ClinicalTrials.gov Protocol and Results Registration System (PRS) Receipt
Release Date: 03/15/2012

Grantor: CDER IND/IDE Number: 103308 Serial Number:

A Study With Pentasa in Patients With Active Crohn's Disease (PEACE)

This study has been terminated.
(Terminated due to poor recruitment)

Sponsor:	Ferring Pharmaceuticals
Collaborators:	
Information provided by (Responsible Party):	Ferring Pharmaceuticals
ClinicalTrials.gov Identifier:	NCT00862121

Purpose

The purpose of this trial is to demonstrate that Pentasa administered as a 2 g morning dose and a 4 g evening dose is efficacious in active mild to moderate CD.

Condition	Intervention	Phase
Crohn´s Disease	Drug: Pentasa Drug: Placebo	Phase 3

Study Type: Interventional
Study Design: Treatment, Parallel Assignment, Double Blind (Subject, Investigator), Randomized, Efficacy Study
Official Title: PENTASA in Active Crohn's Disease: A 10-week, Double-blind, Multi-centre Trial Comparing PENTASA Sachet 6 g/Day (Mesalazine, Mesalamine) With Placebo.

Further study details as provided by Ferring Pharmaceuticals:

Primary Outcome Measure:

- Percentage of Crohn's Disease Activity Index (CDAI) Responders at Week 10. [Time Frame: At Week 10, end of treatment] [Designated as safety issue: No]

The Crohn's Disease Activity Index (CDAI) is a composite score to quantify symptoms of Crohn's disease. It has a range of 0-600; higher scores are worse. A responder is defined as a participant who achieved a reduction in the CDAI score to <150 or a decrease in CDAI score of at least 70.

Secondary Outcome Measures:

- Relative Change From Baseline to Week 10 in Fecal Calprotectin [Time Frame: At Week 10, end of treatment] [Designated as safety issue: No]
  Fecal calprotectin is an inflammatory marker for the gastrointestinal tract. Higher values indicate more serious inflammation.
- Relative Change From Baseline to Each Visit in Serum C-reactive Protein (CRP) [Time Frame: Within the 10 week treatment period] [Designated as safety issue: No]
  Serum CRP is a laboratory measure of acute inflammation. Higher values are worse.
- Relative Change From Baseline to Each Visit in Inflammatory Bowel Disease Questionnaire (IBDQ) Score [Time Frame: Within the 10 week treatment period] [Designated as safety issue: No]
  The IBDQ is a measure of the impact of inflammatory bowel disease (IBD) on health-related quality-of-life (HRQL; mood, social activities, daily life, and IBD-related health worries). Higher scores are better; Total IBDQ score can range from 32 (very poor HRQL) to 224 (perfect HRQL).
- Relative Change From Baseline to Each Visit in Work Productivity & Activity Impairment Questionnaire (WPAI_CD) Score Item 5 (Work Productivity) [Time Frame: Within the 10 week treatment period] [Designated as safety issue: No]
  The WPAI_CD Item 5 measures the impact of Crohn's disease on work productivity (while working). The score is recorded by the patient on a visual analog scale, from 0 to 10. Lower scores are better, while higher scores indicate greater negative effect on work productivity.
- Relative Change From Baseline to Week 10 in Estimated Creatinine Clearance [Time Frame: At Week 10, end of treatment] [Designated as safety issue: Yes]
  A lower creatinine clearance indicates worsening of renal function. Creatinine clearance was estimated from serum creatinine levels, using the Cockcroft-Gault formula.

Enrollment: 20
Study Start Date: April 2009
Primary Completion Date: October 2010
Study Completion Date: October 2010

Arms	Assigned Interventions
Experimental: Mesalazine Mesalazine (Mesalamine) 2 g sachet; 6 g daily	Drug: Pentasa 6 g/day orally, 2 g in the morning and 4 g in the evening
Placebo Comparator: Placebo Placebo to Mesalazine (Mesalamine) 2 g sachet; 6 g daily	Drug: Placebo 6 g/day orally, 2 g in the morning and 4 g in the evening

Eligibility

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

Criteria

Inclusion Criteria (main):

