ClinicalTrials.gov Protocol and Results Registration System (PRS) Receipt
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Evaluation of Long-term Prucalopride Treatment With Chronic Constipation in Subjects Aged ≥ 18 Years (SPD555-401)

This study has been completed.

Sponsor:	Shire
Collaborators:	
Information provided by (Responsible Party):	Shire
ClinicalTrials.gov Identifier:	NCT01424228

Purpose

The purpose of this trial is to evaluate the long-term (24 weeks) efficacy of prucalopride versus placebo in subjects aged 18 years and older with chronic constipation.

Condition	Intervention	Phase
Constipation	Drug: placebo Drug: prucalopride	Phase 4

Study Type: Interventional
Study Design: Treatment, Parallel Assignment, Double Blind (Subject, Investigator), Randomized, Safety/Efficacy Study
Official Title: A Randomised, Double-blind, Placebo-controlled Trial to Evaluate the Efficacy, Quality of Life, Safety and Tolerability of Long-term Treatment (24 Weeks) With Prucalopride in Subjects Aged ≥18 Years With Chronic Constipation

Further study details as provided by Shire:

Primary Outcome Measure:

- The Percentage of Subjects With an Average of ≥3 Spontaneous Complete Bowel Movements (SCBM) Per Week Over the 24 Week Treatment Period [Time Frame: Over 24 week treatment period] [Designated as safety issue: No]

Spontaneous Bowel Movements defined as a bowel movement that is not preceded within a period of 24 hours by the intake of a laxative agent or by the use of an enema.

Secondary Outcome Measures:

- Percentage of Subjects With an Increase of ≥1 Spontaneous Complete Bowel Movement (SCBM) Per Week Up to 24 Weeks [Time Frame: Over 24 week treatment period] [Designated as safety issue: No]
- Average Number of Spontaneous Complete Bowel Movements (SCBM) Per Week Up to 24 Weeks [Time Frame: Over 24 week treatment period] [Designated as safety issue: No]
- Change From Baseline in Spontaneous Complete Bowel Movements Per Week at Up to 24 Weeks [Time Frame: Baseline and Over 24 week treatment period] [Designated as safety issue: No]
- Percent of Subjects With an Average Weekly Frequency of at Least 3 SCBM by Week [Time Frame: Over 24 week treatment period] [Designated as safety issue: No]
- Percent of Subjects With an Average Weekly Frequency of at Least 3 SCBM by 4-Week Treatment Period [Time Frame: Over 24 week treatment period] [Designated as safety issue: No]
- Change From Baseline in Average Consistency Per SCBM at Up to 24 Weeks [Time Frame: Baseline and Over 24 week treatment period] [Designated as safety issue: No]

  Consistency measured using the 7-point Bristol scale where 1-2 indicate constipation (=hard/very hard), 3-4 are ideal stools (=normal), and 5-7 tending toward diarrhea.
- Change From Baseline in Percent SCBM With a Consistency of Normal and Hard/Very Hard at Up to 24 Weeks [Time Frame: Baseline and Over 24 week treatment period] [Designated as safety issue: No]
- Change From Baseline in Straining Per SCBM at Up to 24 Weeks [Time Frame: Baseline and Over 24 week treatment period] [Designated as safety issue: No]

  Straining was evaluated on a 5-point scale (0=none, 1=mild, 2=moderate, 3=severe, or 4=very severe)
- Change From Baseline in Percent SCBM With No Straining and Severe/Very Severe Straining at Up to 24 Weeks [Time Frame: Baseline and Over 24 week treatment period] [Designated as safety issue: No]
- Change From Baseline in Percent SBM With Sensation of Complete Evacuation at Up to 24 Weeks [Time Frame: Baseline and Over 24 week treatment period] [Designated as safety issue: No]
- Time to First SCBM After Investigational Product Intake on Day 1 and Day 28 [Time Frame: Day 1 and 28] [Designated as safety issue: No]
- Change From Baseline in the Number of Bisacodyl Tablets Taken Per Week at Up to 24 Weeks [Time Frame: Baseline and Over 24 week treatment period] [Designated as safety issue: No]
- Change From Baseline in the Number of Days With Rescue Medication Taken Per Week at Up to 24 Weeks [Time Frame: Baseline and Over 24 week treatment period] [Designated as safety issue: No]

