ClinicalTrials.gov Protocol and Results Registration System (PRS) Receipt
Release Date: 06/06/2014

Grantor: CDER IND/IDE Number: 66193 Serial Number:

Prevention of Recurrence of Diverticulitis (PREVENT1)

This study has been completed.

Sponsor:	Shire
Collaborators:	
Information provided by (Responsible Party):	Shire
ClinicalTrials.gov Identifier:	NCT00545740

Purpose

The purpose of this study is to determine whether SPD476 is effective in reducing recurrence of diverticulitis.

Condition	Intervention	Phase
Diverticulitis	Drug: SPD476 (1.2g) Drug: SPD476 (2.4 g) Drug: SPD476 (4.8 g) Drug: Placebo	Phase 3

Study Type: Interventional
Study Design: Prevention, Parallel Assignment, Double Blind (Subject, Caregiver, Investigator, Outcomes Assessor), Randomized, Safety/Efficacy Study
Official Title: A Phase III, Randomised, Double-Blind, Dose-Response, Stratified, Placebo-Controlled Study Evaluating the Safety and Efficacy of SPD476 Versus Placebo Over 104 Weeks in the Prevention of Recurrence of Diverticulitis.

Further study details as provided by Shire:

Primary Outcome Measure:

- Percent of Subjects Without Recurrence of Diverticulitis [Time Frame: Up to 104 weeks] [Designated as safety issue: No]

Recurrence of diverticulitis is defined as the presence of each and all of the following 3 items: 1) abdominal pain, 2) a 15% increase in white blood cell count from baseline, 3) bowel wall thickening (>5 mm) and/or fat stranding as evidenced by spiral computerized axial tomography (CT) scan; OR surgical intervention for diverticular disease. Withdrawals are considered as recurrences.

Secondary Outcome Measures:

- Percent of Subjects Who Were CT-Recurrence Free of Diverticulitis [Time Frame: Up to 104 weeks] [Designated as safety issue: No]
  CT-recurrence of diverticulitis is defined as: a positive spiral CT scan for diverticulitis showing, at a minimum, fat stranding with or without bowel wall thickening >5 mm or surgical intervention for diverticular disease. Withdrawals considered as CT-recurrences.
- Number of CT Scans Performed Within 7 Days of Suspected Recurrence of Diverticulitis That Were Positive [Time Frame: Up to 104 weeks] [Designated as safety issue: No]
  A positive CT scan was defined as a CT scan that showed bowel wall thickening (>5 mm) and/or fat stranding as read by the central reader.
- Number of CT Scans Performed Within 7 Days of Suspected Recurrence of Diverticulitis That Were Negative [Time Frame: Up to 104 weeks] [Designated as safety issue: No]
  A negative CT scan was defined as a CT scan that did not show bowel wall thickening (>5 mm) and/or fat stranding as read by the central reader.
- Number of CT Scans Performed More Than 7 Days From Suspected Recurrence of Diverticulitis That Were Positive [Time Frame: Up to 104 weeks] [Designated as safety issue: No]
  A positive CT scan was defined as a CT scan that showed bowel wall thickening (>5 mm) and/or fat stranding as read by the central reader.
- Number of CT Scans Performed More Than 7 Days From Suspected Recurrence of Diverticulitis That Were Negative [Time Frame: Up to 104 weeks] [Designated as safety issue: No]
  A negative CT scan was defined as a CT scan that did not show bowel wall thickening (>5 mm) and/or fat stranding as read by the central reader.
- Percent of Subjects Requiring Surgery for Diverticulitis [Time Frame: Up to 104 weeks] [Designated as safety issue: No]

Enrollment: 590
Study Start Date: November 2007
Primary Completion Date: February 2012
Study Completion Date: March 2012

Arms	Assigned Interventions
Experimental: SPD476 (1.2 g)	Drug: SPD476 (1.2g) 1.2g SPD476 once daily (QD) orally Other Names: Lialda, MMX™ mesalazine
Experimental: SPD476 (2.4 g)	Drug: SPD476 (2.4 g) 2.4g SPD476 QD orally Other Names: Lialda, MMX™ mesalazine
Experimental: SPD476 (4.8 g)	Drug: SPD476 (4.8 g) 4.8g SPD476 QD orally Other Names: Lialda, MMX™ mesalazine
Placebo Comparator: Placebo	Drug: Placebo

Arms	Assigned Interventions
	QD orally

Eligibility

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

Criteria

Inclusion Criteria:

1. Males and females =>18yrs of age.
2. If female of childbearing potential (FOCP), has demonstrated a negative beta HCG (human chorionic gonadotropin) serum pregnancy test, and agrees to comply with any applicable contraceptive requirements of the protocol.
3. An episode of acute diverticulitis that resolved without colonic resection.
4. Confirmation of diverticulosis via endoscopic evaluation of the sigmoid colon with at least three diverticula noted.