- Age: at least 18 years
- CD symptoms/onset of disease: ≥ 3 months prior to Visit 1
- Ileal, ileo-colonic or colonic non-stricturing/non-penetrating disease
- A confirmed location of CD (by MRI, X-ray (small bowel and/or colon), and/or endoscopy)
- A Harvey-Bradshaw score between 5 and 12
- Males and non-pregnant, non-nursing women
- Mild to moderate active CD, defined by a CDAI score between 180 and 350
- Active inflammatory disease (C-Reactive Protein (CRP) level above or equal to 5 mg/L), or a biopsy verified inflammation, or fecal calprotectin level above or equal to 50 µg/g)
- Estimated creatinine clearance should be above 75 ml/min

Exclusion Criteria (main):

- Any significant disease or disorder which, in the opinion of the Investigator, may either put the patient at risk because of participation in the trial, or may influence the results of the trial or the patient's ability to participate in the trial
- CD located to the upper gastrointestinal tract and/or jejunal part of the small intestine, and/or to colon below the left colon flexure and/or isolated proctitis and/or anal disease
- Prior treatment resistance to Pentasa (mesalazine)
- Chronic, dominant arthralgia or rheumatoid arthritis
- Palpable abdominal mass
- Biologics (eg anti-TNF-α) must not be used during the trial or 6 months before Visit 1
- Continuous usage of systemic steroids (excluding budesonide) for 3 months or more within the past year
- Positive pregnancy test

Contacts and Locations

Locations

United States, California
Gold Clinical Research
Beverly Hills, California, United States
North County Gastroenterology
Oceanside, California, United States
San Diego Clinical Trials
San Diego, California, United States
United States, Colorado
Rocky Mountain Gastroenterology Associates
Denver, Colorado, United States
United States, Florida
Clinical Research of West Florida
Clearwater, Florida, United States
Southeastern Integrated Medical, PL dba Florida Medical Research, Suite 17
Gainesville, Florida, United States
United States, Georgia
Atlanta Gastroenterology Specialists
John's Creek, Georgia, United States

United States, Iowa
Gastrointestinal Clinic of Quad Cities
Davenport, Iowa, United States
United States, Kansas
Wichita Clinic PA
Wichita, Kansas, United States
United States, Montana
Center for Digestive and Liver Disease, Inc
Mexico, Montana, United States
United States, New Jersey
CRI Worldwide
Mt. Laurel, New Jersey, United States
United States, New York
Synergy First Medical
Brooklyn, New York, United States
Long Island Clinical Research Associates, LLP
Great Neck, New York, United States
United States, North Carolina
Wake Research Associates
Raleigh, North Carolina, United States
United States, Ohio
Consultants for Clinical Research Inc.
Cincinnati, Ohio, United States
United States, Oklahoma
York Clinical Consulting - Oklahoma
Oklahoma City, Oklahoma, United States
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Tulsa, Oklahoma, United States
United States, South Carolina
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United States, Texas
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Houston, Texas, United States
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Brasschaat, Belgium
AZ Sint Elisabeth

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CHC Saint Joseph
Liège, Belgium
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Aalborg Sygehus
Aalborg, Denmark
Herlev University Hospital
Copenhagen, Denmark
Med Dep F Gentofte Hospital
Hellerup, Denmark
Hvidovre Hospital
Hvidovre, Denmark
Amager Hospital
Kobenhavn S., Denmark
Køge Hospital
Koge, Denmark
Regionshospitalet Randers
Randers, Denmark
Regionshospitalet Viborg
Viborg, Denmark
France
Investigational Site
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Guadalajara, Spain
Hospital Ramon y Cajal
Madrid, Spain
Fundación Hospital Alcorcón
Madrid, Spain
Hospital General Universitario Gregorio Marañón
Madrid, Spain
Corporació Sanitària del Parc Taulí
Sabadell, Spain
Hospital Clinico Zaragoza
Zaragoza, Spain
Sweden
Medicinkliniken, SU/Östra sjukhuset
Göteborg, Sweden
Lunds Lasaret
Lund, Sweden
UMAS
Malmö, Sweden
Kärnsjukhuset Skövde
Skövde, Sweden
Sophiahemmet
Stockholm, Sweden
Medicinmottagningen, Södersjukhuset
Stockholm, Sweden
Karolinska University Hospital
Stockholm, Sweden
Varberg Hospital
Varberg, Sweden
United Kingdom
Addenbrookes Hospital

Cambridge, United Kingdom
St Thomas' Hospital
London, United Kingdom
Chelsea and Westminster Hospital
London, United Kingdom
Royal Victoria Infirmary
Newcastle, United Kingdom
Royal Gwent Hospital
Newport, United Kingdom
John Radcliffe Hospital
Oxford, United Kingdom
Royal Hampshire County Hospital
Winchester, United Kingdom