  Rescue medications include laxatives and enemas.
- Change From Baseline in the Patient Assessment of Constipation - Symptom (PAC-SYM) Questionnaire Score at Up to the Final On Treatment Assessment Value [Time Frame: Baseline and Over 24 week treatment period] [Designated as safety issue: No]

  The PAC-SYM is a validated 12-item questionnaire for the evaluation of severity of symptoms of constipation in subjects with constipation. Items are rated on a 5-point Likert scale: 0=absent, 1=mild, 2=moderate, 3=severe, 4=very severe. Total score ranges from 0 to 48. Lower scores indicate improvement in symptoms. A 1-point improvement in PAC-SYM total score was considered clinically meaningful.
- Change From Baseline in the Patient Assessment of Constipation - Quality of Life (PAC-QOL) Score at Up to the Final On Treatment Assessment Value [Time Frame: Baseline and Over 24 week treatment period] [Designated as safety issue: No]

  The PAC-QOL is a validated 28-item questionnaire for the evaluation of quality of life in subjects with constipation. Items are rated on a 5-point Likert scale: 0=not at all/none of the time, 1=a little bit/a little bit of the time, 2=moderately/some of the time, 3=quite a bit/most of the time, 4=extremely/all of the time. Total score ranges from 0-112. Lower scores indicate improvement in symptoms. A 1-point improvement in PAC-QOL total score was considered clinically meaningful.

- Change From Baseline in the Short Form-36 Health Survey (SF-36) Score at Up to the Final On Treatment Assessment Value [Time Frame: Baseline and Over 24 week treatment period] [Designated as safety issue: No]
  The SF-36 consists of eight scaled scores, which are the weighted sums of the questions in their section. Total score ranges from 0 (lowest level of health) - 100 (highest level of health) on the assumption that each question carries equal weight. The lower the score the more disability. The higher the score the less disability (i.e. a score of zero is equivalent to maximum disability and a score of 100 is equivalent to no disability). Higher scores are associated with better quality of life.

Enrollment: 364
Study Start Date: June 2011
Primary Completion Date: December 2012
Study Completion Date: December 2012

Arms	Assigned Interventions
Placebo Comparator: Placebo Placebo 2 mg tablet once daily before breakfast	Drug: placebo Placebo matching tablet 2 mg once daily before breakfast for 24 weeks
Active Comparator: prucalopride Prucalopride 2 mg once daily before breakfast	Drug: prucalopride Prucalopride 2 mg daily before breakfast 1 mg for subjects >65 years; in case of insufficient response 2 mg at week 2 or week 4

Detailed Description:

In this phase IV trial a total of 340 subjects (170 subjects per treatment group), with chronic constipation, are planned to be randomly assigned to double-blind treatment.

The trial duration for a subject can be 26 to 28 weeks in total, including a 2- to 4-week run-in phase followed by a 24-week double-blind treatment phase. The patient will complete an e-diary.

Adult subjects (≥18 to <65 years of age) will take 2 mg prucalopride or matching placebo throughout the entire 24-week treatment period. Elderly subjects (≥65 years of age) will start at a dose of 1 mg prucalopride or matching placebo. In case of insufficient response the daily dose has to be increased to 2 mg (i.e. changed to 2 mg prucalopride or matching placebo).

Eligibility

Ages Eligible for Study: 18 Years and older
Genders Eligible for Study: Both
Accepts Healthy Volunteers: No

Criteria

Inclusion Criteria:

1. Subject is a male or non-pregnant, non-breastfeeding female out-patient ≥18 years of age (no upper age limit).

2. Subject has a history of constipation. The subject reports an average of ≤2 SBM/week that result in a feeling of complete evacuation (SCBM).
3. Subject agrees to stop his/her current laxative treatment and is willing to use rescue medication according to the rescue rule [bisacodyl/enemas].

