	Female Laxative Failures		Complete Intent-to-Treat (ITT)	
Parameter	PLA N=478	PRU 2 mg N=458	PLA N=661	PRU 2 mg N=657
Primary endpoint ≥ 3 SCBM/week Weeks 1-12	9.2%	24.7%*	11.0%	24.4%*
Increase of ≥ 1 SCBM/week Weeks 1-12	22.6%	44.2%*	24.8%	43.5%*
Number of SCBM/week Run-in Weeks 1-12, mean (mean change)	0.38 1.00(0.63)	0.43 2.02(1.60)*	0.43 1.11(0.68)	0.42 1.91(1.52)*
Number of SBM/week Run-in Weeks 1-12, mean (mean change)	3.39 4.11(0.71)	3.71 6.39(2.72)*	3.38 4.23(0.84)	3.73 6.31(2.61)*
%BM with: Normal consistency No straining Feeling of complete evacuation	33.5% 18.1% 24.7%	42.7%* 21.5%# 30.9%*	34.9% 18.6% 26.9%	43.0%* 21.8%# 30.6%*
Rescue medication use (no. of bisacodyl tablets/week) Run-in Weeks 1-12, mean (mean change)	2.18 2.06(-0.11)	1.92 1.07(-0.89)*	2.09 1.91(-0.14)	1.93 1.12(-0.86)*
Median time to first SBM (h)	26:77	2:46$	26:50	2:50$
Increase of ≥ 1 in PAC-SYM overall score[a]	20.8%	34.9%*	21.3%	33.3%*
Increase of ≥ 1 in PAC-QOL overall score[a]	17.0%	39.8%*	18.5%	36.5%*
Increase of ≥ 1 in PAC-QOL satisfaction score[a]	19.0%	46.9%*	22.4%	44.1%*
% of patients rating: Constipation is severe/very severe[a] Treatment is extremely/quite a bit effective[a]	50.9% 16.2%	28.5%* 36.5%*	47.9% 17.5%	29.2%* 35.0%*

PLA: placebo; PRU: prucalopride; (S)(C)BM: (spontaneous)(complete) bowel movement; PAC-(QOL)(SYM):Patient Assessment of Constipation-(Quality of Life)(Symptoms) questionnaires [a]Week 12 endpoint $p<0.0001 *vs.* PLA; *p<0.001 *vs.* PLA; #p<0.05 *vs.* PLA

Tu1395

Efficacy and Tolerability of Alpha-Galactosidase on Gas Related Symptoms in Pediatric Irritable Bowel Syndrome. a Randomized, Double-Blind, Placebo Controlled Trial

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Introduction: Bloating, abdominal distension and flatulence represent very frequent complaints in children with irritable bowel syndrome (IBS). These symptoms are frequently associated to excessive intestinal gas. Hence the reduction of gas production can be considered an effective therapeutic strategy. Alpha-Galactosidase has been shown to reduce gas production and related symptoms in adults. Aim: to evaluate the efficacy and tolerability of Alpha-galactosidase on gas related symptoms in pediatric IBS patients. Patients and Methods: this was a single center, randomized, double-blind, placebo-controlled, parallel-group study performed in tertiary care setting. Fifty-two pediatric patients (32 female, median age 8 yrs, range 4-17) with IBS according to Rome III criteria were randomized to receive placebo (n = 25) or Alpha-galactosidase (n = 27) (Sinaire, Promefarm). Both treatments were given as drops or tablets according to body weight at the beginning of each of three meals for 2 weeks. Children were followed up two weeks after the end of treatment. Parent and/or self-assessment of the severity of gas related symptoms (bloating, flatulence, abdominal distension and abdominal spasms) were recorded 3 times daily during the treatment period using a validated visual score. The primary endpoint was reduction in the severity of bloating at the end of treatment compared to baseline. Secondary endpoints were reduction in the severity of other symptoms. As a measure of intestinal gas production, breath hydrogen concentration was measured at baseline and at the end of treatment. Results: α-galactosidase significantly reduced the severity of bloating (p = 0,023) and flatulence (p = 0,005) as compared with placebo. No significant differences were found for abdominal spasms and abdominal distension. The administration of Alpha-galactosidase had no significant effect on breath hydrogen excretion as compared with placebo (p = 0,54). The benefical effects of treatment tended to disappear in both groups at the end of follow-up. No treatment-related adverse events were reported during treatment. Conclusions: Although larger and longer trials are needed to confirm our results, Alpha-galattosidase looks a safe and effective agent for managing gas related symptoms in pediatric IBS.

Tu1396

Identification of Pro-Secretory Components in STW 5, a Fixed Herbal Combination Medicine to Treat Functional Gut Disorders