Investigators

Study Director:	Clinical Development Support	Ferring Pharmaceuticals

More Information

Responsible Party:	Ferring Pharmaceuticals
Study ID Numbers:	FE999907 CS05 EudraCT no: 2008-002100-26
Health Authority:	Belgium: Federal Agency for Medicinal Products and Health Products Denmark: Danish Medicines Agency France: Afssaps - Agence française de sécurité sanitaire des produits de santé (Saint-Denis) Germany: Federal Institute for Drugs and Medical Devices Spain: Spanish Agency of Medicines Sweden: Medical Products Agency United Kingdom: Medicines and Healthcare Products Regulatory Agency United States: Food and Drug Administration

Study Results

Participant Flow

Reporting Groups

	Description
Mesalazine	Mesalazine (Mesalamine) 2 g sachet; 6 g daily

	Description
Placebo	Placebo to Mesalazine (Mesalamine) 2 g sachet; 6 g daily

Overall Study

	Mesalazine	Placebo
Started	8	12 [1]
Full Analysis Set (FAS)	7 [2]	11 [3]
Safety Analysis Set	8 [4]	11
Completed	7	4
Not Completed	1	8
Adverse Event	1	2
Lack of Efficacy	0	3
Protocol Violation	0	1
Exclusion criterion violation	0	1
Incorrect randomisation	0	1

[1] Randomised, intent-to-treat (ITT)
[2] One participant had no evaluable post-baseline CDAI score.
[3] One participant randomised in error (no IMP taken).
[4] The participant with no evaluable post-baseline CDAI score was included in the Safety Analysis Set.

Baseline Characteristics

Reporting Groups

	Description
Mesalazine	Mesalazine (Mesalamine) 2 g sachet; 6 g daily
Placebo	Placebo to Mesalazine (Mesalamine) 2 g sachet; 6 g daily

Baseline Measures

	Mesalazine	Placebo	Total
Number of Participants	7	11	18
Age, Categorical			

	Mesalazine	Placebo	Total
[units: participants]			
<=18 years	0	0	0
Between 18 and 65 years	7	11	18
>=65 years	0	0	0
Age, Continuous [units: years] Mean (Standard Deviation)	37.6 (13.2)	37.5 (12.6)	37.5 (12.4)
Gender, Male/Female [units: participants]			
Female	6	8	14
Male	1	3	4
Region of Enrollment [units: participants]			
France	0	1	1
United States	3	6	9
Belgium	0	1	1
Denmark	0	1	1
Germany	4	2	6
United Kingdom	0	1	1
Sweden	1	0	1

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Percentage of Crohn's Disease Activity Index (CDAI) Responders at Week 10.
Measure Description	The Crohn's Disease Activity Index (CDAI) is a composite score to quantify symptoms of Crohn's disease. It has a range of 0-600; higher scores are worse. A responder is defined as a participant who achieved a reduction in the CDAI score to <150 or a decrease in CDAI score of at least 70.
Time Frame	At Week 10, end of treatment
Safety Issue?	No

Analysis Population Description

The percentage of CDAI responders at Week 10 was analysed for the FAS (treated participants with post-baseline CDAI), Last Observation Carried Forward (LOCF).

Reporting Groups

	Description
Mesalazine	Mesalazine (Mesalamine) 2 g sachet; 6 g daily
Placebo	Placebo to Mesalazine (Mesalamine) 2 g sachet; 6 g daily

Measured Values

	Mesalazine	Placebo
Number of Participants Analyzed	7	11
Percentage of Crohn's Disease Activity Index (CDAI) Responders at Week 10. [units: percentage of participants]	43	55

Statistical Analysis 1 for Percentage of Crohn's Disease Activity Index (CDAI) Responders at Week 10.

Statistical Analysis Overview	Comparison Groups	Mesalazine, Placebo
	Comments	The odds ratio (OR) for Baseline CDAI measures the effect of an increase of one unit on the outcome. The OR [95% CI] and p-value (likelihood-based) are for Pentasa versus placebo estimated in a logistic regression analysis including TREATMENT and CDAI at baseline as covariates. Power to demonstrate superiority of PENTASA Sachet 6 g/day over placebo in the primary efficacy analysis was 90% for a planned sample size of 255 participants per treatment arm (assuming 10% nonassessable participants).
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.231
	Comments	[Not specified]
	Method	Regression, Logistic
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Odds Ratio (OR)
	Estimated Value	0.212

	Confidence Interval	(2-Sided) 95% 0.017 to 2.683
	Estimation Comments	[Not specified]

2. Secondary Outcome Measure:

Measure Title	Relative Change From Baseline to Week 10 in Fecal Calprotectin
Measure Description	Fecal calprotectin is an inflammatory marker for the gastrointestinal tract. Higher values indicate more serious inflammation.
Time Frame	At Week 10, end of treatment
Safety Issue?	No

Analysis Population Description

Full Analysis Set (FAS), observed cases (OC), descriptive statistics only.

