ClinicalTrials.gov Protocol Registration and Results System (PRS) Receipt
Release Date: February 14, 2017

ClinicalTrials.gov ID: NCT01358708

Study Identification

Unique Protocol ID:	MA-LA-IBS09-01
Brief Title:	Treatment of Diarrhea-predominant Irritable Bowel Syndrome (IBS-D) With LACTEOL® 340 mg
Official Title:	Treatment of Diarrhea-predominant Irritable Bowel Syndrome With LACTEOL® 340 mg: A Pilot Study Evaluating Safety and Efficacy
Secondary IDs:	

Study Status

Record Verification:	February 2017
Overall Status:	Terminated [Administrative reasons]
Study Start:	June 2010 []
Primary Completion:	September 2011 [Actual]
Study Completion:	September 2011 [Actual]

Sponsor/Collaborators

Sponsor:	Forest Laboratories
Responsible Party:	Sponsor
Collaborators:	

Oversight

U.S. FDA-regulated Drug:	
U.S. FDA-regulated Device:	

U.S. FDA IND/IDE:	No
Human Subjects Review:	Board Status: Approved Approval Number: 2010-003 Board Name: Comité de Protection des Personnes Nord-Ouest 1 Board Affiliation: Hopital Charles Nicolle Phone: +33 (0)2 32 88 84 46 Email: cppnordouest1@chu-rouen.fr Address: 1 rue Germont 76081 Rouen, France
Data Monitoring:	No
FDA Regulated Intervention:	No

Study Description

Brief Summary:	Irritable bowel syndrome is a complex condition with a high unmet medical need for effective and safe treatment options. Lacteol® is a lactobacillus product used for adjunctive and symptomatic treatment of diarrhea. In this study, Lacteol® 340 mg will be evaluated as a potential therapy for the treatment of diarrhea-predominant irritable bowel syndrome (IBS-D).
Detailed Description:	This study will include the following phases: Screening Phase, Run-In Phase, Double-Blind Treatment Phase and Open-Label Treatment Phase. Screening: Eligibility of subjects will be evaluated following informed consent signature. Screening procedures/evaluations (physical exam, concomitant medications, clinical laboratory tests) and confirmation of eligibility following Rome III Diagnostic questionnaire will be performed. Run-In: Subjects will enter a 2-week Run-In Phase during which IBS Symptoms and Stool Characteristics will be recorded. At the end of the Run-In Phase, data collected over the last week will be reviewed. Upon confirmation of IBS-D severity status, subjects may be randomized. Double-Blind Treatment: Subjects will take study medication (either LACTEOL® 340 mg or Placebo) for 28 days. During this time, IBS Symptoms and Stool Characteristics and global assessment of relief will be recorded, and clinical laboratory tests will be performed. HAD score will be assessed at the end of the double blind treatment. Open-Label Treatment: All study completers will be eligible for a second 28 day Open-Label Treatment in the event that IBS-D symptoms remain or recur within the month following the end of Double-Blind Treatment. Subjects will take the study medication (LACTEOL® 340 mg) for 28 days. During this time, IBS Symptoms and Stool Characteristics and global assessment of relief will be recorded, and clinical laboratory tests will be performed.

Conditions

Conditions:	Diarrhea-predominant Irritable Bowel Syndrome

Keywords:

Study Design

Study Type: Interventional
Primary Purpose: Treatment
Study Phase: Phase 3
Interventional Study Model: Parallel Assignment
Number of Arms: 2
Masking: Quadruple (Participant, Care Provider, Investigator, Outcomes Assessor)
Allocation: Randomized
Enrollment: 26 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: LACTEOL® 340 mg	Drug: LACTEOL® 340 mg LACTEOL® 340 mg will be taken for a 4-week duration (28 days) as three capsules a day: two capsules in the morning and one capsule in the evening.
Placebo Comparator: PLACEBO	Drug: PLACEBO Matched LACTEOL® 340 mg Placebo will be taken for a 4-week duration (28 days) as three capsules a day: two capsules in the morning and one capsule in the evening.