Exclusion Criteria:

1. Previous colorectal surgery, including surgical intervention for diverticular disease (with the exception of haemorrhoidectomy, colonic removal of polyps, and appendectomy)
2. Active peptic ulcer disease
3. History of or current presence of inflammatory bowel disease (IBD)
4. Subjects with active irritable bowel syndrome (IBS) requiring ongoing medication
5. Allergy or hypersensitivity to aspirin or related compounds
6. Allergy to radiologic contrast agents
7. Use of another Investigational product within 30 days of Baseline
8. Use of antibiotic therapy within 4 weeks of Baseline
9. Within 14 days of Baseline, use of prebiotic, probiotic or 5-ASA medications, as well as drugs active at the 5HT-receptor or anti-spasmodic agents
10. Use of systemic or rectal steroids within 6 weeks of Baseline. Use of inhaled or nasal steroids is acceptable
11. Use of anti-inflammatory drugs, (NSIADs, COX-2 inhibitors) including aspirin (except for cardiac prophylaxis) and ibuprofen, on a regular and ongoing basis
12. History of alcohol or other substance abuse within the previous year
13. Active or recent history of endometriosis or dysmenorrhoea within 6 months prior to Baseline
14. Females who are lactating

Contacts and Locations

Locations
United States, Arizona
Dedicated Clinical Research
Litchfield Park, Arizona, United States, 85340
United States, Arkansas

Lynn Institute of the Ozarks
Little Rock, Arkansas, United States, 72205
United States, California
Advanced Clinical Research Institute
Anaheim, California, United States, 92108
GW Research
Chula Vista, California, United States, 91910
Monterey Bay GI Research Institute, Inc
Monterey, California, United States, 93940
Rancho Cucamonga C. Trials
Rancho Cucamonga, California, United States, 91730
Clinical Trials Research
Roseville, California, United States, 95661
Medical Associates Research
San Diego, California, United States, 92123
Torrance Clinical Research
Torrance, California, United States, 90505
United States, Colorado
Rocky Mountain Gastroenterology Associates
Thornton, Colorado, United States, 80229
United States, Connecticut
Gastroenterology Associates of Fairfield County
Bridgeport, Connecticut, United States, 06606
Yale Center for Clinical Investigation
New Haven, Connecticut, United States, 06520
United States, Florida
ZASA Clinical Research
Boynton Beach, Florida, United States, 33472
Clinical Research of West Florida, Inc.
Clearwater, Florida, United States, 33765
Borland-Groover Clinic
Jacksonville, Florida, United States, 32256
Compass Research
Orlando, Florida, United States, 32806
Accord Clinic Research, LLC
Port Orange, Florida, United States, 32129
Florida Medical Clinic/Tampa Clinical Trials
Tampa, Florida, United States, 33613
United States, Georgia
Gastroenterology Associates of Central Georgia, LLC
Macon, Georgia, United States, 31201
United States, Indiana
Saint John's Research Institute
Anderson, Indiana, United States, 46016
United States, Iowa

Digestive & Liver Disease Consultants
Clive, Iowa, United States, 50325
United States, Louisiana
New Orleans Research Institute
Metairie, Louisiana, United States, 70006
United States, Maryland
Digestive Disease Associates
Baltimore, Maryland, United States, 21229
Endoscopic Microsurgery Associates, PA
Towson, Maryland, United States, 21204
United States, Michigan
Borgess Research Institute
Kalamazoo, Michigan, United States, 49048
United States, Missouri
Jefferson City Medical Group
Jefferson City, Missouri, United States, 65109
United States, New Jersey
South Jersey Gastroenterology, P.A.
Marlton, New Jersey, United States, 08053
Howard Guss, DO
Ocean, New Jersey, United States, 07712
New Jersey Physicians, LLC
Passaic, New Jersey, United States, 07055
Allied Gastrointestinal Associates, P.A.
Voorhees, New Jersey, United States, 08043
United States, New York
Regional Clinical Research
Endwell, New York, United States, 13760
Long Island Gastrointestinal Research Group
Great Neck, New York, United States, 11023
Long Island Clinical Research Associates
Great Neck, New York, United States, 11021
Research Associates of New York
New York, New York, United States, 10075
United States, North Carolina
Vital Research
Greensboro, North Carolina, United States, 27408
United States, Ohio
Gastroenterology Specialists, Inc
Canton, Ohio, United States, 44718
United States, Tennessee
Memorial Research Center
Chattanooga, Tennessee, United States, 37404
Gastroenterology Associates Clinical Research
Kingsport, Tennessee, United States, 37660

Nashville Medical Research Institute
Nashville, Tennessee, United States, 37205
United States, Texas
Harris Methodist Fort Worth Hospital
Fort Worth, Texas, United States, 76104
Kelsey-Seybold Clinic
Houston, Texas, United States, 77005
Stone Oak Research Foundation
San Antonio, Texas, United States, 78258
Clinical Trials of Texas, Inc.
San Antonio, Texas, United States, 78229
United States, Virginia
Blue Ridge Medical Research
Lynchburg, Virginia, United States, 24502
Digestive and Liver Disease Specialists
Norfolk, Virginia, United States, 23502
United States, Wisconsin
Aurora Advanced Healthcare, Inc. - Clinical Research Center
Milwaukee, Wisconsin, United States, 53209
Argentina
Sanatorio Guemes
Buenos Aires, Argentina, C1180AAX
Hospital Bocalandro
Buenos Aires, Argentina, B1657BHD
Hospital Heroes de Malvinas
Buenos Aires, Argentina, B1722FJN
GEDYT
Buenos Aires, Buenos Aires, Argentina, C1117AAA
CIMEL
Lanus, Buenos Aires, Argentina, B1824KAS
Instituto Gamma
Rosario, Santa Fe, Argentina, S2000DFD
CIBIC S.A.
Santa Fe, Santa Fe, Argentina, S2000BCG
Australia
Royal Adelaide Hospital
Adelaide, Australia, 5000
Royal Prince Albert Hospital
Camperdown, Australia, 2050
Frankston Private
Frankston, Australia, 3199
Bayside Gastroenterology
Frankston, Australia, VIC 3199
Fremantle Hospital
Fremantle, Australia, 6160

