Clinical trial results:
A Phase 2b, Multicenter, Randomized, Double-blind, Placebo-controlled, Parallel-group, Dose-response Study Evaluating the Efficacy and Safety of JNJ-54781532 in Subjects with Moderately to Severely Active Ulcerative Colitis

Summary

EudraCT number	2013-000263-88
Trial protocol	DE BE HU NL PL BG RO
Global end of trial date	05 December 2015

Results information

Result version number	v1 (current)
This version publication date	21 December 2016
First version publication date	21 December 2016

Trial information

Trial identification

Sponsor protocol code	54781532UCO2001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01959282
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Janssen Research and Development, LLC
Sponsor organisation address	Antwerpseweg 15-17, Beerse, Belgium, B-2340
Public contact	Clinical Registry Group, Janssen Research and Development, ClinicalTrialsEU@its.jnj.com
Scientific contact	Clinical Registry Group, Janssen Research and Development, ClinicalTrialsEU@its.jnj.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	05 December 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	05 December 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main obective of trial was to evaluate the dose response of JNJ-54781532 at Week 8 in subjects with moderately to severely active ulcerative colitis (UC) and to evaluate the safety of JNJ-54781532 in subjects with moderately to severely active UC.

Protection of trial subjects:

Safety evaluations included the collection of adverse events (AEs), clinical laboratory tests, vital signs, physical examinations, electrocardiograms (ECG), tuberculosis (TB) evaluations and pregnancy testing.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	26 November 2013
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 11
Country: Number of subjects enrolled	Belgium: 8
Country: Number of subjects enrolled	Bulgaria: 11
Country: Number of subjects enrolled	Canada: 16
Country: Number of subjects enrolled	Germany: 17
Country: Number of subjects enrolled	France: 1
Country: Number of subjects enrolled	Hungary: 14
Country: Number of subjects enrolled	Israel: 3
Country: Number of subjects enrolled	Netherlands: 5
Country: Number of subjects enrolled	Poland: 18
Country: Number of subjects enrolled	Romania: 2
Country: Number of subjects enrolled	Russian Federation: 45
Country: Number of subjects enrolled	Ukraine: 42
Country: Number of subjects enrolled	United States: 26
Worldwide total number of subjects	219
EEA total number of subjects	76

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	206
From 65 to 84 years	13
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was conducted from 26 November 2013 to 05 December 2015.

Pre-assignment

Screening details:

A total of 219 subjects were enrolled; among these 176 subjects were randomized to 4 JNJ-54781532 treatment groups and 43 subjects were randomized to the placebo group.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Subjects received placebo once daily from Week 0 to Week 8. Subjects in clinical response at Week 8 continued to receive placebo through Week 32. Subjects not in clinical response at Week 8 received treatment with 150 milligram (mg) JNJ-54781532 orally once daily from Week 8 to Week 16. Among subjects who were not in clinical response at Week 8, subjects who achieved a partial Mayo score response (i.e., a decrease from baseline of greater than or equal to (>=) 3 in the partial Mayo score) at Week 16 continued to receive 150 mg JNJ-54781532 once daily through Week 32; subjects who did not achieve a partial Mayo score response were discontinued from study medication.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received placebo once daily from Week 0 to Week 8. Subjects in clinical response at Week 8 continued to receive placebo through Week 32.

Arm title	JNJ-54781532 25 mg once daily (QD)

Arm description:

Subjects received 25 mg of JNJ-54781532 orally once daily from Week 0 to Week 8. Subjects in clinical response at Week 8 continued to receive the same dosage through Week 32. Subjects not in clinical response at Week 8 continued to receive the same dosage through Week 16. Among subjects who were not in clinical response at Week 8, subjects who achieved a partial Mayo score response (i.e. a decrease from baseline >= 3 in the partial Mayo score) at Week 16 continued to receive JNJ- 54781532 25 mg once daily through Week 32; subjects who did not achieve a partial Mayo score response were discontinued from study medication.

Arm type	Experimental
Investigational medicinal product name	JNJ-54781532 25 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received 25 mg of JNJ-54781532 once daily from Week 0 to Week 8. Subjects in clinical response at Week 8 continued to receive the same dosage through Week 32. Subjects not in clinical

response at Week 8 continued to receive the same dosage through Week 16; subjects who achieved a partial Mayo score response at week 16 continued to receive JNJ-54781532 25 mg once daily through Week 32.

Arm title	JNJ-54781532 75 mg QD

Arm description:

Subjects received 75 mg of JNJ-54781532 orally once daily from Week 0 to Week 8. Subjects in clinical response at Week 8 continued to receive the same dosage through Week 32. Subjects not in clinical response at Week 8 continued to receive the same dosage through Week 16. Among subjects who were not in clinical response at Week 8, subjects who achieved a partial Mayo score response (i.e. a decrease from baseline >= 3 in the partial Mayo score) at Week 16 continued to receive JNJ- 54781532 75 mg once daily through Week 32; subjects who did not achieve a partial Mayo score response were discontinued from study medication.