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age: 18 Years
Maximum Age: 100 Years
Sex: All
Gender Based:
Accepts Healthy Volunteers: No

Criteria: Inclusion Criteria:

- IBS-D diagnosis using the Rome III questionnaire
- IBS Symptoms Severity Scale (IBS-SSS) score ranging between 100 and 400
- Bristol Stool Form Scale score exceeding two (> 2) but less than seven (< 7)
- Stable diet
- Mental and legal ability to sign informed consent

Exclusion Criteria:

- Diagnosis of Inflammatory Bowel Disease (IBD)
- Chronic use of systemic steroids
- Diagnosis of autoimmune Diseases or Disorders
- Invasive abdominal surgery
- Use of antibiotics prior to screening
- Allergy to active substance or any other ingredient in LACTEOL® 340 mg
- Congenital galactosemia, glucose, fructose and/or galactose malabsorption syndrome, lactase deficiency or lactose intolerance
- Diagnosis of exocrine pancreatic insufficiency
- Use of any experimental drug within the 30 days prior to screening

Contacts/Locations

Central Contact Person: Valérie Ratheau, MSc
Telephone: 1-450-467-5138 Ext. 2096
Email: vratheau@aptalispharma.com

Central Contact Backup: Ivan T. Shaw, PhD
Telephone: 1-450-467-5138 Ext. 2608
Email: ishaw@aptalispharma.com

Study Officials: Ivan T Shaw, PhD
Study Director
Axcan Pharma Inc.

Locations: France
Lyon, France

Nice, France

Marseille, France

Rouen, France

Colombes, France

Germany
Berlin, Germany

Mannheim, Germany

Hamburg, Germany

France
Bordeaux, France

Germany
Berlin, Germany

IPDSharing

Plan to Share IPD:

References

Citations:

Links:

Available IPD/Information:

Study Results

Participant Flow

Recruitment Details	First subject in: 22 June 2010; last subject out: 12 September 2011; ten (10) sites were recruited to participate in this trial and 7 of these (4 in France and 3 in Germany) enrolled subjects.
Pre-assignment Details	Inclusion criteria related to symptom severity and stool characteristics assessed during 2nd week of Run-In Phase; ≥ 5 days of symptom data necessary for randomization; Double-Blind Phase completers eligible for a 28-day open-label treatment with LACTEOL® if symptoms not improved or recurring within 1 month after end of blinded treatment.

Reporting Groups

	Description
LACTEOL® 340 mg	LACTEOL® active medication was taken for a 4-week duration (28 days) as three capsules a day: two capsules in the morning and one capsule in the evening.
PLACEBO	Matched LACTEOL® placebo was taken for a 4-week duration (28 days) as three capsules a day: two capsules in the morning and one capsule in the evening.

Double-Blind Treatment Phase

	LACTEOL® 340 mg	PLACEBO
Started	13	13
Randomized	13	13
Received Study Medication	12 [1]	13
Completed	10	13
Not Completed	3	0
Lost to Follow-up	2	0
Protocol Violation	1	0

[1] For 1 subject, unused med not returned to the site and intake of study medication not confirmed.

Open-Label Treatment Phase

	LACTEOL® 340 mg	PLACEBO
Started	5 [1]	12 [2]
Completed	5	12
Not Completed	0	0

[1] Number of subjects on LACTEOL® during double-blind treatment and entering the Open-Label Phase
[2] Number of subjects on PLACEBO during double-blind treatment and entering the Open-Label Phase

Baseline Characteristics

Baseline Analysis Population Description
Analysis conducted on the Intent-to-Treat population defined as all randomized subjects

Reporting Groups

	Description
LACTEOL® 340 mg	LACTEOL® active medication was taken for a 4-week duration (28 days) as three capsules a day: two capsules in the morning and one capsule in the evening.
PLACEBO	Matched LACTEOL® placebo was taken for a 4-week duration (28 days) as three capsules a day: two capsules in the morning and one capsule in the evening.

