ClinicalTrials.gov Protocol and Results Registration System (PRS) Receipt
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Prevention of Recurrence of Diverticulitis (PREVENT2)

This study has been completed.

Sponsor:	Shire
Collaborators:	
Information provided by (Responsible Party):	Shire
ClinicalTrials.gov Identifier:	NCT00545103

Purpose

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

Condition	Intervention	Phase
Diverticulitis	Drug: SPD476, MMX™ mesalazine, 1.2g extended release tablet 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 Are 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: 592
Study Start Date: December 2007
Primary Completion Date: November 2011
Study Completion Date: November 2011

Arms	Assigned Interventions
Experimental: SPD476 (1.2 g)	Drug: SPD476, MMX™ mesalazine, 1.2g extended release tablet SPD476 1.2g administered Once Daily (QD) Other Names: LIALDA
Experimental: SPD476 (2.4 g)	Drug: SPD476, MMX™ mesalazine, 1.2g extended release tablet SPD476 2.4g administered Once Daily (QD) Other Names: LIALDA
Experimental: SPD476 (4.8 g)	Drug: SPD476, MMX™ mesalazine, 1.2g extended release tablet SPD476 4.8g administered Once Daily (QD)

Arms	Assigned Interventions
	Other Names: LIALDA
Placebo Comparator: Placebo	Drug: Placebo Placebo administered Once Daily (QD)

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

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Investigators

Principal Investigator:	Jeffrey B. Raskin, M.D.	University of Miami Miller School of Medicine

More Information

Responsible Party:	Shire
Study ID Numbers:	SPD476-314
	2007-004896-20 [EudraCT Number]
Health Authority:	United States: Food and Drug Administration

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	148	148	150	146
Completed	73	70	74	76
Not Completed	75	78	76	70
Lack of Efficacy	48	45	31	27
Withdrawal by Subject	6	10	18	22
Adverse Event	11	12	17	10
Lost to Follow-up	4	6	3	4
Protocol Violation	1	2	3	0
Suspected recurrence of diverticulitis	1	0	0	3
Difficult to open package	0	0	0	1
Investigational product not taken	1	0	0	1
Wish to start a family	0	0	0	1
Diverticulitis crisis	0	0	0	1
Personal reasons	1	0	0	0
Subject's decision	1	0	0	0
Noncompliance	0	1	0	0
Investigator decision	0	0	1	0

	SPD476 (1.2 g)	SPD476 (2.4 g)	SPD476 (4.8 g)	Placebo
Subject moved	0	1	0	0
Use of prohibited medication	0	0	1	0
Does not want to take study drug anymore	1	0	1	0
Subject met endpoint under protocol v. 1	0	0	1	0
Death	0	1	0	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	148	147	149	142	586
Age, Continuous [1] [units: years] Mean (Standard Deviation)	57.8 (10.88)	54.2 (10.10)	56.7 (11.76)	55.7 (11.15)	56.1 (11.04)
Age, Customized [1] [units: participants]					
18 to < 35 years	1	4	5	6	16
35 to < 45 years	16	21	18	16	71
45 to < 55 years	42	50	41	40	173
55 to < 65 years	45	48	45	45	183
>= 65 years	44	24	40	35	143
Gender, Male/Female [1] [units: participants]					

	SPD476 (1.2 g)	SPD476 (2.4 g)	SPD476 (4.8 g)	Placebo	Total
Female	83	71	88	72	314
Male	65	76	61	70	272
Region of Enrollment [2] [units: participants]					
United States	89	88	88	86	351
Hungary	2	3	6	3	14
Canada	5	5	4	5	19
Finland	4	5	5	4	18
Brazil	10	9	10	11	40
Romania	10	12	11	9	42
South Africa	14	16	15	15	60
Netherlands	5	3	5	5	18
Germany	7	6	4	4	21
Italy	2	1	2	4	9

[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 592 subjects randomized, 6 were never dosed with investigational product. Therefore, 586 subjects are in the Safety Population.

[2] This baseline measure consists of all randomized subjects (n = 592).