Arm type	Experimental
Investigational medicinal product name	JNJ-54781532 75 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received 75 mg of JNJ-54781532 once daily from Week 0 to Week 8. Subjects in clinical response at Week 8 continued to receive the same dosage through Week 32. Subjects not in clinical response at Week 8 continued to receive the same dosage through Week 16; subjects who achieved a partial Mayo score response at week 16 continued to receive JNJ 54781532 75 mg once daily through Week 32.

Arm title	JNJ-54781532 150 mg QD

Arm description:

Subjects received 150 mg of JNJ-54781532 orally once daily from Week 0 to Week 8. Subjects in clinical response at Week 8 continued to receive the same dosage through Week 32. Subjects not in clinical response at Week 8 continue to receive the same dosage through Week 16. Among subjects who were not in clinical response at Week 8, subjects who achieved a partial Mayo score response (ie a decrease from baseline >= 3 in the partial Mayo score) at Week 16 continued to receive JNJ-54781532 150 mg once daily through Week 32; subjects who did not achieve a partial Mayo score response were discontinued from study medication.

Arm type	Experimental
Investigational medicinal product name	JNJ-54781532 150 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received 150 mg of JNJ-54781532 once daily from Week 0 to Week 8. Subjects in clinical response at Week 8 continued to receive the same dosage through Week 32. Subjects not in clinical response at Week 8 continue to received the same dosage through Week 16; subjects who achieved a partial Mayo score response at week 16 continued to receive JNJ-54781532 150 mg once daily through Week 32.

Arm title	JNJ-54781532 75 mg twice daily (BID)

Arm description:

Subjects received 75 mg of JNJ-54781532 orally twice daily from Week 0 to Week 8. Subjects in clinical response at Week 8 continued to receive the same dosage through Week 32. Subjects not in clinical response at Week 8 continued to receive the same dosage through Week 16. Among subjects who were not in clinical response at Week 8, subjects who achieved a partial Mayo score response (ie a decrease from baseline >= 3 in the partial Mayo score) at Week 16 continued to receive JNJ- 54781532 75 mg twice daily through Week 32; subjects who did not achieve a partial Mayo score response were discontinued from study medication.

Arm type	Experimental

Investigational medicinal product name	JNJ-54781532 75 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received 75 mg of JNJ-54781532 twice daily from Week 0 to Week 8. Subjects in clinical response at Week 8 were continued to receive the same dosage through Week 32 and subjects not in clinical response at Week 8 were continued to receive the same dosage through Week 16. At Week 16, subjects who achieved a partial Mayo score response at Week 16 could continued to receive JNJ-54781532 75 mg twice daily through Week 32.

Number of subjects in period 1	Placebo	JNJ-54781532 25 mg once daily (QD)	JNJ-54781532 75 mg QD
Started	43	44	44
Completed	39	40	40
Not completed	4	4	4
Consent withdrawn by subject	2	2	4
Other	-	1	-
Lost to follow-up	2	1	-
Sponsor decision	-	-	-

Number of subjects in period 1	JNJ-54781532 150 mg QD	JNJ-54781532 75 mg twice daily (BID)
Started	44	44
Completed	40	39
Not completed	4	5
Consent withdrawn by subject	2	2
Other	1	1
Lost to follow-up	-	1
Sponsor decision	1	1

Baseline characteristics

Reporting groups

Reporting group title	Placebo

Reporting group description:

Subjects received placebo once daily from Week 0 to Week 8. Subjects in clinical response at Week 8 continued to receive placebo through Week 32. Subjects not in clinical response at Week 8 received treatment with 150 milligram (mg) JNJ-54781532 orally once daily from Week 8 to Week 16. Among subjects who were not in clinical response at Week 8, subjects who achieved a partial Mayo score response (i.e., a decrease from baseline of greater than or equal to (>=) 3 in the partial Mayo score) at Week 16 continued to receive 150 mg JNJ-54781532 once daily through Week 32; subjects who did not achieve a partial Mayo score response were discontinued from study medication.

Reporting group title	JNJ-54781532 25 mg once daily (QD)

Reporting group description:

Subjects received 25 mg of JNJ-54781532 orally once daily from Week 0 to Week 8. Subjects in clinical response at Week 8 continued to receive the same dosage through Week 32. Subjects not in clinical response at Week 8 continued to receive the same dosage through Week 16. Among subjects who were not in clinical response at Week 8, subjects who achieved a partial Mayo score response (i.e. a decrease from baseline >= 3 in the partial Mayo score) at Week 16 continued to receive JNJ- 54781532 25 mg once daily through Week 32; subjects who did not achieve a partial Mayo score response were discontinued from study medication.

Reporting group title	JNJ-54781532 75 mg QD

Reporting group description:

Subjects received 75 mg of JNJ-54781532 orally once daily from Week 0 to Week 8. Subjects in clinical response at Week 8 continued to receive the same dosage through Week 32. Subjects not in clinical response at Week 8 continued to receive the same dosage through Week 16. Among subjects who were not in clinical response at Week 8, subjects who achieved a partial Mayo score response (i.e. a decrease from baseline >= 3 in the partial Mayo score) at Week 16 continued to receive JNJ- 54781532 75 mg once daily through Week 32; subjects who did not achieve a partial Mayo score response were discontinued from study medication.