Baseline Measures

		LACTEOL® 340 mg	PLACEBO	Total
Overall Number of Participants		13	13	26
Age, Categorical Measure Type: Count of Participants Unit of measure: participants	Number Analyzed	13 participants	13 participants	26 participants
	<=18 years	0 0%	0 0%	0 0%
	Between 18 and 65 years	10 76.92%	11 84.62%	21 80.77%
	>=65 years	3 23.08%	2 15.38%	5 19.23%
Sex: Female, Male Measure Type: Count of Participants Unit of measure: participants	Number Analyzed	13 participants	13 participants	26 participants
	Female	9 69.23%	8 61.54%	17 65.38%
	Male	4 30.77%	5 38.46%	9 34.62%
Region of Enrollment Measure Type: Number Unit of measure: participants	Number Analyzed	13 participants	13 participants	26 participants
France		6	6	12
Germany		7	7	14

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Global Assessment of Relief During the Double-Blind Treatment Phase Using the Subject Global Assessment (SGA)

Measure Description	Subjects were considered as responders if they had answered “Yes” to the following question at least 50% of the time during the 4-week treatment phase: “Over the past week, do you consider that you have had satisfactory relief from your IBS symptoms?"
Time Frame	Weekly Assessment (every 7 days)

Analysis Population Description

Analysis conducted on the Intent-to-Treat population defined as all randomized subjects; observed case (OC) data with no imputation made

Reporting Groups

	Description
LACTEOL® 340 mg	LACTEOL® active medication was taken for a 4-week duration (28 days) as three capsules a day: two capsules in the morning and one capsule in the evening.
PLACEBO	Matched LACTEOL® placebo was taken for a 4-week duration (28 days) as three capsules a day: two capsules in the morning and one capsule in the evening.

Measured Values

	LACTEOL® 340 mg	PLACEBO
Overall Number of Participants Analyzed	13	13
Global Assessment of Relief During the Double-Blind Treatment Phase Using the Subject Global Assessment (SGA) Measure Type: Number Unit of measure: percentage of participants		
Responders	30.8	30.8
Non-responders	69.2	69.2

2. Secondary Outcome Measure:

Measure Title	Global Assessment of Relief During the Open-Label Treatment Phase Using the Subject Global Assessment (SGA)
Measure Description	Subjects were considered as responders if they had answered "Yes" to the following question at least 50% of the time during the 4-week treatment phase: "Over the past week, do you consider that you have had satisfactory relief from your IBS symptoms?"
Time Frame	Weekly Assessment (every 7 days)

Analysis Population Description

Analysis conducted on the Intent-to-Treat population defined as all subjects randomized to double-blind treatment and who subsequently entered the Open-Label Treatment Phase; observed case (OC) data with no imputation made; SGA data not available for one patient so that the analysis was performed on 16 rather than 17 patients

Reporting Groups

	Description
LACTEOL® 340 mg	LACTEOL® active medication was taken for a 4-week duration (28 days) as three capsules a day: two capsules in the morning and one capsule in the evening.

Measured Values

	LACTEOL® 340 mg
Overall Number of Participants Analyzed	16
Global Assessment of Relief During the Open-Label Treatment Phase Using the Subject Global Assessment (SGA) Measure Type: Number Unit of measure: percentage of participants	
Responders	50.0
Non-responders	50.0

3. Secondary Outcome Measure:

Measure Title	Symptom Severity During the Double-Blind Treatment Phase Using the IBS Symptom Severity Scale (IBS-SSS) Total Score
Measure Description	The IBS-SSS has five questions related to four domains: abdominal pain severity and duration, abdominal distension, dissatisfaction with bowel habit and quality of life. The IBS-SSS score ranges from 0 (best outcome) to 500 (worst outcome).
Time Frame	Weekly assessment (every 7 days)

Analysis Population Description

Analysis conducted on the Intent-to-Treat population defined as all randomized subjects; observed case (OC) data with no imputation made. Number of participants analyzed refers to number of participants at Baseline.

Reporting Groups

	Description
LACTEOL® 340 mg	LACTEOL® active medication was taken for a 4-week duration (28 days) as three capsules a day: two capsules in the morning and one capsule in the evening.
PLACEBO	Matched LACTEOL® placebo was taken for a 4-week duration (28 days) as three capsules a day: two capsules in the morning and one capsule in the evening.