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	148	147	149	142
Percent of Subjects Without Recurrence of Diverticulitis [units: percentage of subjects]	62.8	59.2	69.1	67.6

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	0.778
	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	0.159
	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	0.368
	Comments	[Not specified]
	Method	Cochran-Mantel-Haenszel
	Comments	[Not specified]

2. Secondary Outcome Measure:

Measure Title	Percent of Subjects Who Are 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

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	148	147	149	142
Percent of Subjects Who Are CT-Recurrence Free of Diverticulitis [units: percentage of subjects]	62.8	59.2	69.1	66.9

Statistical Analysis 1 for Percent of Subjects Who Are 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	0.685
	Comments	[Not specified]
	Method	Cochran-Mantel-Haenszel
	Comments	[Not specified]

Statistical Analysis 2 for Percent of Subjects Who Are 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	0.198
	Comments	[Not specified]
	Method	Cochran-Mantel-Haenszel
	Comments	[Not specified]

Statistical Analysis 3 for Percent of Subjects Who Are 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	0.441
	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	55	52	51	40

	SPD476 (1.2 g)	SPD476 (2.4 g)	SPD476 (4.8 g)	Placebo
Number of CT Scans Performed Within 7 Days of Suspected Recurrence of Diverticulitis That Were Positive [units: Number of CT Scans]				
Positive	49	45	35	30
Presence of abdominal pain	48	39	34	29
15% increase in WBC from baseline	23	24	18	11
Abdominal pain + 15% increase in WBC	23	22	18	11

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
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	55	52	51	40
Number of CT Scans Performed Within 7 Days of Suspected Recurrence of Diverticulitis That Were Negative				

	SPD476 (1.2 g)	SPD476 (2.4 g)	SPD476 (4.8 g)	Placebo
[units: Number of CT Scans]				
Negative	9	8	22	15
Presence of abdominal pain	8	6	17	12
15% increase in WBC from Baseline	1	2	4	4
Abdominal pain + 15% increase in WBC	1	2	4	3

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
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	55	52	51	40
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

	SPD476 (1.2 g)	SPD476 (2.4 g)	SPD476 (4.8 g)	Placebo
Presence of abdominal pain	0	0	0	1
15% increase in WBC from baseline	0	0	0	0
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
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	55	52	51	40
Number of CT Scans Performed More Than 7 Days From Suspected Recurrence of Diverticulitis That Were Negative [units: Number of CT Scans]				
Negative	1	0	0	0
Presence of abdominal pain	1	0	0	0
15% increase in WBC from baseline	0	0	0	0

	SPD476 (1.2 g)	SPD476 (2.4 g)	SPD476 (4.8 g)	Placebo
Abdominal pain + 15% increase in WBC	0	0	0	0

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

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	148	147	149	142
Percent of Subjects Requiring Surgery for Diverticulitis [units: percentage of subjects]	4.7	2.7	2.0	1.4