Exclusion Criteria:

1. Subjects in whom constipation is thought to be drug-induced
2. Subjects using any disallowed medication.
3. Subjects who previously used prucalopride.
4. Subjects suffering from secondary causes of chronic constipation.

Contacts and Locations

Locations

- Belgium
  - Cliniques Universitaires St. Luc
    - Brussel, Belgium, 1200
  - Huisartspraktijk Jaak Mortelmans
    - Ham, Belgium, 3945
  - Universitaire Ziekenhuizen Leuven
    - Leuven, Flemish Brabant, Belgium, 3000
  - Centre Hospitalier Universitaire Sart Tilman Liège
    - Liège, Liège, Belgium, 4000
- Czech Republic
  - Derma Plus s.r.o.
    - Ceské Budejovice, Czech Republic, 370 01
  - Oblastní nemocnice Kolín, a.s.
    - Kolin, Czech Republic, 280 20
  - PIGEAS s.r.o.
    - Martin, Czech Republic, 03601
  - Diagnostika a Lécba Zažívacích Chorob, s.r.o.
    - Ostrava-Hrabuvka, Czech Republic, 700 30
  - MONSE s.r.o
    - Praha 1, Czech Republic, 118 33
  - Nemocnice Tábor, a.s.
    - Tabor, Czech Republic, 390 03
  - Orlickoústecká Nemocnice a.s
    - Ústí nad Orlicí, Czech Republic, 562 18
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    - Praha 4 - Krc, Praha, Czech Republic, 140 59
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    - Budapest, Hungary, 1136
  - BAZ Megyei és Egyetemi Oktató Kórház
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More Information

Responsible Party: Shire
Study ID Numbers: M0001-C401
2011-000670-62 [EudraCT Number]
Health Authority: Belgium: Federal Agency for Medicinal Products and Health Products
Czech Republic: State Institute for Drug Control
Hungary: National Institute of Pharmacy
Poland: CEBK
Romania: National Medicines Agency
Slovakia: State Institute for Drug Control
Spain: Agencia Española de Medicamentos y Productos Sanitarios
Sweden: Medical Products Agency

Study Results

Participant Flow

Reporting Groups

	Description
Placebo	Tablet once daily before breakfast
Prucalopride	1 mg or 2 mg tablet once daily before breakfast

Overall Study

	Placebo	Prucalopride
Started	182	182
Completed	126	135
Not Completed	56	47
Withdrawal by Subject	27	11

	Placebo	Prucalopride
Adverse Event	10	14
Sponsor's decision	9	12
Lack of Efficacy	5	7
inclusion/exclusion criteria not met	2	2
Non-compliance	2	0
Worsening of symptoms	1	0
Unplanned journey	0	1

Baseline Characteristics

Analysis Population Description

The Safety Population was used for demographics. The Safety Population includes all subjects randomized into the study who took at least 1 dose of investigational product. Three subjects did not receive investigational product and therefore were not included in the Safety Population (n = 361).

Reporting Groups

	Description
Placebo	Tablet once daily before breakfast
Prucalopride	1 mg or 2 mg tablet once daily before breakfast

Baseline Measures

	Placebo	Prucalopride	Total
Number of Participants	180	181	361
Age, Continuous [units: years] Mean (Standard Deviation)	48.3 (16.25)	49.4 (15.78)	48.9 (16.00)
Age, Customized [units: participants]			
<65 years	149	146	295
> = 65 years to <75 years	20	26	46
>=75 years	11	9	20
Gender, Male/Female [units: participants]			

	Placebo	Prucalopride	Total
Female	153	155	308
Male	27	26	53
Region of Enrollment [1] [units: participants]			
Romania	38	37	75
Poland	34	31	65
Hungary	29	31	60
Slovakia	28	29	57
Italy	19	18	37
Spain	11	8	19
Belgium	8	11	19
Sweden	9	9	18
Czech Republic	6	8	14

[1] This includes all randomized subjects (n = 364).