Measured Values

	LACTEOL® 340 mg	PLACEBO
Overall Number of Participants Analyzed	13	13
Symptom Severity During the Double-Blind Treatment Phase Using the IBS Symptom Severity Scale (IBS-SSS) Total Score Mean (Standard Deviation) Unit of measure: units on a scale (from 0 to 500)		
Baseline IBS-SSS score	245.0 (87.3)	307.5 (72.36)
IBS-SSS score at end of Week 1 (Day 7)	219.2 (76.36)	271.2 (109.72)
IBS-SSS score at end of Week 2 (Day 14)	229.5 (81.95)	265.4 (99.93)
IBS-SSS score at end of Week 3 (Day 21)	233.6 (87.78)	254.8 (103.75)
IBS-SSS score at end of Week 4 (Day 28)	228.6 (91.82)	241.4 (99.23)

4. Secondary Outcome Measure:

Measure Title	Stool Characteristics During the Double-Blind Treatment Phase Using the Bristol Stool Form Scale
Measure Description	The Bristol Stool Form Scale score ranges from 1 to 7 from hard (score of 1) to watery (score of 7). Data are presented as the mean of daily assessments over a week.
Time Frame	Daily assessment

Analysis Population Description

Analysis conducted on the Intent-to-Treat population defined as all randomized subjects; observed case (OC) data with no imputation made. Number of participants analyzed refers to number of participants at Baseline.

Reporting Groups

	Description
LACTEOL® 340 mg	LACTEOL® active medication was taken for a 4-week duration (28 days) as three capsules a day: two capsules in the morning and one capsule in the evening.
PLACEBO	Matched LACTEOL® placebo was taken for a 4-week duration (28 days) as three capsules a day: two capsules in the morning and one capsule in the evening.

Measured Values

	LACTEOL® 340 mg	PLACEBO
Overall Number of Participants Analyzed	13	13
Stool Characteristics During the Double-Blind Treatment Phase Using the Bristol Stool Form Scale Mean (Standard Deviation) Unit of measure: units on a scale (from 1 ato 7)		
Baseline Bristol Stool Form Scale Score	4.8 (1.14)	4.9 (0.64)
Bristol Stool Form Score during Week 1	4.3 (1.29)	4.8 (0.61)
Bristol Stool Form Score during Week 2	4.6 (1.33)	4.8 (0.83)
Bristol Stool Form Score during Week 3	4.4 (1.52)	4.4 (0.78)
Bristol Stool Form Score during Week 4	4.4 (1.32)	4.8 (0.81)

5. Secondary Outcome Measure:

Measure Title	Hospital Anxiety and Depression Scale (HADS) Score During the Double-Blind Phase
Measure Description	The HADS has 14 questions related to 2 domains: Anxiety subscale (7 questions) and Depression subscale (7 questions). Each question is graded from 0 (best outcome) to 3 (worst outcome), for a total score ranging from 0 (best outcome) to 42 (worst outcome).
Time Frame	At Screening and End of Double-Blind Treatment Phase

Analysis Population Description

Analysis conducted on the Intent-to-Treat population defined as all randomized subjects; observed case (OC) data with no imputation made

Reporting Groups

	Description
LACTEOL® 340 mg	LACTEOL® active medication was taken for a 4-week duration (28 days) as three capsules a day: two capsules in the morning and one capsule in the evening.
PLACEBO	Matched LACTEOL® placebo was taken for a 4-week duration (28 days) as three capsules a day: two capsules in the morning and one capsule in the evening.