Reporting group title	JNJ-54781532 150 mg QD

Reporting group description:

Subjects received 150 mg of JNJ-54781532 orally once daily from Week 0 to Week 8. Subjects in clinical response at Week 8 continued to receive the same dosage through Week 32. Subjects not in clinical response at Week 8 continue to receive the same dosage through Week 16. Among subjects who were not in clinical response at Week 8, subjects who achieved a partial Mayo score response (ie a decrease from baseline >= 3 in the partial Mayo score) at Week 16 continued to receive JNJ-54781532 150 mg once daily through Week 32; subjects who did not achieve a partial Mayo score response were discontinued from study medication.

Reporting group title	JNJ-54781532 75 mg twice daily (BID)

Reporting group description:

Subjects received 75 mg of JNJ-54781532 orally twice daily from Week 0 to Week 8. Subjects in clinical response at Week 8 continued to receive the same dosage through Week 32. Subjects not in clinical response at Week 8 continued to receive the same dosage through Week 16. Among subjects who were not in clinical response at Week 8, subjects who achieved a partial Mayo score response (ie a decrease from baseline >= 3 in the partial Mayo score) at Week 16 continued to receive JNJ- 54781532 75 mg twice daily through Week 32; subjects who did not achieve a partial Mayo score response were discontinued from study medication.

Reporting group values	Placebo	JNJ-54781532 25 mg once daily (QD)	JNJ-54781532 75 mg QD
Number of subjects	43	44	44
Title for AgeCategorical Units: subjects			
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	39	42	41
From 65 to 84 years	4	2	3

85 years and over	0	0	0

Title for AgeContinuous			
Units: years			
arithmetic mean	40.8	44.2	42.7
standard deviation	± 14.63	± 12.77	± 14.35
Title for Gender			
Units: subjects			
Female	11	19	19
Male	32	25	25

Reporting group values	JNJ-54781532 150 mg QD	JNJ-54781532 75 mg twice daily (BID)	Total
Number of subjects	44	44	219
Title for AgeCategorical			
Units: subjects			
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	43	41	206
From 65 to 84 years	1	3	13
85 years and over	0	0	0
Title for AgeContinuous			
Units: years			
arithmetic mean	38	40.5	
standard deviation	± 13.69	± 13.22	-
Title for Gender			
Units: subjects			
Female	22	18	89
Male	22	26	130

End points

End points reporting groups

Reporting group title	Placebo

Reporting group description:

Subjects received placebo once daily from Week 0 to Week 8. Subjects in clinical response at Week 8 continued to receive placebo through Week 32. Subjects not in clinical response at Week 8 received treatment with 150 milligram (mg) JNJ-54781532 orally once daily from Week 8 to Week 16. Among subjects who were not in clinical response at Week 8, subjects who achieved a partial Mayo score response (i.e., a decrease from baseline of greater than or equal to (>=) 3 in the partial Mayo score) at Week 16 continued to receive 150 mg JNJ-54781532 once daily through Week 32; subjects who did not achieve a partial Mayo score response were discontinued from study medication.

Reporting group title	JNJ-54781532 25 mg once daily (QD)

Reporting group description:

Subjects received 25 mg of JNJ-54781532 orally once daily from Week 0 to Week 8. Subjects in clinical response at Week 8 continued to receive the same dosage through Week 32. Subjects not in clinical response at Week 8 continued to receive the same dosage through Week 16. Among subjects who were not in clinical response at Week 8, subjects who achieved a partial Mayo score response (i.e. a decrease from baseline >= 3 in the partial Mayo score) at Week 16 continued to receive JNJ- 54781532 25 mg once daily through Week 32; subjects who did not achieve a partial Mayo score response were discontinued from study medication.

Reporting group title	JNJ-54781532 75 mg QD

Reporting group description:

Subjects received 75 mg of JNJ-54781532 orally once daily from Week 0 to Week 8. Subjects in clinical response at Week 8 continued to receive the same dosage through Week 32. Subjects not in clinical response at Week 8 continued to receive the same dosage through Week 16. Among subjects who were not in clinical response at Week 8, subjects who achieved a partial Mayo score response (i.e. a decrease from baseline >= 3 in the partial Mayo score) at Week 16 continued to receive JNJ- 54781532 75 mg once daily through Week 32; subjects who did not achieve a partial Mayo score response were discontinued from study medication.

Reporting group title	JNJ-54781532 150 mg QD

Reporting group description:

Subjects received 150 mg of JNJ-54781532 orally once daily from Week 0 to Week 8. Subjects in clinical response at Week 8 continued to receive the same dosage through Week 32. Subjects not in clinical response at Week 8 continue to receive the same dosage through Week 16. Among subjects who were not in clinical response at Week 8, subjects who achieved a partial Mayo score response (ie a decrease from baseline >= 3 in the partial Mayo score) at Week 16 continued to receive JNJ-54781532 150 mg once daily through Week 32; subjects who did not achieve a partial Mayo score response were discontinued from study medication.