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Background and Aims: STW 5 consists of nine hydroethanolic extracts (bitter candy tuft whole plant, chamomile flower, peppermint leaf (P), caraway fruit, liquorice root, lemon balm leaf (L), angelica root (A), greater celandine herb, and milk thistle fruit) and is used to treat functional dyspepsia and irritable bowel syndrome. We recently reported that STW 5 relaxes the gastric fundus and increases intestinal chloride secretion and proposed that these actions may be involved in its clinical efficacy. The aim of this study was to identify the plant extracts responsible for the secretory action in order to provide an understanding of target oriented herbal combinations. Methods: We used the Ussing chamber method to study the effects of the individual hydroethanolic extracts contained in STW 5 on short circuit currents (Isc) in 552 mucosa/submucosa preparations of human small or large intestinal specimens from 70 patients undergoing abdominal surgery and the human epithelial cell line T84 (142 wells). Results: We first prepared a combination of the individual extracts (sSTW 5) at concentrations which corresponded to their concentrations in 512µg/ml STW 5, a sub-therapeutic dose which evoked a reliable secretory response. Pro-secretory action of sSTW5 was comparable to that of STW5 both in the small and large intestine (17.5±3.9 vs 20.7±6.3 µA/cm2). Of the individual components, only A, L and P had a pro-secretory action yielding a small insignificant Isc increase at a concentration corresponding to 512µg/ml STW 5 and a large significant Isc increase at 5120µg/ml STW 5, which is still sub-therapeutic. A, L and P were equally potent in small and large intestine. A combination of A, L and P (ALP) at concentrations corresponding to 512µg/ml STW 5 evoked a significant Isc increase (13.4±1.6µA/cm2) comparable to sSTW 5 which corresponded well to the sum of their individual responses (17.2µA/cm2). The secretory response of ALP was significantly reduced by the cAMP dependent Cl- channel blocker CFTRinh-172, the Ca++ dependent Cl- channel blocker SITS and cAMP inhibitor MDL12,330A by 33%, 59% and 46%, respectively. The efficacies, potencies and modes of action of the individual extracts were identical in experiments with the epithelial cell line T84. Summary and Conclusion: The results show that the pro-secretory action of STW 5 is due to the additive effects of the three components angelica, lemon balm and peppermint. Their effects must involve direct activation of epithelial cAMP- and Ca++-dependent chloride channels. It is noteworthy, that we identified angelica, chamomile and liquorice as those extracts responsible for fundus relaxation. The identification of region and target specific action of the extracts suggests the potential for selective disease targeted combinations.

Tu1397

Chronic Constipation in Canada - Prevalence and Patient Perspective

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Background and Objectives: Chronic Constipation (CC) is a prevalent condition and a common complaint in clinical practice (Storr 2011). This study was conducted to estimate the CC prevalence in Canada and assess, from a patient perspective, disease impact of CC on quality of life. Methods: A nationwide, regionally-representative sample of 1,049 adult chronic constipation sufferers was polled by Ipsos Marketing July 15th -25th 2011. The sample was generated by the Ipsos Online Consumer Panel ("I-Say Online Panel") and was screened for chronic constipation using Rome II criteria over the previous 12 months - similar criteria used in other surveys (Pare 2001, Johanssen 2007). Responders were excluded if pregnant (current or within the past year); if diagnosed with colon or bowel cancer, diverticulitis, inflammatory bowel disease, Crohn's disease, or if they had an existing diagnosis of irritable bowel syndrome with constipation (IBS-C). Outcome measures included prevalence, symptoms, and quality of life (based on PAC-QOL, SF-8™ questions). Results: Overall CC prevalence was estimated at 10% (95% CI, 7-13%) (female 12%, male 7%) and was consistent across different age groups: 18-39 yrs (12%), 40-49 yrs (10%), 50-59 yrs (9%), 60+yrs (9%). 1.5% suffer physical discomfort most or all of the time related to CC, which would translate into approximately 300,000 Canadians severely affected. Straining (a sense of difficulty) passing stool (88%), hard stools (61%), gas (61%) and sensation of incomplete evacuation (60%) were most commonly experienced, while straining (35%), gas (23%), and abdominal pain (29%) were rated as the most bothersome. Decreased frequency (<3 BM per week) was only experienced in 39%. The mean duration of symptoms was 11 years. Half of respondents had taken a laxative in the preceding 12 months; of these, 56% had taken stimulants, 42% had taken bulking agents, and 14% had taken osmotic laxatives. Only 16% of CC patients overall were very satisfied with laxative treatment, and only 11% were very satisfied in the severely affected group. 54% were less than "very satisfied" with their current quality of life. Ultimately, only 61% of the respondents had spoken to a doctor about CC and these sufferers waited an average of eight months before they consulted a doctor about CC for the first time. Conclusions: Chronic constipation is a prevalent condition in Canada at 10%, with an estimated 1.5% of the population severely affected. Straining, gas and abdominal pain were rated the most bothersome symptoms by patients, which may not be appreciated by physicians as related to constipation. Satisfaction with available treatments is poor.

Tu1398

One Year Treatment of Childhood Constipation Comparing PEG 3350 With Electrolytes Versus PEG 4000: A Double Blind Randomized Controlled Trial

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Background: Currently polyethylene glycols (PEG) with or without electrolytes are the most prescribed laxatives in constipation. However, long-term safety in children has not been assessed yet. 1, 2 It is also unknown whether the PEG dose of 0.4-0.8 g/kg/day found to be effective for short term periods of a maximum of three months, remains effective for long term treatment. Also, no studies have made a head-to-head comparison between PEG 3350 with electrolytes (PEG+E) and PEG 4000 without electrolytes (PEG) in children. Aim: To 1) demonstrate non-inferior long-term safety of PEG+E compared to PEG, 2) assess the dose response during one year of treatment, 3) compare clinical effects of both medications in treating childhood constipation. Methods: Patients, aged 6 months to 15 years, presenting with functional constipation were included for a 12-month double-blind RCT. All participants had a defecation frequency <3 per week and at least one other Rome-III criterion. Subjects were randomly assigned to the treatment groups PEG+E or PEG. Bowel diaries provided among other things information on frequency of defecation, fecal incontinence and adverse events. Treatment success was defined as defecation frequency ≥3 per week together with fecal incontinence ≤ 1per week Results: A total of 97 subjects fulfilled the criteria of whom 82 completed the study. Overall, there were 143 adverse events reported by 56 of the 97 subjects (57.7%) across both treatment groups. There was one serious adverse event in the PEG+E group, and one adverse event in the PEG group leading to discontinuation of the study medication. The dose range used was similar for both treatment groups in all age groups. In PEG+E the range was 0.03 - 0.72 g/kg and in PEG it was 0.10 - 0.86g/kg. At the end of the study, success was achieved in 61.5% in the PEG+E group compared with