Measured Values

	LACTEOL® 340 mg	PLACEBO
Overall Number of Participants Analyzed	13	13
Hospital Anxiety and Depression Scale (HADS) Score During the Double-Blind Phase Mean (Standard Deviation) Unit of measure: units on a scale (from 0 to 42)		
Baseline HADS Total Score	9.7 (5.14)	10.7 (4.82)
HADS Total Score at End of Double-Blind Treatment	9.9 (6.10)	9.5 (5.88)

6. Secondary Outcome Measure:

Measure Title	Symptom Severity During the Open-Label Treatment Phase Using the IBS Symptom Severity Scale (IBS-SSS) Total Score
Measure Description	The IBS-SSS has five questions related to four domains: abdominal pain severity and duration, abdominal distension, dissatisfaction with bowel habit and quality of life. The IBS-SSS score ranges from 0 (best outcome) to 500 (worst outcome).
Time Frame	Weekly assessment (every 7 days)

Analysis Population Description

Analysis conducted on the Intent-to-Treat population defined as all subjects randomized to double-blind treatment and who subsequently entered the Open-Label Treatment Phase; observed case (OC) data with no imputation made; baseline defined as the last non-missing assessment prior to the first dose of double-blind medication.

Reporting Groups

	Description
LACTEOL® 340 mg	LACTEOL® active medication was taken for a 4-week duration (28 days) as three capsules a day: two capsules in the morning and one capsule in the evening.

Measured Values

	LACTEOL® 340 mg
Overall Number of Participants Analyzed	17
Symptom Severity During the Open-Label Treatment Phase Using the IBS Symptom Severity Scale (IBS-SSS) Total Score Mean (Standard Deviation) Unit of measure: units on a scale (from 0 to 500)	
Double-Blind Baseline IBS-SSS score	270.5 (78.2)
IBS-SSS score at end of Week 1 (Day 7)	224.6 (73.06)
IBS-SSS score at end of Week 2 (Day 14)	211.5 (93.58)
IBS-SSS score at end of Week 3 (Day 21)	199.2 (103.68)
IBS-SSS score at end of Week 4 (Day 28)	222.5 (103.14)

7. Secondary Outcome Measure:

Measure Title	Stool Characteristics During the Open-Label Treatment Phase Using the BSFS
Measure Description	The Bristol Stool Form Scale (BSFS) score ranges from 1 to 7 from hard (score of 1) to watery (score of 7). Data are presented as the mean of daily assessments over a week.
Time Frame	Daily assessment

Analysis Population Description

Analysis conducted on the Intent-to-Treat population defined as all subjects randomized to double-blind treatment and who subsequently entered the Open-Label Treatment Phase ; observed case (OC) data with no imputation made; baseline defined as the last non-missing assessment prior to the first dose of double-blind study medication

Reporting Groups

	Description
LACTEOL® 340 mg	LACTEOL® active medication was taken for a 4-week duration (28 days) as three capsules a day: two capsules in the morning and one capsule in the evening.

Measured Values

	LACTEOL® 340 mg
Overall Number of Participants Analyzed	17
Stool Characteristics During the Open-Label Treatment Phase Using the BSFS Mean (Standard Deviation) Unit of measure: units on a scale (from 1 to 7)	
Double-Blind Baseline BSFS Score	5.0 (0.68)
BSFS score during Week 1	4.6 (1.10)
BSFS score during Week 2	4.5 (1.24)
BSFS score during Week 3	4.4 (1.45)
BSFS score during Week 4	4.4 (1.33)

8. Secondary Outcome Measure:

Measure Title	Use of Rescue Medication During the Double-Blind and Open-Label Treatment Phases of the Study
Measure Description	Number of subjects using rescue medication (bisacodyl or loperamide) during each treatment phase of the study
Time Frame	8 weeks

Analysis Population Description

Analysis conducted on the Intent-to-Treat population for both treatment phases

Reporting Groups

	Description
LACTEOL® 340 mg Double-Blind Period	LACTEOL® active medication was taken for a 4-week duration (28 days) as three capsules a day: two capsules in the morning and one capsule in the evening.
PLACEBO Double-Blind Period	Matched LACTEOL® placebo was taken for a 4-week duration (28 days) as three capsules a day: two capsules in the morning and one capsule in the evening.
LACTEOL® 340 mg Open-Label Period	LACTEOL® active medication was taken for a 4-week duration (28 days) as three capsules a day: two capsules in the morning and one capsule in the evening.