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

	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

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	9/148 (6.08%)	13/147 (8.84%)	14/149 (9.4%)	15/142 (10.56%)
Blood and lymphatic system disorders				
Agranulocytosis	0/148 (0%)	0/147 (0%)	1/149 (0.67%)	0/142 (0%)
Cardiac disorders				
Angina pectoris	0/148 (0%)	1/147 (0.68%)	1/149 (0.67%)	1/142 (0.7%)
Atrial fibrillation	1/148 (0.68%)	1/147 (0.68%)	0/149 (0%)	0/142 (0%)
Cardiac failure	0/148 (0%)	0/147 (0%)	1/149 (0.67%)	0/142 (0%)
Supraventricular tachycardia	1/148 (0.68%)	0/147 (0%)	0/149 (0%)	0/142 (0%)
Ventricular extrasystoles	0/148 (0%)	1/147 (0.68%)	0/149 (0%)	0/142 (0%)
Gastrointestinal disorders				
Abdominal pain	0/148 (0%)	1/147 (0.68%)	0/149 (0%)	1/142 (0.7%)
Abdominal pain lower	0/148 (0%)	0/147 (0%)	0/149 (0%)	1/142 (0.7%)
Abdominal pain upper	0/148 (0%)	0/147 (0%)	0/149 (0%)	1/142 (0.7%)
Dyspepsia	0/148 (0%)	0/147 (0%)	0/149 (0%)	1/142 (0.7%)
Esophagitis	0/148 (0%)	1/147 (0.68%)	0/149 (0%)	0/142 (0%)
Gastroesophogeal reflux disease	0/148 (0%)	0/147 (0%)	1/149 (0.67%)	0/142 (0%)
Gastrointestinal hemorrhage	0/148 (0%)	1/147 (0.68%)	0/149 (0%)	0/142 (0%)
Hiatus hernia	0/148 (0%)	1/147 (0.68%)	0/149 (0%)	0/142 (0%)
Mallory-Weiss syndrome	0/148 (0%)	0/147 (0%)	0/149 (0%)	1/142 (0.7%)
Nausea	0/148 (0%)	1/147 (0.68%)	0/149 (0%)	0/142 (0%)
Small intestinal hemorrhage	0/148 (0%)	0/147 (0%)	1/149 (0.67%)	0/142 (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 (%)
General disorders				
Chest discomfort	1/148 (0.68%)	0/147 (0%)	0/149 (0%)	0/142 (0%)
Chest pain	0/148 (0%)	0/147 (0%)	2/149 (1.34%)	0/142 (0%)
Multi-organ failure/Death	0/148 (0%)	1/147 (0.68%)	0/149 (0%)	0/142 (0%)
Hepatobiliary disorders				
Cholangitis acute	0/148 (0%)	0/147 (0%)	1/149 (0.67%)	0/142 (0%)
Cholecystitis	0/148 (0%)	0/147 (0%)	0/149 (0%)	1/142 (0.7%)
Infections and infestations				
Appendicitis	0/148 (0%)	1/147 (0.68%)	0/149 (0%)	0/142 (0%)
Borrelia infection	0/148 (0%)	0/147 (0%)	0/149 (0%)	1/142 (0.7%)
Bronchitis	1/148 (0.68%)	0/147 (0%)	0/149 (0%)	0/142 (0%)
Peridiverticular abscess	1/148 (0.68%)	0/147 (0%)	0/149 (0%)	0/142 (0%)
Pharyngitis	1/148 (0.68%)	0/147 (0%)	0/149 (0%)	0/142 (0%)
Pneumonia	1/148 (0.68%)	0/147 (0%)	1/149 (0.67%)	2/142 (1.41%)
Pneumonia viral	0/148 (0%)	0/147 (0%)	0/149 (0%)	1/142 (0.7%)
Subcutaneous abscess	0/148 (0%)	0/147 (0%)	1/149 (0.67%)	0/142 (0%)
Viral pericarditis	0/148 (0%)	0/147 (0%)	0/149 (0%)	1/142 (0.7%)
Injury, poisoning and procedural complications				
Ankle fracture	0/148 (0%)	1/147 (0.68%)	0/149 (0%)	0/142 (0%)
Hip fracture	1/148 (0.68%)	0/147 (0%)	0/149 (0%)	0/142 (0%)
Humerus fracture	0/148 (0%)	0/147 (0%)	1/149 (0.67%)	0/142 (0%)
Patella fracture	0/148 (0%)	1/147 (0.68%)	0/149 (0%)	0/142 (0%)
Post procedural edema	0/148 (0%)	1/147 (0.68%)	0/149 (0%)	0/142 (0%)
Radius fracture	0/148 (0%)	1/147 (0.68%)	0/149 (0%)	0/142 (0%)
Metabolism and nutrition disorders				
Type 2 diabetes mellitus	0/148 (0%)	0/147 (0%)	1/149 (0.67%)	0/142 (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 (%)
Musculoskeletal and connective tissue disorders				
Arthritis	0/148 (0%)	0/147 (0%)	0/149 (0%)	1/142 (0.7%)
Intervertebral disc protrusion	0/148 (0%)	1/147 (0.68%)	0/149 (0%)	0/142 (0%)
Rotator cuff syndrome	0/148 (0%)	0/147 (0%)	0/149 (0%)	1/142 (0.7%)
Spinal column stenosis	0/148 (0%)	0/147 (0%)	0/149 (0%)	1/142 (0.7%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)				
Breast cancer	0/148 (0%)	1/147 (0.68%)	0/149 (0%)	0/142 (0%)
Cardiac neoplasm unspecified	0/148 (0%)	1/147 (0.68%)	0/149 (0%)	0/142 (0%)
Malignant melanoma	0/148 (0%)	0/147 (0%)	0/149 (0%)	1/142 (0.7%)
Ovarian granulosa-theca cell tumor	0/148 (0%)	0/147 (0%)	1/149 (0.67%)	0/142 (0%)
Prostate cancer	0/148 (0%)	1/147 (0.68%)	0/149 (0%)	0/142 (0%)
Renal cell carcinoma	0/148 (0%)	0/147 (0%)	1/149 (0.67%)	0/142 (0%)
Squamous cell carcinoma	0/148 (0%)	0/147 (0%)	1/149 (0.67%)	0/142 (0%)
Nervous system disorders				
Cerebrovascular accident	0/148 (0%)	2/147 (1.36%)	0/149 (0%)	0/142 (0%)
Syncope	0/148 (0%)	0/147 (0%)	1/149 (0.67%)	0/142 (0%)
Transient ischemic attack	1/148 (0.68%)	0/147 (0%)	0/149 (0%)	0/142 (0%)
Psychiatric disorders				
Panic attack	0/148 (0%)	0/147 (0%)	0/149 (0%)	1/142 (0.7%)
Reproductive system and breast disorders				
Ovarian cyst	0/148 (0%)	0/147 (0%)	1/149 (0.67%)	0/142 (0%)
Uterovaginal prolapse	1/148 (0.68%)	0/147 (0%)	0/149 (0%)	0/142 (0%)
Respiratory, thoracic and mediastinal disorders				
Dyspnea	1/148 (0.68%)	0/147 (0%)	0/149 (0%)	1/142 (0.7%)
Vascular disorders				
Femoral arterial stenosis	0/148 (0%)	0/147 (0%)	0/149 (0%)	1/142 (0.7%)

	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 (%)
Hemorrhage	0/148 (0%)	0/147 (0%)	0/149 (0%)	1/142 (0.7%)
Hypertension	0/148 (0%)	0/147 (0%)	0/149 (0%)	1/142 (0.7%)
Hypotension	0/148 (0%)	1/147 (0.68%)	0/149 (0%)	0/142 (0%)
Intra-abdominal hemorrhage	0/148 (0%)	1/147 (0.68%)	0/149 (0%)	0/142 (0%)
Thrombosis	0/148 (0%)	0/147 (0%)	0/149 (0%)	1/142 (0.7%)

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	108/148 (72.97%)	111/147 (75.51%)	110/149 (73.83%)	105/142 (73.94%)
Gastrointestinal disorders				
Abdominal pain	19/148 (12.84%)	19/147 (12.93%)	15/149 (10.07%)	12/142 (8.45%)
Abdominal pain lower	5/148 (3.38%)	2/147 (1.36%)	10/149 (6.71%)	7/142 (4.93%)
Constipation	9/148 (6.08%)	6/147 (4.08%)	6/149 (4.03%)	12/142 (8.45%)
Diarrhea	15/148 (10.14%)	15/147 (10.2%)	18/149 (12.08%)	12/142 (8.45%)
Dyspepsia	5/148 (3.38%)	11/147 (7.48%)	6/149 (4.03%)	6/142 (4.23%)
Nausea	5/148 (3.38%)	8/147 (5.44%)	10/149 (6.71%)	11/142 (7.75%)
Infections and infestations				
Bronchitis	8/148 (5.41%)	7/147 (4.76%)	9/149 (6.04%)	7/142 (4.93%)
Influenza	11/148 (7.43%)	8/147 (5.44%)	9/149 (6.04%)	11/142 (7.75%)
Nasopharyngitis	5/148 (3.38%)	10/147 (6.8%)	8/149 (5.37%)	9/142 (6.34%)
Sinusitis	12/148 (8.11%)	8/147 (5.44%)	10/149 (6.71%)	11/142 (7.75%)
Urinary tract infection	11/148 (7.43%)	14/147 (9.52%)	10/149 (6.71%)	7/142 (4.93%)
Musculoskeletal and connective tissue disorders				
Back pain	10/148 (6.76%)	11/147 (7.48%)	11/149 (7.38%)	12/142 (8.45%)
Nervous system disorders				
Headache	14/148 (9.46%)	10/147 (6.8%)	14/149 (9.4%)	13/142 (9.15%)

	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 (%)
Respiratory, thoracic and mediastinal disorders				
Cough	9/148 (6.08%)	3/147 (2.04%)	4/149 (2.68%)	2/142 (1.41%)
Vascular disorders				
Hypertension	6/148 (4.05%)	8/147 (5.44%)	2/149 (1.34%)	8/142 (5.63%)

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.

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