Reporting Groups

	Description
Mesalazine	Mesalazine (Mesalamine) 2 g sachet; 6 g daily
Placebo	Placebo to Mesalazine (Mesalamine) 2 g sachet; 6 g daily

Measured Values

	Mesalazine	Placebo
Number of Participants Analyzed	7	11
Relative Change From Baseline to Week 10 in Fecal Calprotectin [units: microgram/gram faeces] Mean (Standard Deviation)		
Baseline	244.5 (212.09)	362 (311.57)
Week 10	181.57 (216.15)	1180.17 (2295.34)

3. Secondary Outcome Measure:

Measure Title	Relative Change From Baseline to Each Visit in Serum C-reactive Protein (CRP)
Measure Description	Serum CRP is a laboratory measure of acute inflammation. Higher values are worse.

Time Frame	Within the 10 week treatment period
Safety Issue?	No

Analysis Population Description

Full Analysis Set (OC). Descriptive statistics only.

Reporting Groups

	Description
Mesalazine	Mesalazine (Mesalamine) 2 g sachet; 6 g daily
Placebo	Placebo to Mesalazine (Mesalamine) 2 g sachet; 6 g daily

Measured Values

	Mesalazine	Placebo
Number of Participants Analyzed	7	11
Relative Change From Baseline to Each Visit in Serum C-reactive Protein (CRP) [units: mg/L] Mean (Standard Deviation)		
Baseline	8.23 (5.71)	10.25 (6.96)
Week 10	7.76 (6)	9.48 (8.41)

4. Secondary Outcome Measure:

Measure Title	Relative Change From Baseline to Each Visit in Inflammatory Bowel Disease Questionnaire (IBDQ) Score
Measure Description	The IBDQ is a measure of the impact of inflammatory bowel disease (IBD) on health-related quality-of-life (HRQL; mood, social activities, daily life, and IBD-related health worries). Higher scores are better; Total IBDQ score can range from 32 (very poor HRQL) to 224 (perfect HRQL).
Time Frame	Within the 10 week treatment period
Safety Issue?	No

Analysis Population Description

Full Analysis Set (OC). Descriptive statistics only.

Reporting Groups

	Description
Mesalazine	Mesalazine (Mesalamine) 2 g sachet; 6 g daily
Placebo	Placebo to Mesalazine (Mesalamine) 2 g sachet; 6 g daily

Measured Values

	Mesalazine	Placebo
Number of Participants Analyzed	7	11
Relative Change From Baseline to Each Visit in Inflammatory Bowel Disease Questionnaire (IBDQ) Score [units: IBDQ score] Mean (Standard Deviation)		
Baseline	138.57 (32.07)	130.27 (29.32)
Week 10	164 (24.99)	121.88 (39.96)

5. Secondary Outcome Measure:

Measure Title	Relative Change From Baseline to Each Visit in Work Productivity & Activity Impairment Questionnaire (WPAI_CD) Score Item 5 (Work Productivity)
Measure Description	The WPAI_CD Item 5 measures the impact of Crohn's disease on work productivity (while working). The score is recorded by the patient on a visual analog scale, from 0 to 10. Lower scores are better, while higher scores indicate greater negative effect on work productivity.
Time Frame	Within the 10 week treatment period
Safety Issue?	No

Analysis Population Description

Full Analysis Set (OC). Descriptive statistics only.

Reporting Groups

	Description
Mesalazine	Mesalazine (Mesalamine) 2 g sachet; 6 g daily
Placebo	Placebo to Mesalazine (Mesalamine) 2 g sachet; 6 g daily

Measured Values

	Mesalazine	Placebo
Number of Participants Analyzed	7	11
Relative Change From Baseline to Each Visit in Work Productivity & Activity Impairment Questionnaire (WPAI_CD) Score Item 5 (Work Productivity) [units: WPAI_CD Item 5 score] Mean (Standard Deviation)		
Baseline	4.17 (3.25)	5 (2.33)
Week 10	1.83 (1.47)	4.4 (2.07)

6. Secondary Outcome Measure:

Measure Title	Relative Change From Baseline to Week 10 in Estimated Creatinine Clearance
Measure Description	A lower creatinine clearance indicates worsening of renal function. Creatinine clearance was estimated from serum creatinine levels, using the Cockcroft-Gault formula.
Time Frame	At Week 10, end of treatment
Safety Issue?	Yes

Analysis Population Description

Safety Analysis Set (OC). Descriptive statistics only.