Australia, Australian Capital Territory
- The Canberra Hospital
  - Garran, Australian Capital Territory, Australia, 2605

Australia, Victoria
- Ballarat Base Hospital
  - Ballarat, Victoria, Australia, 3350
- St Vincent's Hospital (Melb) LTD
  - Melbourne, Victoria, Australia, 3065

Colombia
- UGASEND S.A
  - Barranquilla, Colombia
- Fundacion Clinica Abood Shaio
  - Bogota, Colombia
- FOQUS, Centro de Investigacion Clinica
  - Bogota, Colombia
- Clinica Colsinatas SA
  - Bogota, Colombia
- Hospital Universitario San Ignacio
  - Bogota, Colombia
- Clinica Las Americas
  - Medellin, Colombia

France
- Cabinet du Dr Olivier Delette
  - Lille, France, 59000
- Dr Michel Regensberg
  - Paris, France, 75017
- CHU de Strasbourg
  - Strasbourg, Alsace, France, 67200
- Hepato Gastro Enterology
  - Nantes, Brittany, France, 44033
- Hopital Charles Nicolle
  - Rouen, Normandy, France, 76031
- Hopital Beaujon
  - Clichy, Paris, France, 92118
- Cabinet de Gastro-enterologie du Dr Alain Thevenin
  - Saint Quentin, Picardie, France, 02100
- Hopital l'Archet
  - Nice, Provence-Alpes-Côte d'Azur, France, 06200
- Clinique Bouchard
  - Marseille, Provence-Alpes-Côte-d'Azur, France, 13000
- CHU de Grenoble
  - Grenoble, Rhone-Alpes, France, 38043

India
- Brahmin Mitra Mandal Society
  - Gujarat, India, 380006

Institute of Postgraduate Medical Education and Research
Kolkatta, India, 700020
Ruby Hall Clinic
Pune, India, 411 001
Krishna Institute of Medical Sciences
Secunderabad, India, 500 003
Baby Memorial Hospital
Calicut, Kerala, India, 673004
Lakeshore Hospital & Research Centre Ltd
Cochin, Kerala, India, 682304
Sree Gokulam Medical College and Research Foundation
Venjaramoodu, Kerala, India, 695607
Dayanand Medical College and Hospital
Ludhiana, Punjab, India, 141001
S R Kalla Memorial Hospital
Jaipur, Rajasthan, India
Aceer
Chennai, Tamil Nadu, India, 600020

Israel

Emek Medical Center
Afula, Israel, 18101
Barzilai Medical Centre
Ashkelon, Israel, 78278
Soroka Medical Center
Beer Sheva, Israel, 84101
Bnai Zion Medical Center
Haifa, Israel, 31048
Rambam Medical Center
Haifa, Israel, 63106
Hadassah Ein-Karem Medical Center
Jerusalem, Israel
Meir Medical Centre
Kfar-Saba, Israel
Rabin Medical Center
Petah-Tikva, Israel, 49100
Kaplan Medical Center
Rechovot, Israel
The Tel Aviv Sourasky Medical Center
Tel Aviv, Israel, 64239
The Chaim Sheba Medical Center
Tel Hashomer, Israel, 52621
Assaf Harofeh Medical Center
Zerifin, Israel, 70300

New Zealand

Auckland City Hospital

Auckland, New Zealand
CURT Medical Trials Trust Board
Christchurch, New Zealand
Tauranga Hospital
Tauranga, New Zealand
Shakespeare Specialist Group
Takapuna, Auckland, New Zealand
Dunedin Hospital
Dunedin, Dunedin, New Zealand
Waikato Hospital
Hamilton, Hamilton, New Zealand, 3240
Spain
Hospital Valle de Hebron
Barcelona, Spain, 08035
Hospital Universitario de Bellvitge
Barcelona, Spain, 08907
Hospital Son Dureta
Palma de Mallorca, Spain, 07014
Hospital de Donostia
San Sebastian, Spain, 20014
Hospital General Universitario de Valencia
Valencia, Spain, 46014
Sweden
University Hospital/Eastern Hospital
Goteborg, Sweden, 41685
University Hospital Linköping
Linköping, Sweden, 58185
Karolinska University Hospital
Stockholm, Sweden, 17176
Danderyd Hospital
Stockholm, Sweden, 18288
VO Internmedicin
Stockholm, Sweden, 11883
Kirurgkliniken
Uppsala, Sweden
United Kingdom
King's College Hospital
London, United Kingdom, SE5 9RS
Imperial College London
London, United Kingdom, W12 0NN
Norfolk/Norwich University Hospital
Norwich, East Anglia, United Kingdom, NR4 7UY
St Mark's Hospital
Harrow, London, United Kingdom, HA1 3UJ
Chelsea & Westminster Hospital