Reporting group title	JNJ-54781532 75 mg twice daily (BID)

Reporting group description:

Subjects received 75 mg of JNJ-54781532 orally twice daily from Week 0 to Week 8. Subjects in clinical response at Week 8 continued to receive the same dosage through Week 32. Subjects not in clinical response at Week 8 continued to receive the same dosage through Week 16. Among subjects who were not in clinical response at Week 8, subjects who achieved a partial Mayo score response (ie a decrease from baseline >= 3 in the partial Mayo score) at Week 16 continued to receive JNJ- 54781532 75 mg twice daily through Week 32; subjects who did not achieve a partial Mayo score response were discontinued from study medication.

Primary: Change From Baseline in Mayo Score at Week 8

End point title	Change From Baseline in Mayo Score at Week 8

End point description:

The Mayo score is the primary tool for assessing ulcerative colitis activity. The Mayo score consists of 4 subscores (stool frequency, rectal bleeding, findings of endoscopy, and physician's global assessment) which range from 0 to 3. The Mayo score is calculated as the sum of these 4 subscores and can range between 0 and 12. A score of 3 to 5 points indicates mildly active disease; a score of 6 to 10 indicates moderately active disease; and a score of 11 to 12 indicates severe disease. Endoscopy subscores are based on the scores assigned by the central readers. The primary efficacy analysis population consisted

of all subjects who were randomized in this study. Here "n" signifies the number of subjects analysed for this endpoint.

End point type	Primary
End point timeframe:	
Baseline, Week 8	

End point values	Placebo	JNJ-54781532 25 mg once daily (QD)	JNJ-54781532 75 mg QD	JNJ-54781532 150 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	43	43	44	44
Units: Units on a scale				
arithmetic mean (standard deviation)				
Baseline (n= 43,43,44,44,44)	9 (± 1.14)	8.8 (± 1.6)	8.6 (± 1.53)	8.2 (± 1.61)
Change from baseline (n=43,43,44,44,44)	-2.4 (± 2.86)	-2.3 (± 2.81)	-3.1 (± 2.99)	-2.8 (± 2.46)

End point values	JNJ-54781532 75 mg twice daily (BID)			
Subject group type	Reporting group			
Number of subjects analysed	44			
Units: Units on a scale				
arithmetic mean (standard deviation)				
Baseline (n= 43,43,44,44,44)	8.3 (± 1.34)			
Change from baseline (n=43,43,44,44,44)	-3 (± 2.61)			

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Placebo v JNJ-54781532 25 mg once daily (QD)
Number of subjects included in analysis	86
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	= 0.88
Method	ANOVA

Notes:

[1] - 1 subject in JNJ-54781532 25 mg once daily (QD) did not have baseline Mayo score. Analysis based on pair wise comparisons was presented. The primary analysis to establish a dose-response relationship based on the Multiple Comparison Procedures with modeling techniques (MCP-Mod) method was not significant.

Statistical analysis title	Statistical analysis 2

Comparison groups	Placebo v JNJ-54781532 75 mg QD
Number of subjects included in analysis	87
Analysis specification	Pre-specified
Analysis type	superiority[2]
P-value	= 0.232
Method	ANOVA

Notes:

[2] - Analysis based on pairwise comparisons was presented. The primary analysis to establish a dose-response relationship based on the MCP-Mod method was not significant.

Statistical analysis title	Statistical analysis 3
Comparison groups	Placebo v JNJ-54781532 150 mg QD
Number of subjects included in analysis	87
Analysis specification	Pre-specified
Analysis type	superiority[3]
P-value	= 0.517
Method	ANOVA

Notes:

[3] - Analysis based on pairwise comparisons was presented. The primary analysis to establish a dose-response relationship based on the MCP-Mod method was not significant.

Statistical analysis title	Statistical analysis 4
Comparison groups	Placebo v JNJ-54781532 75 mg twice daily (BID)
Number of subjects included in analysis	87
Analysis specification	Pre-specified
Analysis type	superiority[4]
P-value	= 0.248
Method	ANOVA

Notes:

[4] - Analysis based on pair wise comparisons was presented. The primary analysis to establish a dose-response relationship based on the MCP-Mod method was not significant. The JNJ-54781532 75 mg twice daily (BID) group was not included in the dose response analysis due to lack of knowledge about its equivalent once daily dose.

Secondary: Number of Subjects with Clinical Response at Week 8

End point title	Number of Subjects with Clinical Response at Week 8

End point description:

Clinical response is defined as a decrease from baseline in the Mayo score by >= 30 percent (%) and >= 3 points, with either a decrease from baseline in the rectal bleeding subscore of >= 1 or a rectal bleeding subscore of 0 or 1. The primary efficacy analysis population consisted of all subjects including the 75 mg bid group who were randomized in this study.