Reporting Groups

	Description
Mesalazine	Mesalazine (Mesalamine) 2 g sachet; 6 g daily
Placebo	Placebo to Mesalazine (Mesalamine) 2 g sachet; 6 g daily

Measured Values

	Mesalazine	Placebo
Number of Participants Analyzed	8	11
Relative Change From Baseline to Week 10 in Estimated Creatinine Clearance [units: mL/min] Mean (Standard Deviation)		
Baseline	122.63 (26.91)	102.55 (24.13)

	Mesalazine	Placebo
Week 10	124 (32.14)	105.11 (31.09)

Reported Adverse Events

Time Frame	[Not specified]
Additional Description	[Not specified]

Reporting Groups

	Description
Mesalazine	Mesalazine (Mesalamine) 2 g sachet; 6 g daily
Placebo	Placebo to Mesalazine (Mesalamine) 2 g sachet; 6 g daily

Serious Adverse Events

	Mesalazine		Placebo	
	Affected/At Risk (%)	# Events	Affected/At Risk (%)	# Events
Total	0/8 (0%)		0/11 (0%)	

Other Adverse Events

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

	Mesalazine		Placebo	
	Affected/At Risk (%)	# Events	Affected/At Risk (%)	# Events
Total	5/8 (62.5%)		7/11 (63.64%)	
Blood and lymphatic system disorders				
Lymphadenopathy [A]	1/8 (12.5%)	1	0/11 (0%)	0
Gastrointestinal disorders				
Abdominal pain [B]	0/8 (0%)	0	1/11 (9.09%)	1
Abdominal tenderness [B]	0/8 (0%)	0	1/11 (9.09%)	2

	Mesalazine		Placebo	
	Affected/At Risk (%)	# Events	Affected/At Risk (%)	# Events
Constipation [B]	0/8 (0%)	0	1/11 (9.09%)	1
Diarrhoea [B]	0/8 (0%)	0	1/11 (9.09%)	1
Gastric disorder [B]	0/8 (0%)	0	1/11 (9.09%)	1
Gastrointestinal hypermotility [B]	1/8 (12.5%)	1	0/11 (0%)	0
Haemorrhoidal haemorrhage [B]	1/8 (12.5%)	1	0/11 (0%)	0
Nausea [B]	1/8 (12.5%)	1	1/11 (9.09%)	1
Infections and infestations				
Lower respiratory tract infection [B]	0/8 (0%)	0	1/11 (9.09%)	1
Sinusitis [B]	1/8 (12.5%)	1	0/11 (0%)	0
Urinary tract infection [B]	1/8 (12.5%)	1	1/11 (9.09%)	1
Musculoskeletal and connective tissue disorders				
Bursitis [B]	1/8 (12.5%)	1	0/11 (0%)	0
Nervous system disorders				
Headache [B]	0/8 (0%)	0	1/11 (9.09%)	1
Psychiatric disorders				
Depression [B]	0/8 (0%)	0	1/11 (9.09%)	1
Renal and urinary disorders				
Pollakiuria [B]	1/8 (12.5%)	1	0/11 (0%)	0
Skin and subcutaneous tissue disorders				
Pruritus [B]	0/8 (0%)	0	1/11 (9.09%)	4
Rash [B]	0/8 (0%)	0	1/11 (9.09%)	3

A Term from vocabulary, MedDRA 12.0
B Term from vocabulary, MedDRA (12.0)

Limitations and Caveats

Early termination led to small number of participants (20/510; actual/planned). Only the primary efficacy outcome was subject to formal statistical analysis. No conclusions could be drawn on primary and secondary efficacy analyses.

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.

The only disclosure restriction on the PI is that the sponsor can review the draft manuscript prior to publication and can request delay of publication where any contents are deemed patentable by the sponsor or confidential to the sponsor. Comments will be given within four weeks from receipt of the draft manuscript. Additional time may be required to allow Ferring to seek patent protection of the invention.

Results Point of Contact:

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