London, London, United Kingdom, SW10 9NH

Investigators
Principal Investigator: Prof. Michael Kamm St. Vincent's Hospital

More Information

Responsible Party: Shire
Study ID Numbers: SPD476-313
2007-004895-37 [EudraCT Number]
Health Authority: United States: Food and Drug Administration

---

Study Results

Participant Flow

Reporting Groups

	Description
SPD476 (1.2 g)	1.2 g administered orally once daily
SPD476 (2.4 g)	2.4 g administered orally once daily
SPD476 (4.8 g)	4.8 g administered orally once daily
Placebo	Placebo administered orally once daily

Overall Study

	SPD476 (1.2 g)	SPD476 (2.4 g)	SPD476 (4.8 g)	Placebo
Started	145	145	151	149
Completed	70	62	55	78
Not Completed	75	83	96	71
Lack of Efficacy	34	35	47	36
Withdrawal by Subject	17	15	16	18
Adverse Event	10	18	19	9
Lost to Follow-up	7	5	5	6
Protocol Violation	1	3	1	0
Non-compliance	0	2	1	0

	SPD476 (1.2 g)	SPD476 (2.4 g)	SPD476 (4.8 g)	Placebo
Moved	2	0	1	0
Diverticulitis attack	0	0	1	1
Suspected Diverticulitis Recurrence	1	1	1	1
Site closure	1	0	0	0
Missed visit	1	0	0	0
Physician Decision	0	0	3	0
Accepted only monthly telephone calls	1	0	0	0
Sponsor decision	0	1	0	0
Lack of time	0	1	0	0
Non-adherence to visits	0	1	0	0
Patient difficulties	0	1	0	0
Husband against study	0	0	1	0

Baseline Characteristics

Reporting Groups

	Description
SPD476 (1.2 g)	1.2 g administered orally once daily
SPD476 (2.4 g)	2.4 g administered orally once daily
SPD476 (4.8 g)	4.8 g administered orally once daily
Placebo	Placebo administered orally once daily

Baseline Measures

	SPD476 (1.2 g)	SPD476 (2.4 g)	SPD476 (4.8 g)	Placebo	Total
Number of Participants	145	145	151	149	590
Age, Continuous [1] [units: years] Mean (Standard Deviation)	55.1 (11.11)	54.5 (11.96)	54.5 (11.93)	57.1 (10.42)	55.3 (11.39)
Age, Customized [1] [units: participants]					

	SPD476 (1.2 g)	SPD476 (2.4 g)	SPD476 (4.8 g)	Placebo	Total
18 to <35 years	3	11	8	3	25
35 to <45 years	20	17	26	14	77
45 to <55 years	49	39	36	37	161
55 to <65 years	43	46	51	62	202
>= 65 years	28	30	29	31	118
Gender, Male/Female [1] [units: participants]					
Female	64	69	71	71	275
Male	79	74	79	76	308
Region of Enrollment [2] [units: participants]					
Argentina	5	3	4	3	15
Australia	3	5	6	5	19
Colombia	19	18	18	19	74
France	5	6	6	6	23
India	4	2	3	4	13
Israel	24	24	23	24	95
New Zealand	3	4	4	4	15
Spain	1	1	4	2	8
Sweden	9	9	11	9	38
United Kingdom	3	3	3	4	13
United States	69	70	69	69	277

[1] The Safety Population was used for this baseline measure. The Safety Population consists of subjects who were randomized and took at least 1 dose of investigational product. Out of the 590 subjects randomized, 7 were never dosed with investigational product. Therefore, 583 subjects are in the Safety Population.

[2] This baseline measure consists of all randomized subjects (n = 590).

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Percent of Subjects Without Recurrence of Diverticulitis
Measure Description	Recurrence of diverticulitis is defined as the presence of each and all of the following 3 items: 1) abdominal pain, 2) a 15% increase in white blood cell count from baseline, 3) bowel wall thickening (>5 mm) and/or fat stranding as evidenced by spiral computerized axial tomography (CT) scan; OR surgical intervention for diverticular disease. Withdrawals are considered as recurrences.
Time Frame	Up to 104 weeks
Safety Issue?	No

Analysis Population Description

Full Analysis Set (FAS) consists of all subjects who were randomized and took at least 1 dose of investigational product.

Reporting Groups

	Description
SPD476 (1.2 g)	1.2 g administered orally once daily
SPD476 (2.4 g)	2.4 g administered orally once daily
SPD476 (4.8 g)	4.8 g administered orally once daily
Placebo	Placebo administered orally once daily

Measured Values

	SPD476 (1.2 g)	SPD476 (2.4 g)	SPD476 (4.8 g)	Placebo
Number of Participants Analyzed	143	143	150	147
Percent of Subjects Without Recurrence of Diverticulitis [units: percentage of subjects]	62.2	62.9	52.7	64.6

Statistical Analysis 1 for Percent of Subjects Without Recurrence of Diverticulitis

Statistical Analysis Overview	Comparison Groups	SPD476 (4.8 g), Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.047
	Comments	[Not specified]
	Method	Cochran-Mantel-Haenszel
	Comments	[Not specified]

Statistical Analysis 2 for Percent of Subjects Without Recurrence of Diverticulitis