Outcome Measures

1. Primary Outcome Measure:

Measure Title	The Percentage of Subjects With an Average of ≥3 Spontaneous Complete Bowel Movements (SCBM) Per Week Over the 24 Week Treatment Period
Measure Description	Spontaneous Bowel Movements defined as a bowel movement that is not preceded within a period of 24 hours by the intake of a laxative agent or by the use of an enema.
Time Frame	Over 24 week treatment period
Safety Issue?	No

Analysis Population Description

Intent-to-Treat Population (ITT) includes all subjects randomized into the study who took at least 1 dose of investigational product. There were 21 subjects with a risk of potential unblinding due to an error in the randomization system who were excluded from the ITT Population to avoid the risk of bias to the study results.

Reporting Groups

	Description
Placebo	Tablet once daily before breakfast
Prucalopride	1 mg or 2 mg tablet once daily before breakfast

Measured Values

	Placebo	Prucalopride
Number of Participants Analyzed	169	171
The Percentage of Subjects With an Average of ≥3 Spontaneous Complete Bowel Movements (SCBM) Per Week Over the 24 Week Treatment Period [units: percentage of subjects]	20.7	25.1

Statistical Analysis 1 for The Percentage of Subjects With an Average of ≥3 Spontaneous Complete Bowel Movements (SCBM) Per Week Over the 24 Week Treatment Period

Statistical Analysis Overview	Comparison Groups	Placebo, Prucalopride
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.367
	Comments	[Not specified]
	Method	Cochran-Mantel-Haenszel
	Comments	[Not specified]

2. Secondary Outcome Measure:

Measure Title	Percentage of Subjects With an Increase of ≥1 Spontaneous Complete Bowel Movement (SCBM) Per Week Up to 24 Weeks
Measure Description	
Time Frame	Over 24 week treatment period
Safety Issue?	No

Analysis Population Description

Intent-to-Treat Population (ITT) includes all subjects randomized into the study who took at least 1 dose of investigational product. The 21 subjects with a risk of potential unblinding due to an error in the randomization system were excluded from the ITT Population to avoid the risk of bias to the study results.

Reporting Groups

	Description
Placebo	Tablet once daily before breakfast
Prucalopride	1 mg or 2 mg tablet once daily before breakfast

Measured Values

	Placebo	Prucalopride
Number of Participants Analyzed	169	171
Percentage of Subjects With an Increase of ≥1 Spontaneous Complete Bowel Movement (SCBM) Per Week Up to 24 Weeks [units: percentage of subjects]	42.0	48.0

3. Secondary Outcome Measure:

Measure Title	Average Number of Spontaneous Complete Bowel Movements (SCBM) Per Week Up to 24 Weeks
Measure Description	
Time Frame	Over 24 week treatment period
Safety Issue?	No

Analysis Population Description

ITT population. Not all subjects in the ITT population had data for this outcome.

Reporting Groups

	Description
Placebo	Tablet once daily before breakfast
Prucalopride	1 mg or 2 mg tablet once daily before breakfast

Measured Values

	Placebo	Prucalopride
Number of Participants Analyzed	165	158
Average Number of Spontaneous Complete Bowel Movements (SCBM) Per Week Up to 24 Weeks	1.7 (1.86)	2.1 (1.96)

	Placebo	Prucalopride
[units: SCBM/week] Mean (Standard Deviation)		

4. Secondary Outcome Measure:

Measure Title	Change From Baseline in Spontaneous Complete Bowel Movements Per Week at Up to 24 Weeks
Measure Description	
Time Frame	Baseline and Over 24 week treatment period
Safety Issue?	No

Analysis Population Description

ITT population. Not all subjects in the ITT population had data for this outcome.

Reporting Groups

	Description
Placebo	Tablet once daily before breakfast
Prucalopride	1 mg or 2 mg tablet once daily before breakfast

Measured Values

	Placebo	Prucalopride
Number of Participants Analyzed	165	158
Change From Baseline in Spontaneous Complete Bowel Movements Per Week at Up to 24 Weeks [units: SCBM/week] Mean (Standard Deviation)	1.3 (1.77)	1.7 (1.90)

5. Secondary Outcome Measure:

Measure Title	Percent of Subjects With an Average Weekly Frequency of at Least 3 SCBM by Week
Measure Description	
Time Frame	Over 24 week treatment period
Safety Issue?	No

Analysis Population Description

Intent-to-Treat Population (ITT) includes all subjects randomized into the study who took at least 1 dose of investigational product. The 21 subjects with a risk of potential unblinding due to an error in the randomization system were excluded from the ITT Population to avoid the risk of bias to the study results.

Reporting Groups

	Description
Placebo	Tablet once daily before breakfast
Prucalopride	1 mg or 2 mg tablet once daily before breakfast

Measured Values

	Placebo	Prucalopride
Number of Participants Analyzed	169	171
Percent of Subjects With an Average Weekly Frequency of at Least 3 SCBM by Week [units: percentage of subjects]		
Week 1	18.3	32.2
Week 2	23.1	34.5
Week 3	22.5	32.2
Week 4	23.1	31.6
Week 5	26.6	27.5
Week 6	28.4	29.2
Week 7	29.0	29.8
Week 8	26.0	30.4
Week 9	27.8	33.3
Week 10	26.0	30.4
Week 11	25.4	37.4
Week 12	27.2	33.9
Week 13	23.7	30.4
Week 14	30.2	35.7
Week 15	24.9	29.2
Week 16	29.6	35.1
Week 17	28.4	35.1
Week 18	30.2	32.7
Week 19	32.0	32.2

	Placebo	Prucalopride
Week 20	24.9	37.4
Week 21	26.6	30.4
Week 22	27.8	32.7
Week 23	30.2	31.0
Week 24	32.0	31.6

6. Secondary Outcome Measure:

Measure Title	Percent of Subjects With an Average Weekly Frequency of at Least 3 SCBM by 4-Week Treatment Period
Measure Description	
Time Frame	Over 24 week treatment period
Safety Issue?	No

Analysis Population Description

Intent-to-Treat Population (ITT) includes all subjects randomized into the study who took at least 1 dose of investigational product. The 21 subjects with a risk of potential unblinding due to an error in the randomization system were excluded from the ITT Population to avoid the risk of bias to the study results.

Reporting Groups

	Description
Placebo	Tablet once daily before breakfast
Prucalopride	1 mg or 2 mg tablet once daily before breakfast

Measured Values

	Placebo	Prucalopride
Number of Participants Analyzed	169	171
Percent of Subjects With an Average Weekly Frequency of at Least 3 SCBM by 4-Week Treatment Period [units: percentage of subjects]		
First 4-week period	18.3	26.9
Second 4-week period	23.7	25.7
Third 4-week period	23.7	29.2
Fourth 4-week period	22.5	29.2

	Placebo	Prucalopride
Fifth 4-week period	23.7	33.3
Sixth 4-week period	24.9	26.9

7. Secondary Outcome Measure:

Measure Title	Change From Baseline in Average Consistency Per SCBM at Up to 24 Weeks
Measure Description	Consistency measured using the 7-point Bristol scale where 1-2 indicate constipation (=hard/very hard), 3-4 are ideal stools (=normal), and 5-7 tending toward diarrhea.
Time Frame	Baseline and Over 24 week treatment period
Safety Issue?	No

Analysis Population Description

ITT population. Not all subjects in the ITT population had data for this outcome.

Reporting Groups

	Description
Placebo	Tablet once daily before breakfast
Prucalopride	1 mg or 2 mg tablet once daily before breakfast

Measured Values

	Placebo	Prucalopride
Number of Participants Analyzed	67	55
Change From Baseline in Average Consistency Per SCBM at Up to 24 Weeks [units: units on a scale] Mean (Standard Deviation)	-0.1 (1.79)	-0.1 (1.31)

8. Secondary Outcome Measure:

Measure Title	Change From Baseline in Percent SCBM With a Consistency of Normal and Hard/Very Hard at Up to 24 Weeks
Measure Description	
Time Frame	Baseline and Over 24 week treatment period
Safety Issue?	No

Analysis Population Description

ITT population. Not all subjects in the ITT population had data for this outcome.

Reporting Groups

	Description
Placebo	Tablet once daily before breakfast
Prucalopride	1 mg or 2 mg tablet once daily before breakfast

Measured Values

	Placebo	Prucalopride
Number of Participants Analyzed	67	55
Change From Baseline in Percent SCBM With a Consistency of Normal and Hard/Very Hard at Up to 24 Weeks [units: percentage of SCBM] Mean (Standard Deviation)		
Normal consistency	16.82 (42.365)	25.71 (40.1)
Hard/Very Hard consistency	-9.11 (41.495)	-13.82 (31.349)

9. Secondary Outcome Measure:

Measure Title	Change From Baseline in Straining Per SCBM at Up to 24 Weeks
Measure Description	Straining was evaluated on a 5-point scale (0=none, 1=mild, 2=moderate, 3=severe, or 4=very severe)
Time Frame	Baseline and Over 24 week treatment period
Safety Issue?	No

Analysis Population Description

ITT population. Not all subjects in the ITT population had data for this outcome.

Reporting Groups

	Description
Placebo	Tablet once daily before breakfast
Prucalopride	1 mg or 2 mg tablet once daily before breakfast

Measured Values

	Placebo	Prucalopride
Number of Participants Analyzed	67	55
Change From Baseline in Straining Per SCBM at Up to 24 Weeks [units: units on a scale] Mean (Standard Deviation)	-0.44 (0.948)	-0.23 (0.870)

10. Secondary Outcome Measure:

Measure Title	Change From Baseline in Percent SCBM With No Straining and Severe/Very Severe Straining at Up to 24 Weeks
Measure Description	
Time Frame	Baseline and Over 24 week treatment period
Safety Issue?	No

Analysis Population Description

ITT population. Not all subjects in the ITT population had data for this outcome.

Reporting Groups

	Description
Placebo	Tablet once daily before breakfast
Prucalopride	1 mg or 2 mg tablet once daily before breakfast

Measured Values

	Placebo	Prucalopride
Number of Participants Analyzed	67	55
Change From Baseline in Percent SCBM With No Straining and Severe/Very Severe Straining at Up to 24 Weeks [units: percentage of SCBM] Mean (Standard Deviation)		
No straining	11.14 (39.786)	6.61 (33.916)
Severe/Very Severe straining	-9.85 (29.711)	-4.49 (28.177)

11. Secondary Outcome Measure:

Measure Title	Change From Baseline in Percent SBM With Sensation of Complete Evacuation at Up to 24 Weeks

Measure Description	
Time Frame	Baseline and Over 24 week treatment period
Safety Issue?	No

Analysis Population Description

ITT population. Not all subjects in the ITT population had data for this outcome.

Reporting Groups

	Description
Placebo	Tablet once daily before breakfast
Prucalopride	1 mg or 2 mg tablet once daily before breakfast

Measured Values

	Placebo	Prucalopride
Number of Participants Analyzed	149	138
Change From Baseline in Percent SBM With Sensation of Complete Evacuation at Up to 24 Weeks [units: percentage of SBM] Mean (Standard Deviation)	20.94 (32.619)	24.22 (32.878)

12. Secondary Outcome Measure:

Measure Title	Time to First SCBM After Investigational Product Intake on Day 1 and Day 28
Measure Description	
Time Frame	Day 1 and 28
Safety Issue?	No

Analysis Population Description

Intent-to-Treat Population (ITT) includes all subjects randomized into the study who took at least 1 dose of investigational product. The 21 subjects with a risk of potential unblinding due to an error in the randomization system were excluded from the ITT Population to avoid the risk of bias to the study results.

Reporting Groups

	Description
Placebo	Tablet once daily before breakfast
Prucalopride	1 mg or 2 mg tablet once daily before breakfast

Measured Values

	Placebo	Prucalopride
Number of Participants Analyzed	169	171
Time to First SCBM After Investigational Product Intake on Day 1 and Day 28 [units: hours] Median (95% Confidence Interval)		
Day 1	359.67 (179.6 to 461.42)	100.83 (74.0 to 170.75)
Day 28	100.58 (75.2 to 199.02)	81.78 (52.25 to 151.05)

13. Secondary Outcome Measure:

Measure Title	Change From Baseline in the Number of Bisacodyl Tablets Taken Per Week at Up to 24 Weeks
Measure Description	
Time Frame	Baseline and Over 24 week treatment period
Safety Issue?	No

Analysis Population Description

ITT population. Not all subjects in the ITT population had data for this outcome.

Reporting Groups

	Description
Placebo	Tablet once daily before breakfast
Prucalopride	1 mg or 2 mg tablet once daily before breakfast

Measured Values

	Placebo	Prucalopride
Number of Participants Analyzed	140	144
Change From Baseline in the Number of Bisacodyl Tablets Taken Per Week at Up to 24 Weeks [units: tablets/week] Mean (Standard Deviation)	-0.68 (1.583)	-0.97 (1.821)

14. Secondary Outcome Measure:

Measure Title	Change From Baseline in the Number of Days With Rescue Medication Taken Per Week at Up to 24 Weeks

Measure Description	Rescue medications include laxatives and enemas.
Time Frame	Baseline and Over 24 week treatment period
Safety Issue?	No

Analysis Population Description

ITT population. Not all subjects in the ITT population had data for this outcome.

Reporting Groups

	Description
Placebo	Tablet once daily before breakfast
Prucalopride	1 mg or 2 mg tablet once daily before breakfast

Measured Values

	Placebo	Prucalopride
Number of Participants Analyzed	140	144
Change From Baseline in the Number of Days With Rescue Medication Taken Per Week at Up to 24 Weeks [units: days/week] Mean (Standard Deviation)	-0.42 (0.892)	-0.54 (1.018)

15. Secondary Outcome Measure:

Measure Title	Change From Baseline in the Patient Assessment of Constipation - Symptom (PAC-SYM) Questionnaire Score at Up to the Final On Treatment Assessment Value
Measure Description	The PAC-SYM is a validated 12-item questionnaire for the evaluation of severity of symptoms of constipation in subjects with constipation. Items are rated on a 5-point Likert scale: 0=absent, 1=mild, 2=moderate, 3=severe, 4=very severe. Total score ranges from 0 to 48. Lower scores indicate improvement in symptoms. A 1-point improvement in PAC-SYM total score was considered clinically meaningful.
Time Frame	Baseline and Over 24 week treatment period
Safety Issue?	No

Analysis Population Description

ITT population. Not all subjects in the ITT population had data for this outcome.

Reporting Groups

	Description
Placebo	Tablet once daily before breakfast
Prucalopride	1 mg or 2 mg tablet once daily before breakfast

Measured Values

	Placebo	Prucalopride
Number of Participants Analyzed	167	167
Change From Baseline in the Patient Assessment of Constipation - Symptom (PAC-SYM) Questionnaire Score at Up to the Final On Treatment Assessment Value [units: units on a scale] Mean (Standard Deviation)	-0.68 (0.929)	-0.55 (0.794)

16. Secondary Outcome Measure:

Measure Title	Change From Baseline in the Patient Assessment of Constipation - Quality of Life (PAC-QOL) Score at Up to the Final On Treatment Assessment Value
Measure Description	The PAC-QOL is a validated 28-item questionnaire for the evaluation of quality of life in subjects with constipation. Items are rated on a 5-point Likert scale: 0=not at all/none of the time, 1=a little bit/a little bit of the time, 2=moderately/ some of the time, 3=quite a bit/most of the time, 4=extremely/all of the time. Total score ranges from 0-112. Lower scores indicate improvement in symptoms. A 1-point improvement in PAC-QOL total score was considered clinically meaningful.
Time Frame	Baseline and Over 24 week treatment period
Safety Issue?	No

Analysis Population Description

ITT population. Not all subjects in the ITT population had data for this outcome.

Reporting Groups

	Description
Placebo	Tablet once daily before breakfast
Prucalopride	1 mg or 2 mg tablet once daily before breakfast

Measured Values

	Placebo	Prucalopride
Number of Participants Analyzed	162	166
Change From Baseline in the Patient Assessment of Constipation - Quality of Life (PAC-QOL) Score at Up to the Final On Treatment Assessment Value [units: units on a scale] Mean (Standard Deviation)	-0.73 (0.902)	-0.67 (0.932)

17. Secondary Outcome Measure:

Measure Title	Change From Baseline in the Short Form-36 Health Survey (SF-36) Score at Up to the Final On Treatment Assessment Value
Measure Description	The SF-36 consists of eight scaled scores, which are the weighted sums of the questions in their section. Total score ranges from 0 (lowest level of health) - 100 (highest level of health) on the assumption that each question carries equal weight. The lower the score the more disability. The higher the score the less disability (i.e. a score of zero is equivalent to maximum disability and a score of 100 is equivalent to no disability). Higher scores are associated with better quality of life.
Time Frame	Baseline and Over 24 week treatment period
Safety Issue?	No

Analysis Population Description

ITT population. Not all subjects in the ITT population had data for this outcome.

Reporting Groups

	Description
Placebo	Tablet once daily before breakfast
Prucalopride	1 mg or 2 mg tablet once daily before breakfast

Measured Values

	Placebo	Prucalopride
Number of Participants Analyzed	164	167
Change From Baseline in the Short Form-36 Health Survey (SF-36) Score at Up to the Final On Treatment Assessment Value [units: units on a scale] Mean (Standard Deviation)		
Mental component	3.786 (10.0887)	3.179 (10.5714)

	Placebo	Prucalopride
Physical component	3.331 (6.9830)	2.965 (6.9320)

Reported Adverse Events

Time Frame	[Not specified]
Additional Description	The Safety Population includes all subjects randomized into the study who took at least 1 dose of investigational product. Three subjects did not receive investigational product and therefore were not included in the Safety Population (n = 361).

Reporting Groups

	Description
Placebo	Tablet once daily before breakfast
Prucalopride	1 mg or 2 mg tablet once daily before breakfast

Serious Adverse Events

	Placebo	Prucalopride
	Affected/At Risk (%)	Affected/At Risk (%)
Total	4/180 (2.22%)	4/181 (2.21%)
Gastrointestinal disorders		
Colitis ischemic	1/180 (0.56%)	0/181 (0%)
Obstruction gastric	0/180 (0%)	1/181 (0.55%)
Hepatobiliary disorders		
Cholecystitis chronic	1/180 (0.56%)	0/181 (0%)
Infections and infestations		
Vestibular neuronitis	1/180 (0.56%)	0/181 (0%)
Investigations		
Blood pressure decreased	0/180 (0%)	1/181 (0.55%)
Electrocardiogram QT prolonged	0/180 (0%)	1/181 (0.55%)
Nervous system disorders		
Cerebrovascular accident	0/180 (0%)	1/181 (0.55%)

	Placebo	Prucalopride
	Affected/At Risk (%)	Affected/At Risk (%)
Ischemic stroke	1/180 (0.56%)	0/181 (0%)
Psychiatric disorders		
Abnormal behavior	0/180 (0%)	1/181 (0.55%)
Vascular disorders		
Orthostatic hypotension	1/180 (0.56%)	0/181 (0%)

Other Adverse Events
Frequency Threshold Above Which Other Adverse Events are Reported: 5%

	Placebo	Prucalopride
	Affected/At Risk (%)	Affected/At Risk (%)
Total	23/180 (12.78%)	41/181 (22.65%)
Gastrointestinal disorders		
Abdominal pain	8/180 (4.44%)	18/181 (9.94%)
Nausea	7/180 (3.89%)	13/181 (7.18%)
Nervous system disorders		
Headache	10/180 (5.56%)	21/181 (11.6%)

Limitations and Caveats

[Not specified]

More Information

Certain Agreements:

Principal Investigators are NOT employed by the organization sponsoring the study.

There IS an agreement between the Principal Investigator and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

If a multicenter publication is not submitted within twelve (12) months after conclusion, abandonment or termination of the Study at all sites, or after Sponsor confirms there shall be no multicenter Study publication, the Institution and/or such Principal Investigator may publish the results from the Institution site individually.

Results Point of Contact:

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