Measured Values

	LACTEOL® 340 mg Double-Blind Period	PLACEBO Double-Blind Period	LACTEOL® 340 mg Open-Label Period
Overall Number of Participants Analyzed	13	13	17
Use of Rescue Medication During the Double-Blind and Open-Label Treatment Phases of the Study Measure Type: Number Unit of measure: participants	2	0	0

Reported Adverse Events

Time Frame	From Informed Consent Form signature up to 28 days following the end of double-blind treatment (symptom recurrence observation period) or up to End of Open-Label Treatment Phase Visit (Days 29 to 38) for subjects continuing with open-label treatment
Adverse Event Reporting Description	Adverse events collected during study visits as well as via an interactive voice response system (IVRS) while at home; clinical labs performed at baseline and end of each period; only treatment-emergent adverse events are displayed, ie. events that occurred or worsened in intensity on or after the first dose of study medication in each period.

Reporting Groups

	Description
LACTEOL® 340 mg Double-Blind Period	LACTEOL® active medication was taken for a 4-week duration (28 days) as three capsules a day: two capsules in the morning and one capsule in the evening.
PLACEBO Double-Blind Period	Matched LACTEOL® placebo was taken for a 4-week duration (28 days) as three capsules a day: two capsules in the morning and one capsule in the evening.
LACTEOL® 340 mg Open-Label Period	LACTEOL® active medication was taken for a 4-week duration (28 days) as three capsules a day: two capsules in the morning and one capsule in the evening.

All-Cause Mortality

	LACTEOL® 340 mg Double-Blind Period		PLACEBO Double-Blind Period		LACTEOL® 340 mg Open-Label Period	
	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events
Total All-Cause Mortality	/		/		/	

Serious Adverse Events

	LACTEOL® 340 mg Double-Blind Period		PLACEBO Double-Blind Period		LACTEOL® 340 mg Open-Label Period	
	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events
Total	0/13 (0%)		0/13 (0%)		0/17 (0%)	

Other Adverse Events

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

	LACTEOL® 340 mg Double-Blind Period		PLACEBO Double-Blind Period		LACTEOL® 340 mg Open-Label Period	
	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events
Total	2/13 (15.38%)		2/13 (15.38%)		2/17 (11.76%)	
Gastrointestinal disorders						
Toothache [A] *	0/13 (0%)	0	0/13 (0%)	0	1/17 (5.88%)	1
Infections and infestations						
Gastrointestinal infection [A] *	1/13 (7.69%)	1	0/13 (0%)	0	0/17 (0%)	0
Influenza [A] *	0/13 (0%)	0	1/13 (7.69%)	1	0/17 (0%)	0
Lung infection [A] *	0/13 (0%)	0	1/13 (7.69%)	1	0/17 (0%)	0
Pharyngitis [A] *	0/13 (0%)	0	0/13 (0%)	0	1/17 (5.88%)	1
Sinusitis [A] *	0/13 (0%)	0	1/13 (7.69%)	1	0/17 (0%)	0
Nervous system disorders						
Headache [A] *	1/13 (7.69%)	1	0/13 (0%)	0	0/17 (0%)	0

	LACTEOL® 340 mg Double-Blind Period		PLACEBO Double-Blind Period		LACTEOL® 340 mg Open-Label Period	
	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events
Skin and subcutaneous tissue disorders						
Erythema [A] *	0/13 (0%)	0	0/13 (0%)	0	1/17 (5.88%)	1

* Indicates events were collected by non-systematic methods.

A Term from vocabulary, MedDRA 13.0

Limitations and Caveats

Because of early termination of this trial, the number of subjects analyzed was too small to perform statistical analyses and draw conclusions relative to the efficacy and safety of LACTEOL®.

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.

Restrictions vary in accordance with each agreement with the individual investigators. Sponsor will allow publication after a multi-center publication has been published or after an agreed period of time if no such multi-center publication is submitted for publication. Sponsor can ask that Sponsor’s confidential information be removed from any publication and can defer publication for a period of time to allow for Sponsor to obtain patent or other intellectual property right protection.

Results Point of Contact:

Name/Official Title: Robert Winkler MD, VP, Clinical Development and Operations
Organization: Aptalis Pharma US, Inc.
Phone: (908) 429-4479 Ext: 4175
Email: rwinkler@aptalispharma.com