Statistical Analysis Overview	Comparison Groups	SPD476 (2.4 g), Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.741
	Comments	[Not specified]
	Method	Cochran-Mantel-Haenszel
	Comments	[Not specified]

Statistical Analysis 3 for Percent of Subjects Without Recurrence of Diverticulitis

Statistical Analysis Overview	Comparison Groups	SPD476 (1.2 g), Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.780
	Comments	[Not specified]
	Method	Cochran-Mantel-Haenszel
	Comments	[Not specified]

2. Secondary Outcome Measure:

Measure Title	Percent of Subjects Who Were CT-Recurrence Free of Diverticulitis

Measure Description	CT-recurrence of diverticulitis is defined as: a positive spiral CT scan for diverticulitis showing, at a minimum, fat stranding with or without bowel wall thickening >5 mm or surgical intervention for diverticular disease. Withdrawals considered as CT-recurrences.
Time Frame	Up to 104 weeks
Safety Issue?	No

Analysis Population Description

Full Analysis Set (FAS) consists of all subjects who were randomized and took at least 1 dose of investigational product.

Reporting Groups

	Description
SPD476 (1.2 g)	1.2 g administered orally once daily
SPD476 (2.4 g)	2.4 g administered orally once daily
SPD476 (4.8 g)	4.8 g administered orally once daily
Placebo	Placebo administered orally once daily

Measured Values

	SPD476 (1.2 g)	SPD476 (2.4 g)	SPD476 (4.8 g)	Placebo
Number of Participants Analyzed	143	143	150	147
Percent of Subjects Who Were CT-Recurrence Free of Diverticulitis [units: percentage of subjects]	61.5	62.2	52.7	63.9

Statistical Analysis 1 for Percent of Subjects Who Were CT-Recurrence Free of Diverticulitis

Statistical Analysis Overview	Comparison Groups	SPD476 (4.8 g), Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.063
	Comments	[Not specified]
	Method	Cochran-Mantel-Haenszel
	Comments	[Not specified]

Statistical Analysis 2 for Percent of Subjects Who Were CT-Recurrence Free of Diverticulitis

Statistical Analysis Overview	Comparison Groups	SPD476 (2.4 g), Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.736
	Comments	[Not specified]
	Method	Cochran-Mantel-Haenszel
	Comments	[Not specified]

Statistical Analysis 3 for Percent of Subjects Who Were CT-Recurrence Free of Diverticulitis

Statistical Analysis Overview	Comparison Groups	SPD476 (1.2 g), Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.780
	Comments	[Not specified]
	Method	Cochran-Mantel-Haenszel
	Comments	[Not specified]

3. Secondary Outcome Measure:

Measure Title	Number of CT Scans Performed Within 7 Days of Suspected Recurrence of Diverticulitis That Were Positive
Measure Description	A positive CT scan was defined as a CT scan that showed bowel wall thickening (>5 mm) and/or fat stranding as read by the central reader.
Time Frame	Up to 104 weeks
Safety Issue?	No

Analysis Population Description

Suspected Recurrence of Diverticulitis consists of subjects in the Full Analysis Set who had a CT scan performed. Since subjects may have had more than one suspected recurrence, counts are of the number of CT scans, not the number of subjects.

Reporting Groups

	Description
SPD476 (1.2 g)	1.2 g administered orally once daily
SPD476 (2.4 g)	2.4 g administered orally once daily
SPD476 (4.8 g)	4.8 g administered orally once daily
Placebo	Placebo administered orally once daily

Measured Values

	SPD476 (1.2 g)	SPD476 (2.4 g)	SPD476 (4.8 g)	Placebo
Number of Participants Analyzed	52	49	55	46
Number of CT Scans Performed Within 7 Days of Suspected Recurrence of Diverticulitis That Were Positive [units: Number of CT scans]				
Positive	37	39	55	38
Presence of abdominal pain	30	39	54	37
15% increase in WBC from baseline	17	24	28	24
Presence in abdominal pain + 15% increase in WBC	17	24	28	23

4. Secondary Outcome Measure:

Measure Title	Number of CT Scans Performed Within 7 Days of Suspected Recurrence of Diverticulitis That Were Negative
Measure Description	A negative CT scan was defined as a CT scan that did not show bowel wall thickening (>5 mm) and/or fat stranding as read by the central reader.
Time Frame	Up to 104 weeks
Safety Issue?	No

Analysis Population Description

Suspected Recurrence of Diverticulitis consists of subjects in the Full Analysis Set who had a CT scan performed. Since subjects may have had more than one suspected recurrence, counts are of the number of CT scans, not the number of subjects.

Reporting Groups

	Description
SPD476 (1.2 g)	1.2 g administered orally once daily

	Description
SPD476 (2.4 g)	2.4 g administered orally once daily
SPD476 (4.8 g)	4.8 g administered orally once daily
Placebo	Placebo administered orally once daily

Measured Values

	SPD476 (1.2 g)	SPD476 (2.4 g)	SPD476 (4.8 g)	Placebo
Number of Participants Analyzed	52	49	55	46
Number of CT Scans Performed Within 7 Days of Suspected Recurrence of Diverticulitis That Were Negative [units: Number of CT scans]				
Negative	19	10	5	10
Presence of abdominal pain	19	8	5	7
15% increase in WBC from baseline	5	2	2	1
Presence in abdominal pain + 15% increase in WBC	5	2	2	1

5. Secondary Outcome Measure:

Measure Title	Number of CT Scans Performed More Than 7 Days From Suspected Recurrence of Diverticulitis That Were Positive
Measure Description	A positive CT scan was defined as a CT scan that showed bowel wall thickening (>5 mm) and/or fat stranding as read by the central reader.
Time Frame	Up to 104 weeks
Safety Issue?	No

Analysis Population Description

Suspected Recurrence of Diverticulitis consists of subjects in the Full Analysis Set who had a CT scan performed. Since subjects may have had more than one suspected recurrence, counts are of the number of CT scans, not the number of subjects.

Reporting Groups

	Description
SPD476 (1.2 g)	1.2 g administered orally once daily
SPD476 (2.4 g)	2.4 g administered orally once daily

	Description
SPD476 (4.8 g)	4.8 g administered orally once daily
Placebo	Placebo administered orally once daily

Measured Values

	SPD476 (1.2 g)	SPD476 (2.4 g)	SPD476 (4.8 g)	Placebo
Number of Participants Analyzed	52	49	55	46
Number of CT Scans Performed More Than 7 Days From Suspected Recurrence of Diverticulitis That Were Positive [units: Number of CT scans]				
Positive	0	0	1	1
Presence of abdominal pain	0	0	1	1
15% increase in WBC from baseline	0	0	0	0
Presence of abdominal pain + 15% increase in WBC	0	0	0	0

6. Secondary Outcome Measure:

Measure Title	Number of CT Scans Performed More Than 7 Days From Suspected Recurrence of Diverticulitis That Were Negative
Measure Description	A negative CT scan was defined as a CT scan that did not show bowel wall thickening (>5 mm) and/or fat stranding as read by the central reader.
Time Frame	Up to 104 weeks
Safety Issue?	No

Analysis Population Description

Suspected Recurrence of Diverticulitis consists of subjects in the Full Analysis Set who had a CT scan performed. Since subjects may have had more than one suspected recurrence, counts are of the number of CT scans, not the number of subjects.

Reporting Groups

	Description
SPD476 (1.2 g)	1.2 g administered orally once daily
SPD476 (2.4 g)	2.4 g administered orally once daily
SPD476 (4.8 g)	4.8 g administered orally once daily

	Description
Placebo	Placebo administered orally once daily

Measured Values

	SPD476 (1.2 g)	SPD476 (2.4 g)	SPD476 (4.8 g)	Placebo
Number of Participants Analyzed	52	49	55	46
Number of CT Scans Performed More Than 7 Days From Suspected Recurrence of Diverticulitis That Were Negative [units: Number of CT scans]				
Negative	0	3	2	3
Presence of abdominal pain	0	2	2	3
15% increase in WBC from baseline	0	1	0	1
Presence of abdominal pain + 15% increase in WBC	0	0	0	1

7. Secondary Outcome Measure:

Measure Title	Percent of Subjects Requiring Surgery for Diverticulitis
Measure Description	
Time Frame	Up to 104 weeks
Safety Issue?	No

Analysis Population Description

Full Analysis Set consists of all subjects who were randomized and took at least 1 dose of investigational product.

Reporting Groups

	Description
SPD476 (1.2 g)	1.2 g administered orally once daily
SPD476 (2.4 g)	2.4 g administered orally once daily
SPD476 (4.8 g)	4.8 g administered orally once daily
Placebo	Placebo administered orally once daily

Measured Values

	SPD476 (1.2 g)	SPD476 (2.4 g)	SPD476 (4.8 g)	Placebo
Number of Participants Analyzed	143	143	150	147
Percent of Subjects Requiring Surgery for Diverticulitis [units: percentage of subjects]	2.8	2.8	3.3	2.0

Reported Adverse Events

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

Reporting Groups

	Description
SPD476 (1.2 g)	1.2 g administered orally once daily
SPD476 (2.4 g)	2.4 g administered orally once daily
SPD476 (4.8 g)	4.8 g administered orally once daily
Placebo	Placebo administered orally once daily

Serious Adverse Events

	SPD476 (1.2 g)	SPD476 (2.4 g)	SPD476 (4.8 g)	Placebo
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Total	16/143 (11.19%)	15/143 (10.49%)	18/150 (12%)	16/147 (10.88%)
Blood and lymphatic system disorders				
Iron deficiency anemia	0/143 (0%)	1/143 (0.7%)	0/150 (0%)	0/147 (0%)
Cardiac disorders				
Acute myocarcial infarction	1/143 (0.7%)	0/143 (0%)	0/150 (0%)	2/147 (1.36%)
Angina pectoris	2/143 (1.4%)	1/143 (0.7%)	1/150 (0.67%)	0/147 (0%)
Coronary artery disease	0/143 (0%)	1/143 (0.7%)	0/150 (0%)	0/147 (0%)
Coronary artery insufficiency	1/143 (0.7%)	0/143 (0%)	0/150 (0%)	1/147 (0.68%)
Myocardial ischemia	0/143 (0%)	1/143 (0.7%)	0/150 (0%)	0/147 (0%)
Ear and labyrinth disorders				

	SPD476 (1.2 g)	SPD476 (2.4 g)	SPD476 (4.8 g)	Placebo
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Vertigo positional	0/143 (0%)	0/143 (0%)	0/150 (0%)	1/147 (0.68%)
Endocrine disorders				
Autoimmune thyroiditis	0/143 (0%)	0/143 (0%)	0/150 (0%)	1/147 (0.68%)
Eye disorders				
Retinal detachment	0/143 (0%)	0/143 (0%)	0/150 (0%)	1/147 (0.68%)
Gastrointestinal disorders				
Abdominal pain	1/143 (0.7%)	0/143 (0%)	0/150 (0%)	2/147 (1.36%)
Dyspepsia	0/143 (0%)	0/143 (0%)	1/150 (0.67%)	0/147 (0%)
Enterovesical fistula	0/143 (0%)	1/143 (0.7%)	0/150 (0%)	0/147 (0%)
Gastritis	0/143 (0%)	0/143 (0%)	1/150 (0.67%)	0/147 (0%)
Gastrointestinal hemorrhage	0/143 (0%)	1/143 (0.7%)	0/150 (0%)	0/147 (0%)
Large intestine perforation	1/143 (0.7%)	0/143 (0%)	0/150 (0%)	0/147 (0%)
Pancreatitis	0/143 (0%)	0/143 (0%)	1/150 (0.67%)	0/147 (0%)
Pancreatitis acute	0/143 (0%)	0/143 (0%)	1/150 (0.67%)	0/147 (0%)
Peritoneal hematoma	1/143 (0.7%)	0/143 (0%)	0/150 (0%)	0/147 (0%)
General disorders				
Chills	0/143 (0%)	1/143 (0.7%)	0/150 (0%)	0/147 (0%)
Non-cardiac chest pain	1/143 (0.7%)	0/143 (0%)	0/150 (0%)	0/147 (0%)
Pyrexia	0/143 (0%)	0/143 (0%)	1/150 (0.67%)	0/147 (0%)
Infections and infestations				
Cellulitis	0/143 (0%)	1/143 (0.7%)	0/150 (0%)	0/147 (0%)
Clostridial infection	0/143 (0%)	0/143 (0%)	1/150 (0.67%)	0/147 (0%)
Endophthalmitis	0/143 (0%)	0/143 (0%)	0/150 (0%)	1/147 (0.68%)
Gastroenteritis	0/143 (0%)	1/143 (0.7%)	1/150 (0.67%)	0/147 (0%)
Gastrointestinal infection	0/143 (0%)	0/143 (0%)	0/150 (0%)	1/147 (0.68%)
Kidney infection	0/143 (0%)	0/143 (0%)	1/150 (0.67%)	0/147 (0%)

	SPD476 (1.2 g)	SPD476 (2.4 g)	SPD476 (4.8 g)	Placebo
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Pneumonia	1/143 (0.7%)	0/143 (0%)	0/150 (0%)	1/147 (0.68%)
Pneumonia primary atypical	0/143 (0%)	0/143 (0%)	1/150 (0.67%)	0/147 (0%)
Sepsis	1/143 (0.7%)	0/143 (0%)	1/150 (0.67%)	0/147 (0%)
Urinary tract infection	0/143 (0%)	0/143 (0%)	2/150 (1.33%)	0/147 (0%)
Viral infection	0/143 (0%)	0/143 (0%)	1/150 (0.67%)	0/147 (0%)
Injury, poisoning and procedural complications				
Concussion	1/143 (0.7%)	0/143 (0%)	0/150 (0%)	0/147 (0%)
Femoral neck fracture	1/143 (0.7%)	0/143 (0%)	0/150 (0%)	0/147 (0%)
Humerus fracture	0/143 (0%)	0/143 (0%)	0/150 (0%)	1/147 (0.68%)
Joint dislocation	0/143 (0%)	0/143 (0%)	0/150 (0%)	1/147 (0.68%)
Near drowning	0/143 (0%)	0/143 (0%)	1/150 (0.67%)	0/147 (0%)
Road traffic accident	2/143 (1.4%)	0/143 (0%)	0/150 (0%)	0/147 (0%)
Skin injury	1/143 (0.7%)	0/143 (0%)	0/150 (0%)	0/147 (0%)
Metabolism and nutrition disorders				
Hypercalcemia	1/143 (0.7%)	0/143 (0%)	0/150 (0%)	0/147 (0%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)				
Breast cancer	0/143 (0%)	1/143 (0.7%)	0/150 (0%)	0/147 (0%)
Breast cancer in situ	0/143 (0%)	0/143 (0%)	0/150 (0%)	1/147 (0.68%)
Laryngeal cancer	0/143 (0%)	0/143 (0%)	0/150 (0%)	1/147 (0.68%)
Prostate cancer	0/143 (0%)	0/143 (0%)	1/150 (0.67%)	0/147 (0%)
Thyroid cancer	0/143 (0%)	0/143 (0%)	0/150 (0%)	1/147 (0.68%)
Thyroid neoplasm	1/143 (0.7%)	0/143 (0%)	0/150 (0%)	0/147 (0%)
Uterine cancer	2/143 (1.4%)	0/143 (0%)	0/150 (0%)	0/147 (0%)
Nervous system disorders				
Cerebral ischemia	0/143 (0%)	0/143 (0%)	0/150 (0%)	1/147 (0.68%)
Ischemic stroke	0/143 (0%)	1/143 (0.7%)	0/150 (0%)	0/147 (0%)