End point type	Secondary

End point timeframe:

Week 8

End point values	Placebo	JNJ-54781532 25 mg once daily (QD)	JNJ-54781532 75 mg QD	JNJ-54781532 150 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	43	44	44	44
Units: Subjects				
number (not applicable)	17	15	24	24

End point values	JNJ-54781532 75 mg twice daily (BID)			
Subject group type	Reporting group			
Number of subjects analysed	44			
Units: Subjects				
number (not applicable)	24			

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Placebo v JNJ-54781532 25 mg once daily (QD)
Number of subjects included in analysis	87
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.974 [5]
Method	Cochran-Mantel-Haenszel

Notes:

[5] - The study was not powered to detect treatment differences for this endpoint.

Statistical analysis title	Statistical analysis 2
Comparison groups	Placebo v JNJ-54781532 75 mg QD
Number of subjects included in analysis	87
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.139 [6]
Method	Cochran-Mantel-Haenszel

Notes:

[6] - The study was not powered to detect treatment differences for this endpoint.

Statistical analysis title	Statistical analysis 3
Comparison groups	Placebo v JNJ-54781532 150 mg QD
Number of subjects included in analysis	87
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.134 [7]
Method	Cochran-Mantel-Haenszel

Notes:

[7] - The study was not powered to detect treatment differences for this endpoint.

Statistical analysis title	Statistical analysis 4
Comparison groups	Placebo v JNJ-54781532 75 mg twice daily (BID)
Number of subjects included in analysis	87
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.116 [8]
Method	Cochran-Mantel-Haenszel

Notes:

[8] - The study was not powered to detect treatment differences for this endpoint.

Secondary: Number of Subjects with Clinical Remission at Week 8

End point title	Number of Subjects with Clinical Remission at Week 8

End point description:

Clinical remission is defined as a Mayo score less than or equal to (<=) 2 points, with no individual subscore higher than (>)1. The primary efficacy analysis population consisted of all subjects including the 75 mg bid group who were randomized in this study.

End point type	Secondary

End point timeframe:

Week 8

End point values	Placebo	JNJ-54781532 25 mg once daily (QD)	JNJ-54781532 75 mg QD	JNJ-54781532 150 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	43	44	44	44
Units: Subjects				
number (not applicable)	3	7	7	12

End point values	JNJ-54781532 75 mg twice daily (BID)			
Subject group type	Reporting group			
Number of subjects analysed	44			
Units: Subjects				
number (not applicable)	7			

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	JNJ-54781532 25 mg once daily (QD) v Placebo

Number of subjects included in analysis	87
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.091 [9]
Method	Cochran-Mantel-Haenszel

Notes:

[9] - The study was not powered to detect treatment differences for this endpoint

Statistical analysis title	Statistical analysis 2
Comparison groups	Placebo v JNJ-54781532 75 mg QD
Number of subjects included in analysis	87
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.182 [10]
Method	Cochran-Mantel-Haenszel

Notes:

[10] - The study was not powered to detect treatment differences for this endpoint

Statistical analysis title	statistical analysis 3
Comparison groups	Placebo v JNJ-54781532 150 mg QD
Number of subjects included in analysis	87
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.013 [11]
Method	Cochran-Mantel-Haenszel

Notes:

[11] - The study was not powered to detect treatment differences for this endpoint

Statistical analysis title	Statistical analysis 4
Comparison groups	Placebo v JNJ-54781532 75 mg twice daily (BID)
Number of subjects included in analysis	87
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.177 [12]
Method	Cochran-Mantel-Haenszel

Notes:

[12] - The study was not powered to detect treatment differences for this endpoint

Secondary: Number of Subjects With Mucosal Healing at Week 8

End point title	Number of Subjects With Mucosal Healing at Week 8

End point description:

Mucosal healing is an improvement in the endoscopic appearance of the mucosa. An endoscopy subscore of the Mayo score of 0 or 1. The primary efficacy analysis population consisted of all subjects including the 75 mg bid group who were randomized in this study.

End point type	Secondary

End point timeframe:

Week 8

End point values	Placebo	JNJ-54781532 25 mg once daily (QD)	JNJ-54781532 75 mg QD	JNJ-54781532 150 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	43	44	44	44
Units: Subjects				
number (not applicable)	8	9	13	20

End point values	JNJ-54781532 75 mg twice daily (BID)			
Subject group type	Reporting group			
Number of subjects analysed	44			
Units: Subjects				
number (not applicable)	16			

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Placebo v JNJ-54781532 25 mg once daily (QD)
Number of subjects included in analysis	87
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.562 [13]
Method	Cochran-Mantel-Haenszel

Notes:

[13] - The study was not powered to detect treatment differences for this endpoint

Statistical analysis title	Statistical analysis 2
Comparison groups	Placebo v JNJ-54781532 75 mg QD
Number of subjects included in analysis	87
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.246 [14]
Method	Cochran-Mantel-Haenszel

Notes:

[14] - The study was not powered to detect treatment differences for this endpoint

Statistical analysis title	Statistical analysis 3
Comparison groups	Placebo v JNJ-54781532 150 mg QD

Number of subjects included in analysis	87
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.008 [15]
Method	Cochran-Mantel-Haenszel

Notes:

[15] - The study was not powered to detect treatment differences for this endpoint

Statistical analysis title	Statistical analysis 4
Comparison groups	Placebo v JNJ-54781532 75 mg twice daily (BID)
Number of subjects included in analysis	87
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.057 [16]
Method	Cochran-Mantel-Haenszel

Notes:

[16] - The study was not powered to detect treatment differences for this endpoint

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline up to 4 weeks after their last dose of study agent (Final safety visit)

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.1

Reporting groups

Reporting group title	Placebo

Reporting group description:

Subjects received placebo once daily from Week 0 to Week 8. Subjects in clinical response at Week 8 continued to receive placebo through Week 32. Subjects not in clinical response at Week 8 received treatment with 150 milligram (mg) JNJ-54781532 orally once daily from Week 8. For subjects who received JNJ-54781532 150 mg QD at Week 8 , adverse events are presented from Week 0 up to Week 8.

Reporting group title	JNJ-54781532 25 mg QD

Reporting group description:

Subjects received 25 mg of JNJ-54781532 orally once daily from Week 0 to Week 8. Subjects in clinical response at Week 8 continued to receive the same dosage through Week 32. Subjects not in clinical response at Week 8 continued to receive the same dosage through Week 16. Among subjects who were not in clinical response at Week 8, subjects who achieved a partial Mayo score response (i.e. a decrease from baseline >= 3 in the partial Mayo score) at Week 16 continued to receive JNJ- 54781532 25 mg once daily through Week 32; subjects who did not achieve a partial Mayo score response were discontinued from study medication.

Reporting group title	JNJ-54781532 75 mg QD

Reporting group description:

Subjects received 75 mg of JNJ-54781532 orally once daily from Week 0 to Week 8. Subjects in clinical response at Week 8 continued to receive the same dosage through Week 32. Subjects not in clinical response at Week 8 continued to receive the same dosage through Week 16. Among subjects who were not in clinical response at Week 8, subjects who achieved a partial Mayo score response (i.e. a decrease from baseline >= 3 in the partial Mayo score) at Week 16 continued to receive JNJ- 54781532 75 mg once daily through Week 32; subjects who did not achieve a partial Mayo score response were discontinued from study medication.

Reporting group title	JNJ-54781532 150 mg QD

Reporting group description:

Subjects received 150 mg of JNJ-54781532 orally once daily from Week 0 to Week 8. Subjects in clinical response at Week 8 continued to receive the same dosage through Week 32. Subjects not in clinical response at Week 8 continue to receive the same dosage through Week 16. Among subjects who were not in clinical response at Week 8, subjects who achieved a partial Mayo score response (ie a decrease from baseline >= 3 in the partial Mayo score) at Week 16 continued to receive JNJ-54781532 150 mg once daily through Week 32; subjects who did not achieve a partial Mayo score response were discontinued from study medication.

Reporting group title	JNJ-54781532 75 mg BID

Reporting group description:

Subjects received 75 mg of JNJ-54781532 orally twice daily from Week 0 to Week 8. Subjects in clinical response at Week 8 continued to receive the same dosage through Week 32. Subjects not in clinical response at Week 8 continued to receive the same dosage through Week 16. Among subjects who were not in clinical response at Week 8, subjects who achieved a partial Mayo score response (ie a decrease from baseline >= 3 in the partial Mayo score) at Week 16 continued to receive JNJ- 54781532 75 mg twice daily through Week 32; subjects who did not achieve a partial Mayo score response were discontinued from study medication..

Reporting group title	Placebo to JNJ-54781532 150 mg QD

Reporting group description:

Subjects received placebo once daily from Week 0 to Week 8. Subjects not in clinical response at Week 8 received treatment with 150 mg JNJ-54781532 orally once daily from Week 8 to Week 16. Among subjects who were not in clinical response at Week, subjects who achieved a partial Mayo score response (i.e., a decrease from baseline of greater than or equal to (>=) 3 in the partial Mayo score) at

Week 16 continued receiving 150 mg JNJ-54781532 orally once daily through Week 32. For subjects who received JNJ-54781532 150 mg QD at Week 8 , adverse events are presented from Week 8 up to final safety visit.

Serious adverse events	Placebo	JNJ-54781532 25 mg QD	JNJ-54781532 75 mg QD
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 43 (9.30%)	3 / 44 (6.82%)	3 / 44 (6.82%)
number of deaths (all causes)	1	0	0
number of deaths resulting from adverse events			
Investigations			
Clostridium Test Positive			
subjects affected / exposed	0 / 43 (0.00%)	0 / 44 (0.00%)	0 / 44 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lung Neoplasm			
subjects affected / exposed	0 / 43 (0.00%)	0 / 44 (0.00%)	0 / 44 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatic Neoplasm			
subjects affected / exposed	1 / 43 (2.33%)	0 / 44 (0.00%)	0 / 44 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Cardiac disorders			
Aortic Valve Incompetence			
subjects affected / exposed	1 / 43 (2.33%)	0 / 44 (0.00%)	0 / 44 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mitral Valve Incompetence			
subjects affected / exposed	1 / 43 (2.33%)	0 / 44 (0.00%)	0 / 44 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			

subjects affected / exposed	0 / 43 (0.00%)	2 / 44 (4.55%)	0 / 44 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Colitis Ulcerative			
subjects affected / exposed	2 / 43 (4.65%)	1 / 44 (2.27%)	3 / 44 (6.82%)
occurrences causally related to treatment / all	0 / 2	0 / 1	2 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Megacolon			
subjects affected / exposed	1 / 43 (2.33%)	0 / 44 (0.00%)	0 / 44 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	JNJ-54781532 150 mg QD	JNJ-54781532 75 mg BID	Placebo to JNJ-54781532 150 mg QD
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 44 (4.55%)	4 / 44 (9.09%)	2 / 21 (9.52%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Investigations			
Clostridium Test Positive			
subjects affected / exposed	0 / 44 (0.00%)	1 / 44 (2.27%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lung Neoplasm			
subjects affected / exposed	0 / 44 (0.00%)	0 / 44 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatic Neoplasm			
subjects affected / exposed	0 / 44 (0.00%)	0 / 44 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Aortic Valve Incompetence			

subjects affected / exposed	0 / 44 (0.00%)	0 / 44 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mitral Valve Incompetence			
subjects affected / exposed	0 / 44 (0.00%)	0 / 44 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 44 (2.27%)	0 / 44 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Colitis Ulcerative			
subjects affected / exposed	1 / 44 (2.27%)	3 / 44 (6.82%)	2 / 21 (9.52%)
occurrences causally related to treatment / all	0 / 1	2 / 3	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Megacolon			
subjects affected / exposed	0 / 44 (0.00%)	0 / 44 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Placebo	JNJ-54781532 25 mg QD	JNJ-54781532 75 mg QD
Total subjects affected by non-serious adverse events			
subjects affected / exposed	13 / 43 (30.23%)	16 / 44 (36.36%)	23 / 44 (52.27%)
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	0 / 43 (0.00%)	0 / 44 (0.00%)	1 / 44 (2.27%)
occurrences (all)	0	0	1
Aspartate Aminotransferase Increased			
subjects affected / exposed	0 / 43 (0.00%)	0 / 44 (0.00%)	1 / 44 (2.27%)
occurrences (all)	0	0	1

Blood Creatine Phosphokinase Increased			
subjects affected / exposed	2 / 43 (4.65%)	0 / 44 (0.00%)	10 / 44 (22.73%)
occurrences (all)	2	0	12
Lymphocyte Count Decreased			
subjects affected / exposed	0 / 43 (0.00%)	3 / 44 (6.82%)	0 / 44 (0.00%)
occurrences (all)	0	4	0
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 43 (2.33%)	4 / 44 (9.09%)	0 / 44 (0.00%)
occurrences (all)	1	4	0
Blood and lymphatic system disorders			
Anaemia			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 43 (6.98%)	3 / 44 (6.82%)	1 / 44 (2.27%)
occurrences (all)	3	4	1
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 43 (0.00%)	1 / 44 (2.27%)	3 / 44 (6.82%)
occurrences (all)	0	1	3
Gastrointestinal disorders			
Colitis Ulcerative			
subjects affected / exposed	2 / 43 (4.65%)	4 / 44 (9.09%)	2 / 44 (4.55%)
occurrences (all)	2	5	2
Dyspepsia			
subjects affected / exposed	0 / 43 (0.00%)	0 / 44 (0.00%)	1 / 44 (2.27%)
occurrences (all)	0	0	1
Nausea			
subjects affected / exposed	0 / 43 (0.00%)	3 / 44 (6.82%)	0 / 44 (0.00%)
occurrences (all)	0	3	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 43 (2.33%)	1 / 44 (2.27%)	6 / 44 (13.64%)
occurrences (all)	1	1	7
Myalgia			
subjects affected / exposed	0 / 43 (0.00%)	1 / 44 (2.27%)	1 / 44 (2.27%)
occurrences (all)	0	1	1

Infections and infestations			
Influenza			
subjects affected / exposed	1 / 43 (2.33%)	0 / 44 (0.00%)	3 / 44 (6.82%)
occurrences (all)	1	0	3
Nasopharyngitis			
subjects affected / exposed	2 / 43 (4.65%)	2 / 44 (4.55%)	3 / 44 (6.82%)
occurrences (all)	2	3	5
Respiratory Tract Infection Viral			
subjects affected / exposed	2 / 43 (4.65%)	3 / 44 (6.82%)	1 / 44 (2.27%)
occurrences (all)	2	3	1
Upper Respiratory Tract Infection			
subjects affected / exposed	1 / 43 (2.33%)	0 / 44 (0.00%)	1 / 44 (2.27%)
occurrences (all)	1	0	1
Urinary Tract Infection			
subjects affected / exposed	0 / 43 (0.00%)	0 / 44 (0.00%)	1 / 44 (2.27%)
occurrences (all)	0	0	1

Non-serious adverse events	JNJ-54781532 150 mg QD	JNJ-54781532 75 mg BID	Placebo to JNJ-54781532 150 mg QD
Total subjects affected by non-serious adverse events			
subjects affected / exposed	27 / 44 (61.36%)	22 / 44 (50.00%)	6 / 21 (28.57%)
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	1 / 44 (2.27%)	3 / 44 (6.82%)	1 / 21 (4.76%)
occurrences (all)	2	4	1
Aspartate Aminotransferase Increased			
subjects affected / exposed	1 / 44 (2.27%)	4 / 44 (9.09%)	1 / 21 (4.76%)
occurrences (all)	2	5	1
Blood Creatine Phosphokinase Increased			
subjects affected / exposed	6 / 44 (13.64%)	7 / 44 (15.91%)	2 / 21 (9.52%)
occurrences (all)	7	12	2
Lymphocyte Count Decreased			
subjects affected / exposed	2 / 44 (4.55%)	0 / 44 (0.00%)	0 / 21 (0.00%)
occurrences (all)	2	0	0
Nervous system disorders			

Headache			
subjects affected / exposed	1 / 44 (2.27%)	4 / 44 (9.09%)	0 / 21 (0.00%)
occurrences (all)	1	5	0
Blood and lymphatic system disorders			
Anaemia			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 44 (6.82%)	4 / 44 (9.09%)	1 / 21 (4.76%)
occurrences (all)	5	4	1
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	2 / 44 (4.55%)	1 / 44 (2.27%)	1 / 21 (4.76%)
occurrences (all)	4	1	1
Gastrointestinal disorders			
Colitis Ulcerative			
subjects affected / exposed	9 / 44 (20.45%)	6 / 44 (13.64%)	1 / 21 (4.76%)
occurrences (all)	17	6	1
Dyspepsia			
subjects affected / exposed	3 / 44 (6.82%)	2 / 44 (4.55%)	0 / 21 (0.00%)
occurrences (all)	4	2	0
Nausea			
subjects affected / exposed	2 / 44 (4.55%)	1 / 44 (2.27%)	0 / 21 (0.00%)
occurrences (all)	4	1	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 44 (4.55%)	2 / 44 (4.55%)	0 / 21 (0.00%)
occurrences (all)	2	2	0
Myalgia			
subjects affected / exposed	1 / 44 (2.27%)	3 / 44 (6.82%)	0 / 21 (0.00%)
occurrences (all)	1	3	0
Infections and infestations			
Influenza			
subjects affected / exposed	1 / 44 (2.27%)	1 / 44 (2.27%)	1 / 21 (4.76%)
occurrences (all)	1	1	1
Nasopharyngitis			
subjects affected / exposed	2 / 44 (4.55%)	3 / 44 (6.82%)	2 / 21 (9.52%)
occurrences (all)	2	6	2

Respiratory Tract Infection Viral			
subjects affected / exposed	0 / 44 (0.00%)	1 / 44 (2.27%)	0 / 21 (0.00%)
occurrences (all)	0	2	0
Upper Respiratory Tract Infection			
subjects affected / exposed	3 / 44 (6.82%)	0 / 44 (0.00%)	1 / 21 (4.76%)
occurrences (all)	3	0	1
Urinary Tract Infection			
subjects affected / exposed	3 / 44 (6.82%)	1 / 44 (2.27%)	0 / 21 (0.00%)
occurrences (all)	3	2	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 October 2013	Amendment was done to add an ECG at the final safety visit, eligibility criteria were revised to clarify the threshold for glomerular filtration rate, permit fentanyl use during endoscopy, and the ineligibility of subjects who were pregnant, nursing or planning pregnancy. In addition, the amendment clarified that medications that are CYP3A substrates with a narrow therapeutic window are prohibited medications.
21 January 2014	Amendment was done to exclude subjects with a diagnosis of monoclonal gammopathy of undetermined significance. In addition, criteria for discontinuation of study agent for subjects who develop an opportunistic infection or worsening of ulcerative colitis was provided.
31 July 2014	Amendment was done to allow subjects with appropriately treated latent tuberculosis (TB) and persistently indeterminate QuantiFERON (QFT)-TB Gold test results to enter study. Eligibility criteria were updated to reference the first dose of study agent for the duration of stable dosing for allowed ulcerative colitis (UC) medications or discontinuation of prohibited medications. A maximal threshold for screening creatine kinase levels was removed and guidance for targeted examinations following identification of abnormal CK levels and discontinuation of study agent related to CK elevations was updated. Additionally, a discontinuation criterion for elevated serum creatinine in the presence of reduced glomerular filtration was added.
02 December 2014	Amendment included an update to an eligibility criterion to exclude subjects with a shortened QT interval or who were taking medications that are known to shorten the QT interval. Additionally, the minimum duration of required treatment for latent TB prior to the first dose of study agent was clarified.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

This study is limited by its small sample size. The study was powered at 80% for detecting a dose response signal for JNJ-54781532 based on the primary endpoint, and was not powered to detect treatment differences for the major secondary endpoints.

Notes: