at repeated doses up to 20 mg daily. This is 10 times the recommended dose for treatment of chronic constipation.

Mean differences between PRU and PLA

	Heart Rate (bpm)		QT (ms)		QTcF (ms)	
	GBR-9	GBR-10	GBR-9	GBR-10	GBR-9	GBR-10
2 mg (day 1): 3 h 2 mg (day 1): 24 h	+5.0 +3.9	+8.1 +4.8	-10.1 -10.2	-12.0 -10.3	-0.7 -1.7	+3.3 +0.5
10 mg (day 8): 3 h 10 mg (day 8): 24 h	+6.1 +3.3	- -	-9.1 -7.4	- -	+2.6 -1.2	- -
20 mg (day 13): 3 h 20 mg (day 13): 24 h	- -	+6.3 +3.2	- -	-11.2 -6.4	- -	+1.2 -0.3

T1266

Z-338 Improves Meal-Induced Symptoms in Functional Dyspepsia: A Double-Blind, Randomized, Placebo Controlled Crossover Study

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Background: Functional dyspepsia is a highly prevalent disorder in which pathophysiology is incompletely understood and treatment options are limited. Thus, in this phase-II trial a novel prokinetic agent, Z-338, was tested patients with functional dyspepsia (FD) and healthy controls (HC) to evaluate its effects on meal-related symptoms as the primary endpoint. Aim: To assess the effects of Z-338 on 1. type and severity of symptoms and; 2. gastric nutrient distribution and gastric emptying in response to a standardized nutrient challenge; 3. association of the above with the manifestations of symptoms and symptom pattern. Methods: After a screening visit, Z-338 or placebo (P), was administered during two treatment periods (7 to 9 days) separated by a two week wash-out period in a randomized, double-blind, placebo-controlled, cross-over design. Dosing was one tablet (100mg) orally before food, 3 times daily. Treatment efficacy was assessed during a standardized nutrient challenge test with visual analogue scales yielding a composite symptom score (CSS) and a modified Gastrointestinal Symptom Score. A gastric emptying (GE) test was performed at the end of each treatment phase. An ECG was recorded at screening and after each treatment period. All analyses were two sided with <α>=0.05, unless explicitly mentioned otherwise. Results: 57 subjects participated (30FD/27HC; Female/Male: 38/19). In FD patients, global symptom assessment revealed well controlled symptoms in 23% on placebo vs. 35% on Z-338 (p>0.05). Whilst this treatment difference was considered clinically relevant, it was not statistically significant due to the small sample size (p=0.43). During the standardized nutrient challenge, FD patients had augmented meal-induced symptoms compared to HC (CSS 380.59±323.48 vs. 332.9±269.01, p=0.0003). During treatment with Z338, compared to placebo, the symptom response to the standardized nutrient challenge was diminished for bloating (p=0.048), belching (p=0.039), fullness (p=0.179), burping (p=0.067), upper discomfort (p=0.459) and stomach pain (p=0.956) in FD patients. GE time did not change significantly on Z-338 although a trend towards a differential effect in FD patients vs. HC was noted; such that in FD GE tended to be faster on treatment, whilst in HC no change was apparent (FD: P: 166±100 min, Z-338: 144±58 p=0.23; HC: P:135±52, Z-338:143±46, p=0.50). No serious adverse events were reported. Conclusion: A standardized nutrient challenge can be used to assess treatment effects in FD. These data show that Z-338 improves meal-induced symptoms specifically in patients with functional gastrointestinal disorders.

T1267

Content Validity of a Gastroparesis Cardinal Symptom Index Daily Diary

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Few psychometrically sound patient-reported symptom scales are available for evaluating treatments for gastroparesis and none are based on daily recall. We developed a daily diary version of the Gastroparesis Cardinal Symptom Index (CGSI) originally developed using a 2 week recall period. The **aim** of this study was to evaluate the content validity of this new GCSI daily diary in patients with gastroparesis. This 11 item GCSI daily diary includes nausea/vomiting (3 items), postprandial fullness/early satiety (4 items), bloating (2 items), and 2 exploratory items on abdominal pain. **Methods:** A qualitative study was conducted in patients with confirmed delayed gastric emptying based on 4 hour gastric emptying scintigraphy. Semi-structured cognitive debriefing interviews were conducted by trained research assistants. Debriefing included the open-ended elicitation of the patient's perspective on relevant symptoms of gastroparesis, and detailed questions to obtain patient input on appropriate recall periods, instrument instructions, content of symptom items, and response scales. **Results:** The sample included 12 gastroparesis patients, including 5 with diabetic gastroparesis, recruited from one clinical center, 75% women, 100% Caucasian, and average age of 43.9 (SD=10.6) years (range 25 to 62 years). All or most participants reported that nausea (100%), vomiting (100%), stomach fullness (75%), bloating (58%), and loss of appetite (50%) were important symptoms of gastroparesis. Four (33%) participants stated that abdominal pain or discomfort were important symptoms. The symptom variability over time described by patients suggested that a 1-2 week recall period may fail to capture important symptom change. A 24-hour recall period was well accepted by participants. All participants understood the instructions and content of the diary symptom items and content,