	SPD476 (1.2 g)	SPD476 (2.4 g)	SPD476 (4.8 g)	Placebo
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Movement disorder	0/143 (0%)	1/143 (0.7%)	0/150 (0%)	0/147 (0%)
Syncope	0/143 (0%)	1/143 (0.7%)	0/150 (0%)	0/147 (0%)
Psychiatric disorders				
Alcoholism	0/143 (0%)	0/143 (0%)	1/150 (0.67%)	0/147 (0%)
Bipolar II disorder	0/143 (0%)	0/143 (0%)	1/150 (0.67%)	0/147 (0%)
Bipolar disorder	0/143 (0%)	0/143 (0%)	0/150 (0%)	1/147 (0.68%)
Confusional state	0/143 (0%)	1/143 (0.7%)	0/150 (0%)	0/147 (0%)
Renal and urinary disorders				
Bladder prolapse	0/143 (0%)	1/143 (0.7%)	0/150 (0%)	0/147 (0%)
Nephrolithiasis	0/143 (0%)	0/143 (0%)	1/150 (0.67%)	0/147 (0%)
Pelvi-ureteric obstruction	0/143 (0%)	0/143 (0%)	1/150 (0.67%)	0/147 (0%)
Renal colic	1/143 (0.7%)	0/143 (0%)	0/150 (0%)	0/147 (0%)
Renal failure acute	1/143 (0.7%)	0/143 (0%)	0/150 (0%)	0/147 (0%)
Stress urinary incontinence	0/143 (0%)	0/143 (0%)	0/150 (0%)	1/147 (0.68%)
Reproductive system and breast disorders				
Benign prostatic hyperplasia	0/143 (0%)	1/143 (0.7%)	0/150 (0%)	0/147 (0%)
Ovarian cyst	0/143 (0%)	0/143 (0%)	0/150 (0%)	1/147 (0.68%)
Respiratory, thoracic and mediastinal disorders				
Asthma	0/143 (0%)	0/143 (0%)	0/150 (0%)	1/147 (0.68%)
Chronic obstructive pulmonary disease	1/143 (0.7%)	0/143 (0%)	1/150 (0.67%)	0/147 (0%)
Nasal septum deviation	0/143 (0%)	1/143 (0.7%)	0/150 (0%)	0/147 (0%)
Pulmonary hypertension	1/143 (0.7%)	0/143 (0%)	0/150 (0%)	0/147 (0%)
Sinus polyp	0/143 (0%)	1/143 (0.7%)	0/150 (0%)	0/147 (0%)
Vascular disorders				
Aortic Aneurysm	0/143 (0%)	0/143 (0%)	0/150 (0%)	1/147 (0.68%)
Hypertension	0/143 (0%)	0/143 (0%)	0/150 (0%)	1/147 (0.68%)

Other Adverse Events

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

	SPD476 (1.2 g)	SPD476 (2.4 g)	SPD476 (4.8 g)	Placebo
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Total	109/143 (76.22%)	106/143 (74.13%)	101/150 (67.33%)	112/147 (76.19%)
Gastrointestinal disorders				
Abdominal pain	17/143 (11.89%)	16/143 (11.19%)	18/150 (12%)	16/147 (10.88%)
Constpation	7/143 (4.9%)	3/143 (2.1%)	5/150 (3.33%)	8/147 (5.44%)
Diarrhea	13/143 (9.09%)	12/143 (8.39%)	12/150 (8%)	12/147 (8.16%)
Flatulence	9/143 (6.29%)	5/143 (3.5%)	3/150 (2%)	4/147 (2.72%)
General disorders				
Nausea	10/143 (6.99%)	1/143 (0.7%)	6/150 (4%)	5/147 (3.4%)
Infections and infestations				
Bronchitis	7/143 (4.9%)	8/143 (5.59%)	3/150 (2%)	3/147 (2.04%)
Influenza	5/143 (3.5%)	11/143 (7.69%)	4/150 (2.67%)	3/147 (2.04%)
Nasopharyngitis	6/143 (4.2%)	15/143 (10.49%)	7/150 (4.67%)	13/147 (8.84%)
Sinusitis	9/143 (6.29%)	7/143 (4.9%)	5/150 (3.33%)	8/147 (5.44%)
Upper respiratory tract infection	9/143 (6.29%)	3/143 (2.1%)	10/150 (6.67%)	14/147 (9.52%)
Urinary tract infection	14/143 (9.79%)	12/143 (8.39%)	8/150 (5.33%)	17/147 (11.56%)
Musculoskeletal and connective tissue disorders				
Arthralgia	7/143 (4.9%)	5/143 (3.5%)	4/150 (2.67%)	13/147 (8.84%)
Back pain	8/143 (5.59%)	5/143 (3.5%)	8/150 (5.33%)	12/147 (8.16%)
Nervous system disorders				
Headache	13/143 (9.09%)	6/143 (4.2%)	14/150 (9.33%)	10/147 (6.8%)
Vascular disorders				
Hypertension	5/143 (3.5%)	8/143 (5.59%)	6/150 (4%)	1/147 (0.68%)

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:

Name/Official Title: Study Physician
Organization: Shire Development LLC
Phone: +1 866 842 5335
Email: