Clinical trial results:
A Phase 2a Study Evaluating the Safety, Efficacy, and Pharmacodynamic Effects of ABT-981 in Patients with Knee Osteoarthritis

Summary

EudraCT number	2013-003467-60
Trial protocol	DK GB NL ES IT
Global end of trial date	13 December 2016

Results information

Result version number	v2
This version publication date	10 July 2019
First version publication date	06 December 2017
Version creation reason	• Correction of full data set correct values in two endpoint descriptions

Trial information

Trial identification

Sponsor protocol code	M13-741

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02087904
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AbbVie Deutschland GmbH & Co.KG
Sponsor organisation address	AbbVie House, Vanwall Business Park, Vanwall Road, Maidenhead, Berkshire, United Kingdom, SL6-4UB
Public contact	Marc Levesque, MD, Abbvie, 1 847-936-7855, marc.levesque@abbvie.com
Scientific contact	Marc Levesque, MD, Abbvie, 1 847-936-7855, marc.levesque@abbvie.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	13 December 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	13 December 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the effect of ABT-981 on osteoarthritis (OA) knee pain using the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) at Week 16 and synovitis/effusion volume of the index knee using quantitative measures and semi-quantitative magnetic resonance imaging (MRI) scoring at Week 26 in subjects with knee osteoarthritis.

Protection of trial subjects:

Participant and/or legal guardian read and understood the information provided about the study and gave written permission.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	04 June 2014
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	Spain: 58
Country: Number of subjects enrolled	Netherlands: 2
Country: Number of subjects enrolled	United Kingdom: 1
Country: Number of subjects enrolled	Denmark: 61
Country: Number of subjects enrolled	France: 3
Country: Number of subjects enrolled	Italy: 3
Country: Number of subjects enrolled	Australia: 3
Country: Number of subjects enrolled	Canada: 33
Country: Number of subjects enrolled	Mexico: 31
Country: Number of subjects enrolled	Puerto Rico: 5
Country: Number of subjects enrolled	United States: 150
Worldwide total number of subjects	350
EEA total number of subjects	128

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)	219
From 65 to 84 years	131
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The study included a screening period (approximately 45 days prior to first study drug dose) and a washout period (5 half-lives of the longest acting analgesic used, or 48 hours, whichever was longer, in which all standard of care analgesic medications were discontinued prior to the first study drug dose).

Pre-assignment period milestones

Number of subjects started	350
Number of subjects completed	347

Pre-assignment subject non-completion reasons

Reason: Number of subjects	did not receive study drug: 3

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	Investigator, Carer, Assessor, Subject

Blinding implementation details:

The study was conducted in a double-blind manner such that the investigator and subjects were blinded to the treatment assignments. All clinical site personnel, except for the unblinded licensed pharmacist or unblinded, qualified pharmacy technician and an unblinded monitor, remained blinded to the treatment.

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Matching placebo SC E2W

Arm type	Placebo
Investigational medicinal product name	placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Study drug (placebo) was provided as a lyophilized powder in vials that were reconstituted to a solution for injection at the clinical site by the unblinded pharmacist or unblinded, qualified designees as permitted by local/state law.

Arm title	ABT-981 25 mg

Arm description:

25 mg ABT-981 SC E2W

Arm type	Experimental

Investigational medicinal product name	ABT-981
Investigational medicinal product code	
Other name	lutikizumab
Pharmaceutical forms	Powder for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Study drug (ABT-981) was provided as a lyophilized powder in vials that were reconstituted to a solution for injection at the clinical site by the unblinded pharmacist or unblinded, qualified designees as permitted by local/state law.

Arm title	ABT-981 100 mg

Arm description:

100 mg ABT-981 SC E2W

Arm type	Experimental
Investigational medicinal product name	ABT-981
Investigational medicinal product code	
Other name	lutikizumab
Pharmaceutical forms	Powder for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Study drug (ABT-981) was provided as a lyophilized powder in vials that were reconstituted to a solution for injection at the clinical site by the unblinded pharmacist or unblinded, qualified designees as permitted by local/state law.

Arm title	ABT-981 200 mg

Arm description:

200 mg ABT-981 SC E2W

Arm type	Experimental
Investigational medicinal product name	ABT-981
Investigational medicinal product code	
Other name	lutikizumab
Pharmaceutical forms	Powder for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Study drug (ABT-981) was provided as a lyophilized powder in vials that were reconstituted to a solution for injection at the clinical site by the unblinded pharmacist or unblinded, qualified designees as permitted by local/state law.

Number of subjects in period 1[1]	Placebo	ABT-981 25 mg	ABT-981 100 mg
Started	85	89	85
Completed	60	70	65
Not completed	25	19	20
Consent withdrawn by subject	8	3	7
Not specified	6	2	4
Adverse event	8	4	4
Lost to follow-up	-	4	2
Lack of efficacy	3	6	3

Number of subjects in period 1[1]	ABT-981 200 mg
Started	88
Completed	64
Not completed	24
Consent withdrawn by subject	4
Not specified	4
Adverse event	12
Lost to follow-up	2
Lack of efficacy	2

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Three subjects did not receive study drug.

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Matching placebo SC E2W	
Reporting group title	ABT-981 25 mg
Reporting group description:	
25 mg ABT-981 SC E2W	
Reporting group title	ABT-981 100 mg
Reporting group description:	
100 mg ABT-981 SC E2W	
Reporting group title	ABT-981 200 mg
Reporting group description:	
200 mg ABT-981 SC E2W	

Reporting group values	Placebo	ABT-981 25 mg	ABT-981 100 mg
Number of subjects	85	89	85
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean	59.53	61.63	60.21
standard deviation	± 8.850	± 7.546	± 8.194
Gender categorical			
Units: Subjects			
Female	52	63	53
Male	33	26	32

Reporting group values	ABT-981 200 mg	Total	
Number of subjects	88	347	
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean	59.05		
standard deviation	± 10.273	-	
Gender categorical			
Units: Subjects			
Female	57	225	
Male	31	122	

End points

End points reporting groups	
Reporting group title	Placebo
Reporting group description: Matching placebo SC E2W	
Reporting group title	ABT-981 25 mg
Reporting group description: 25 mg ABT-981 SC E2W	
Reporting group title	ABT-981 100 mg
Reporting group description: 100 mg ABT-981 SC E2W	
Reporting group title	ABT-981 200 mg
Reporting group description: 200 mg ABT-981 SC E2W	

Primary: Change from Baseline in WOMAC Pain Scores of the Index Knee at Week 16

End point title	Change from Baseline in WOMAC Pain Scores of the Index Knee at Week 16

End point description:

The WOMAC was developed to assess pain, stiffness, and physical function in subjects with hip and/or knee osteoarthritis. The WOMAC consists of 24 items divided into 3 subscales: Pain (5 items); Stiffness (2 items); and Physical Function (17 items). Each item is rated on an 11-point (0 to 10) numerical rating scale (NRS). The pain sub-score has a range of 0 (no pain) to 50 (maximum pain). A negative change from baseline indicates improvement.

Modified Intent to Treat population: all subjects who received at least 1 dose of study drug, LOCF (missing responses were imputed by calculation based on the last non-missing post-baseline component values).

End point type	Primary

End point timeframe:

Baseline, Week 16

End point values	Placebo	ABT-981 25 mg	ABT-981 100 mg	ABT-981 200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	85	88	84	88
Units: units on a scale				
least squares mean (confidence interval 95%)	-8.9 (-10.96 to -6.90)	-9.2 (-11.23 to -7.23)	-11.8 (-13.84 to -9.75)	-10.1 (-12.10 to -8.10)

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v ABT-981 25 mg

Number of subjects included in analysis	173
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.834 [1]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.13
upper limit	2.53

Notes:

[1] - P-value for test of difference between ABT-981 25 mg dose group and Placebo at each post-baseline time point was from an ANCOVA model with treatment, age, and Kellgren-Lawrence (K-L) grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v ABT-981 100 mg
Number of subjects included in analysis	169
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.05 [2]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-2.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.73
upper limit	0.01

Notes:

[2] - P-value for test of difference between ABT-981 100 mg dose group and Placebo at each post-baseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo v ABT-981 200 mg
Number of subjects included in analysis	173
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.415 [3]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4
upper limit	1.66

Notes:

[3] - P-value for test of difference between ABT-981 200 mg dose group and Placebo at each post-baseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Primary: Change from Baseline in Quantitative Synovitis of the Index Knee at Week 26

End point title	Change from Baseline in Quantitative Synovitis of the Index Knee at Week 26
End point description:	
Modified Intent to Treat population: all subjects who received at least 1 dose of study drug, observed cases.	
End point type	Primary
End point timeframe:	
Baseline, Week 26	

End point values	Placebo	ABT-981 25 mg	ABT-981 100 mg	ABT-981 200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	59	65	59	63
Units: mm				
least squares mean (confidence interval 95%)	-0.05 (-0.107 to 0.011)	0.01 (-0.045 to 0.068)	-0.08 (-0.134 to -0.016)	0.01 (-0.047 to 0.067)

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v ABT-981 25 mg
Number of subjects included in analysis	124
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.145 [4]
Method	ANCOVA
Parameter estimate	LS
Point estimate	0.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.021
upper limit	0.141

Notes:

[4] - P-value for test of difference between ABT-981 25 mg dose group and Placebo at each post-baseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v ABT-981 100 mg

Number of subjects included in analysis	118
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.52 [5]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.11
upper limit	0.056

Notes:

[5] - P-value for test of difference between ABT-981 100 mg dose group and Placebo at each post-baseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo v ABT-981 200 mg
Number of subjects included in analysis	122
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.159 [6]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	0.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.023
upper limit	0.139

Notes:

[6] - P-value for test of difference between ABT-981 200 mg dose group and Placebo at each post-baseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Primary: Change from Baseline in Effusion Volume of the Index Knee at Week 26

End point title	Change from Baseline in Effusion Volume of the Index Knee at Week 26

End point description:

Modified Intent to Treat population: all subjects who received at least 1 dose of study drug, observed cases.

End point type	Primary

End point timeframe:

Baseline, Week 26

End point values	Placebo	ABT-981 25 mg	ABT-981 100 mg	ABT-981 200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	60	69	67	68
Units: mL				
least squares mean (confidence interval 95%)	0.03 (-2.498 to 2.562)	0.26 (-2.113 to 2.624)	-1.04 (-3.421 to 1.347)	-1.49 (-3.868 to 0.898)

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v ABT-981 25 mg
Number of subjects included in analysis	129
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.897 [7]
Method	ANCOVA
Parameter estimate	LS mean Difference
Point estimate	0.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.193
upper limit	3.642

Notes:

[7] - P-value for test of difference between ABT-981 25 mg dose group and Placebo at each post-baseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v ABT-981 100 mg
Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.542 [8]
Method	ANCOVA
Parameter estimate	LS mean Difference
Point estimate	-1.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.515
upper limit	2.377

Notes:

[8] - P-value for test of difference between ABT-981 100 dose group and Placebo at each post-baseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo v ABT-981 200 mg

Number of subjects included in analysis	128
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.385 [9]
Method	ANCOVA
Parameter estimate	LS mean Difference
Point estimate	-1.52
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.95
upper limit	1.916

Notes:

[9] - P-value for test of difference between ABT-981 200 dose group and Placebo at each post-baseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Primary: Change from Baseline in Whole-Organ Magnetic Resonance Imaging Score (WORMS) Semi-Quantitative Synovitis/Effusion Score of the Index Knee at Week 26

End point title	Change from Baseline in Whole-Organ Magnetic Resonance Imaging Score (WORMS) Semi-Quantitative Synovitis/Effusion Score of the Index Knee at Week 26

End point description:

Semi-quantitative synovitis/effusion volume WORMS scores were scored as normal (0), < 33% of maximum estimated distention (1), 33% – 66% of maximum estimated distention (2), or > 66% of maximum estimated distention (3).

Modified Intent to Treat population: all subjects who received at least 1 dose of study drug, observed cases.

End point type	Primary

End point timeframe:

Baseline, Week 26

End point values	Placebo	ABT-981 25 mg	ABT-981 100 mg	ABT-981 200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	70	76	70	75
Units: units on a scale				
least squares mean (confidence interval 95%)	0.07 (-0.057 to 0.193)	-0.01 (-0.130 to 0.113)	-0.08 (-0.205 to 0.043)	-0.07 (-0.196 to 0.048)

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v ABT-981 25 mg

Number of subjects included in analysis	146
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.384 [10]
Method	ANCOVA
Parameter estimate	LS mean Difference
Point estimate	-0.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.249
upper limit	0.096

Notes:

[10] - P-value for test of difference between ABT-981 25 mg dose group and Placebo at each post-baseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v ABT-981 100 mg
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.095 [11]
Method	ANCOVA
Parameter estimate	LS mean Difference
Point estimate	-0.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.324
upper limit	0.026

Notes:

[11] - P-value for test of difference between ABT-981 100 mg dose group and Placebo at each post-baseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo v ABT-981 200 mg
Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.106 [12]
Method	ANCOVA
Parameter estimate	LS mean Difference
Point estimate	-0.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.314
upper limit	0.03

Notes:

[12] - P-value for test of difference between ABT-981 200 mg dose group and Placebo at each post-baseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Secondary: Change From Baseline in WOMAC Physical Function Scores of the Index Knee at Week 16

End point title	Change From Baseline in WOMAC Physical Function Scores of the Index Knee at Week 16

End point description:

The WOMAC was developed to assess pain, stiffness, and physical function in subjects with hip and/or knee osteoarthritis. The WOMAC consists of 24 items divided into 3 subscales: Pain (5 items); Stiffness (2 items); and Physical Function (17 items). Each item is rated on an 11-point (0 to 10) NRS. The WOMAC physical function subscale score was 0 (normal) to 170 (least physical function). A negative change from baseline indicates improvement.

Modified intent to Treat population: all subjects who received at least 1 dose of study drug, LOCF (missing responses were imputed by calculation based on the last non-missing post-baseline component values).

End point type	Secondary

End point timeframe:

Baseline, Week 16

End point values	Placebo	ABT-981 25 mg	ABT-981 100 mg	ABT-981 200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	85	88	84	87
Units: units on a scale				
least squares mean (confidence interval 95%)	-28.7 (-35.30 to -22.15)	-29.8 (-36.27 to -23.32)	-36.3 (-42.90 to -29.69)	-32.1 (-38.64 to -25.63)

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v ABT-981 25 mg
Number of subjects included in analysis	173
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.818 [13]
Method	ANCOVA
Parameter estimate	LS mean Difference
Point estimate	-1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.22
upper limit	8.08

Notes:

[13] - P-value for test of difference between ABT-981 25 mg dose group and placebo at each post-baseline time point is from an ANCOVA model with treatment, age, K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v ABT-981 100 mg
Number of subjects included in analysis	169
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.109 [14]
Method	ANCOVA
Parameter estimate	LS mean Difference
Point estimate	-7.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-16.83
upper limit	1.69

Notes:

[14] - P-value for test of difference between ABT-981 100 mg dose group and placebo at each post-baseline time point is from an ANCOVA model with treatment, age, K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo v ABT-981 200 mg
Number of subjects included in analysis	172
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.465 [15]
Method	ANCOVA
Parameter estimate	LS mean Difference
Point estimate	-3.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.58
upper limit	5.76

Notes:

[15] - P-value for test of difference between ABT-981 200 mg dose group and placebo at each post-baseline time point is from an ANCOVA model with treatment, age, K-L grade as the main factors and baseline as a covariate.

Secondary: Change From Baseline in WOMAC Physical Function Scores of the Index Knee at Week 26

End point title	Change From Baseline in WOMAC Physical Function Scores of the Index Knee at Week 26

End point description:

The WOMAC was developed to assess pain, stiffness, and physical function in subjects with hip and/or knee osteoarthritis. The WOMAC consists of 24 items divided into 3 subscales: Pain (5 items); Stiffness (2 items); and Physical Function (17 items). Each item is rated on an 11-point (0 to 10) NRS. The WOMAC physical function subscale score was 0 (normal) to 170 (least physical function). A negative change from baseline indicates improvement.

Modified Intent to Treat population: all subjects who received at least 1 dose of study drug, LOCF (missing responses were imputed by calculation based on the last non-missing post-baseline component values).

End point type	Secondary

End point timeframe:

Baseline, Week 26

End point values	Placebo	ABT-981 25 mg	ABT-981 100 mg	ABT-981 200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	85	88	84	87
Units: units on a scale				
least squares mean (confidence interval 95%)	-29.7 (-36.61 to -22.75)	-31.8 (-38.62 to -24.98)	-38.9 (-45.83 to -31.92)	-36.9 (-43.71 to -30.00)

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v ABT-981 25 mg
Number of subjects included in analysis	173
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.666 [16]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-2.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.76
upper limit	7.52

Notes:

[16] - P-value for test of difference between ABT-981 25 mg dose group and placebo at each postbaseline time point is from an ANCOVA model with treatment, age, K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v ABT-981 100 mg
Number of subjects included in analysis	169
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.065 [17]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-9.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-18.95
upper limit	0.56

Notes:

[17] - P-value for test of difference between ABT-981 100 mg dose group and placebo at each postbaseline time point is from an ANCOVA model with treatment, age, K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo v ABT-981 200 mg
Number of subjects included in analysis	172
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.145 [18]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-7.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-16.84
upper limit	2.49

Notes:

[18] - P-value for test of difference between ABT-981 200 mg dose group and placebo at each postbaseline time point is from an ANCOVA model with treatment, age, K-L grade as the main factors and baseline as a covariate.

Secondary: Change From Baseline in WOMAC Physical Function Scores of the Index Knee at Week 52

End point title	Change From Baseline in WOMAC Physical Function Scores of the Index Knee at Week 52

End point description:

The WOMAC was developed to assess pain, stiffness, and physical function in subjects with hip and/or knee osteoarthritis. The WOMAC consists of 24 items divided into 3 subscales: Pain (5 items); Stiffness (2 items); and Physical Function (17 items). Each item is rated on an 11-point (0 to 10) NRS. The WOMAC physical function subscale score was 0 (normal) to 170 (least physical function). A negative change from baseline indicates improvement.

Modified Intent to Treat population: all subjects who received at least 1 dose of study drug, LOCF (missing responses were imputed by calculation based on the last non-missing post-baseline component values).

End point type	Secondary

End point timeframe:

Baseline, Week 52

End point values	Placebo	ABT-981 25 mg	ABT-981 100 mg	ABT-981 200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	85	88	84	87
Units: units on a scale				
least squares mean (confidence interval 95%)	-32.9 (-40.66 to -25.12)	-36.1 (-43.76 to -28.46)	-38.7 (-46.52 to -30.92)	-39.7 (-47.37 to -32.00)

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v ABT-981 25 mg

Number of subjects included in analysis	173
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.558 [19]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-3.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.03
upper limit	7.59

Notes:

[19] - P-value for test of difference between ABT-981 25 mg dose group and placebo at each postbaseline time point is from an ANCOVA model with treatment, age, K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v ABT-981 100 mg
Number of subjects included in analysis	169
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.295 [20]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-5.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-16.77
upper limit	5.11

Notes:

[20] - P-value for test of difference between ABT-981 100 mg dose group and placebo at each postbaseline time point is from an ANCOVA model with treatment, age, K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo v ABT-981 200 mg
Number of subjects included in analysis	172
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.218 [21]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-6.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-17.63
upper limit	4.04

Notes:

[21] - P-value for test of difference between ABT-981 200 mg dose group and placebo at each postbaseline time point is from an ANCOVA model with treatment, age, K-L grade as the main factors and baseline as a covariate.

Secondary: Change From Baseline in WOMAC Pain Scores of the Index Knee at Week 26

End point title	Change From Baseline in WOMAC Pain Scores of the Index Knee at Week 26

End point description:

The WOMAC was developed to assess pain, stiffness, and physical function in subjects with hip and/or knee osteoarthritis. The WOMAC consists of 24 items divided into 3 subscales: Pain (5 items); Stiffness (2 items); and Physical Function (17 items). Each item is rated on an 11-point (0 to 10) numerical rating scale (NRS). The pain sub-score has a range of 0 (no pain) to 50 (maximum pain). A negative change from baseline indicates improvement.

Modified intent to Treat population: all subjects who received at least 1 dose of study drug, LOCF (missing responses were imputed by calculation based on the last non-missing post-baseline component values).

End point type	Secondary

End point timeframe:

Baseline, Week 26

End point values	Placebo	ABT-981 25 mg	ABT-981 100 mg	ABT-981 200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	85	88	84	88
Units: units on a scale				
least squares mean (confidence interval 95%)	-9.2 (-11.29 to -7.07)	-9.8 (-11.90 to -7.75)	-11.9 (-13.99 to -9.76)	-11.6 (-13.65 to -9.51)

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v ABT-981 25 mg
Number of subjects included in analysis	173
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.664 [22]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.58
upper limit	2.28

Notes:

[22] - P-value for test of difference between ABT-981 25 mg dose group and placebo at each postbaseline time point is from an ANCOVA model with treatment, age, K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v ABT-981 100 mg
Number of subjects included in analysis	169
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.075 [23]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-2.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.67
upper limit	0.28

Notes:

[23] - P-value for test of difference between ABT-981 100 mg dose group and placebo at each postbaseline time point is from an ANCOVA model with treatment, age, K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo v ABT-981 200 mg
Number of subjects included in analysis	173
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.107 [24]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-2.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.33
upper limit	0.52

Notes:

[24] - P-value for test of difference between ABT-981 200 mg dose group and placebo at each postbaseline time point is from an ANCOVA model with treatment, age, K-L grade as the main factors and baseline as a covariate.

Secondary: Change From Baseline in WOMAC Pain Scores of the Index Knee at Week 52

End point title	Change From Baseline in WOMAC Pain Scores of the Index Knee at Week 52

End point description:

The WOMAC was developed to assess pain, stiffness, and physical function in subjects with hip and/or knee osteoarthritis. The WOMAC consists of 24 items divided into 3 subscales: Pain (5 items); Stiffness (2 items); and Physical Function (17 items). Each item is rated on an 11-point (0 to 10) numerical rating scale (NRS). The pain sub-score has a range of 0 (no pain) to 50 (maximum pain). A negative change from baseline indicates improvement.

Modified intent to Treat population: all subjects who received at least 1 dose of study drug, LOCF (missing responses were imputed by calculation based on the last non-missing post-baseline component values).

End point type	Secondary

End point timeframe:

Baseline, Week 52

End point values	Placebo	ABT-981 25 mg	ABT-981 100 mg	ABT-981 200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	85	88	84	88
Units: units on a scale				
least squares mean (confidence interval 95%)	-10.0 (-12.24 to -7.68)	-11.0 (-13.29 to -8.80)	-12.1 (-14.42 to -9.84)	-12.2 (-14.49 to -10.00)

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v ABT-981 25 mg
Number of subjects included in analysis	173
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5 [25]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.26
upper limit	2.08

Notes:

[25] - P-value for test of difference between ABT-981 25 mg dose group and placebo at each postbaseline time point is from an ANCOVA model with treatment, age, K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v ABT-981 100 mg
Number of subjects included in analysis	169
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.186 [26]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-2.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.39
upper limit	1.05

Notes:

[26] - P-value for test of difference between ABT-981 100 mg dose group and placebo at each postbaseline time point is from an ANCOVA model with treatment, age, K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo v ABT-981 200 mg
Number of subjects included in analysis	173
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.157 [27]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-2.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.46
upper limit	0.88

Notes:

[27] - P-value for test of difference between ABT-981 200 mg dose group and placebo at each postbaseline time point is from an ANCOVA model with treatment, age, K-L grade as the main factors and baseline as a covariate.

Secondary: Change from Baseline in Global Total Bone Marrow Lesion (BML) Score of the Index Knee Magnetic Resonance Imaging (MRI) at Week 26

End point title	Change from Baseline in Global Total Bone Marrow Lesion (BML) Score of the Index Knee Magnetic Resonance Imaging (MRI) at Week 26

End point description:

BMLs in 15 regions were measured with MRI, and graded as 0 (normal), 1 (mild; < 25% of region), 2 (moderate; 25% – 50% of region), or 3 (severe; > 50% of region). The global total BML score was the sum of the 15 component scores, and ranged from 0 (normal) to 45 (severe).

Modified Intent to Treat population: all subjects who received at least 1 dose of study drug, observed cases.

End point type	Secondary

End point timeframe:

Baseline, Week 26

End point values	Placebo	ABT-981 25 mg	ABT-981 100 mg	ABT-981 200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	69	76	69	75
Units: units on a scale				
least squares mean (confidence interval 95%)	0.1 (-0.24 to 0.43)	0.3 (0.01 to 0.65)	-0.0 (-0.37 to 0.29)	0.1 (-0.22 to 0.43)

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	ABT-981 25 mg v Placebo

Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.319 [28]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.23
upper limit	0.69

Notes:

[28] - P-value for test of difference between ABT-981 25 mg dose group and Placebo at each post-baseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v ABT-981 100 mg
Number of subjects included in analysis	138
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.564 [29]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6
upper limit	0.33

Notes:

[29] - P-value for test of difference between ABT-981 100 mg dose group and Placebo at each post-baseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo v ABT-981 200 mg
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.966 [30]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.45
upper limit	0.47

Notes:

[30] - P-value for test of difference between ABT-981 200 mg dose group and Placebo at each post-baseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Secondary: Change from Baseline in Global Total BML Score of the Index Knee MRI at Week 52

End point title	Change from Baseline in Global Total BML Score of the Index Knee MRI at Week 52

End point description:

BMLs in 15 regions were measured with MRI, and graded as 0 (normal), 1 (mild; < 25% of region), 2 (moderate; 25% – 50% of region), or 3 (severe; > 50% of region). The global total BML score was the sum of the 15 component scores, and ranged from 0 (normal) to 45 (severe).

Modified Intent to Treat population: all subjects who received at least 1 dose of study drug, observed cases.

End point type	Secondary

End point timeframe:

Baseline, Week 52

End point values	Placebo	ABT-981 25 mg	ABT-981 100 mg	ABT-981 200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	56	66	61	66
Units: units on a scale				
least squares mean (confidence interval 95%)	0.1 (-0.34 to 0.48)	0.2 (-0.16 to 0.60)	0.1 (-0.30 to 0.48)	0.0 (-0.36 to 0.39)

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v ABT-981 25 mg
Number of subjects included in analysis	122
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.602 [31]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.41
upper limit	0.7

Notes:

[31] - P-value for test of difference between ABT-981 25 mg dose group and Placebo at each post-baseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v ABT-981 100 mg

Number of subjects included in analysis	117
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.953 [32]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.55
upper limit	0.58

Notes:

[32] - P-value for test of difference between ABT-981 100 mg dose group and Placebo at each post-baseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo v ABT-981 200 mg
Number of subjects included in analysis	122
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.83 [33]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.61
upper limit	0.49

Notes:

[33] - P-value for test of difference between ABT-981 200 mg dose group and Placebo at each post-baseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Secondary: Change from Baseline in Index Knee Intermittent and Constant Osteoarthritis Pain (ICOAP) Scores at Week 16

End point title	Change from Baseline in Index Knee Intermittent and Constant Osteoarthritis Pain (ICOAP) Scores at Week 16

End point description:

The ICOAP is a multidimensional osteoarthritis-specific measure designed to comprehensively evaluate the pain experience in patients with hip or knee osteoarthritis. The ICOAP includes 11 items (5 constant pain items; 6 intermittent pain items). Each item is rated on a 0 to 4 point scale with a 7-day recall period. The raw maximum intermittent pain score ranges from 0 to 24, transformed to a reported scale of 0 (no pain) to 100 (worst pain). The raw maximum constant pain score ranges from 0 to 20, transformed to a reported scale of 0 (no pain) to 100 (worst pain).

Modified Intent to Treat population: all subjects who received at least 1 dose of study drug, observed cases.

End point type	Secondary

End point timeframe:

Baseline, Week 16

End point values	Placebo	ABT-981 25 mg	ABT-981 100 mg	ABT-981 200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	75	84	76	77
Units: units on a scale				
least squares mean (confidence interval 95%)				
Intermittent pain	-20.2 (-24.32 to -16.08)	-19.5 (-23.40 to -15.58)	-21.3 (-25.40 to -17.26)	-18.8 (-22.92 to -14.71)
Constant pain	-18.6 (-22.88 to -14.33)	-17.7 (-21.73 to -13.62)	-24.2 (-28.39 to -19.94)	-20.0 (-24.24 to -15.72)

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description: Intermittent pain	
Comparison groups	Placebo v ABT-981 25 mg
Number of subjects included in analysis	159
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.804 [34]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.91
upper limit	6.33

Notes:

[34] - P-value for test of difference between ABT-981 25 mg dose group and Placebo at each post-baseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 2
Statistical analysis description: Intermittent pain	
Comparison groups	Placebo v ABT-981 100 mg
Number of subjects included in analysis	151
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.699 [35]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-1.1

Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.9
upper limit	4.63

Notes:

[35] - P-value for test of difference between ABT-981 100 mg dose group and Placebo at each post-baseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 3

Statistical analysis description:

Intermittent pain

Comparison groups	Placebo v ABT-981 200 mg
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.636 [36]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.37
upper limit	7.14

Notes:

[36] - P-value for test of difference between ABT-981 200 mg dose group and Placebo at each post-baseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 4

Statistical analysis description:

Constant pain

Comparison groups	Placebo v ABT-981 25 mg
Number of subjects included in analysis	159
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.756 [37]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.91
upper limit	6.76

Notes:

[37] - P-value for test of difference between ABT-981 25 mg dose group and Placebo at each post-baseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 5

Statistical analysis description:	
Constant pain	
Comparison groups	Placebo v ABT-981 100 mg
Number of subjects included in analysis	151
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.068 [38]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-5.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.55
upper limit	0.42

Notes:

[38] - P-value for test of difference between ABT-981 100 mg dose group and Placebo at each post-baseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 6
Statistical analysis description:	
Constant pain	
Comparison groups	Placebo v ABT-981 200 mg
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.649 [39]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.34
upper limit	4.58

Notes:

[39] - P-value for test of difference between ABT-981 200 mg dose group and Placebo at each post-baseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Secondary: Change from Baseline in ICOAP Scores at Week 26

End point title	Change from Baseline in ICOAP Scores at Week 26

End point description:

The ICOAP is a multidimensional osteoarthritis-specific measure designed to comprehensively evaluate the pain experience in patients with hip or knee osteoarthritis. The ICOAP includes 11 items (5 constant pain items; 6 intermittent pain items). Each item is rated on a 0 to 4 point scale with a 7-day recall period. The raw maximum intermittent pain score ranges from 0 to 24, transformed to a reported scale of 0 (no pain) to 100 (worst pain). The raw maximum constant pain score ranges from 0 to 20, transformed to a reported scale of 0 (no pain) to 100 (worst pain).

Modified Intent to Treat population: all subjects who received at least 1 dose of study drug, observed cases.

End point type	Secondary

End point timeframe:
Baseline, Week 26

End point values	Placebo	ABT-981 25 mg	ABT-981 100 mg	ABT-981 200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	68	75	72	73
Units: units on a scale				
least squares mean (confidence interval 95%)				
Intermittent pain	-18.7 (-23.21 to -14.21)	-19.7 (-23.99 to -15.42)	-21.3 (-25.66 to -16.98)	-21.7 (-26.11 to -17.38)
Constant pain	-19.6 (-24.22 to -14.96)	-18.8 (-23.26 to -14.42)	-21.6 (-26.05 to -17.08)	-22.1 (-26.61 to -17.61)

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description: Intermittent pain	
Comparison groups	Placebo v ABT-981 25 mg
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.75 [40]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.14
upper limit	5.14

Notes:
[40] - P-value for test of difference between ABT-981 25 mg dose group and Placebo at each post-baseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 2
Statistical analysis description: Intermittent pain	
Comparison groups	Placebo v ABT-981 100 mg
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.409 [41]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-2.6

Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.82
upper limit	3.6

Notes:

[41] - P-value for test of difference between ABT-981 100 mg dose group and Placebo at each post-baseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 3

Statistical analysis description:

Intermittent pain

Comparison groups	Placebo v ABT-981 200 mg
Number of subjects included in analysis	141
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.338 [42]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.24
upper limit	3.18

Notes:

[42] - P-value for test of difference between ABT-981 200 mg dose group and Placebo at each post-baseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 4

Statistical analysis description:

Constant pain

Comparison groups	Placebo v ABT-981 25 mg
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.817 [43]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.59
upper limit	7.08

Notes:

[43] - P-value for test of difference between ABT-981 25 mg dose group and Placebo at each post-baseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 5

Statistical analysis description:

Constant pain

Comparison groups	Placebo v ABT-981 100 mg
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.544 [44]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.37
upper limit	4.43

Notes:

[44] - P-value for test of difference between ABT-981 100 mg dose group and Placebo at each post-baseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 6

Statistical analysis description:

Constant pain

Comparison groups	Placebo v ABT-981 200 mg
Number of subjects included in analysis	141
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.437 [45]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-2.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.91
upper limit	3.86

Notes:

[45] - P-value for test of difference between ABT-981 200 mg dose group and Placebo at each post-baseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Secondary: Change from Baseline in ICOAP Scores at Week 52

End point title	Change from Baseline in ICOAP Scores at Week 52

End point description:

The ICOAP is a multidimensional osteoarthritis-specific measure designed to comprehensively evaluate the pain experience in patients with hip or knee osteoarthritis. The ICOAP includes 11 items (5 constant pain items; 6 intermittent pain items). Each item is rated on a 0 to 4 point scale with a 7-day recall period. The raw maximum intermittent pain score ranges from 0 to 24, transformed to a reported scale of 0 (no pain) to 100 (worst pain). The raw maximum constant pain score ranges from 0 to 20, transformed to a reported scale of 0 (no pain) to 100 (worst pain).

Modified Intent to Treat population: all subjects who received at least 1 dose of study drug, observed cases.

End point type	Secondary

End point timeframe:
Baseline, Week 52

End point values	Placebo	ABT-981 25 mg	ABT-981 100 mg	ABT-981 200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	58	70	66	66
Units: units on a scale				
least squares mean (confidence interval 95%)				
Intermittent pain	-23.2 (-28.51 to -17.83)	-25.4 (-30.21 to -20.51)	-23.6 (-28.53 to -18.64)	-27.2 (-32.19 to -22.14)
Constant pain	-20.6 (-25.93 to -15.21)	-21.8 (-26.70 to -16.94)	-25.2 (-30.14 to -20.17)	-29.7 (-34.78 to -24.66)

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description: Intermittent pain	
Comparison groups	Placebo v ABT-981 25 mg
Number of subjects included in analysis	128
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.545 [46]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-2.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.31
upper limit	4.92

Notes:
[46] - P-value for test of difference between ABT-981 25 mg dose group and Placebo at each postbaseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 2
Statistical analysis description: Intermittent pain	
Comparison groups	Placebo v ABT-981 100 mg
Number of subjects included in analysis	124
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.909 [47]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.4

Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.65
upper limit	6.81

Notes:

[47] - P-value for test of difference between ABT-981 100 mg dose group and Placebo at each postbaseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 3

Statistical analysis description:

Intermittent pain

Comparison groups	Placebo v ABT-981 200 mg
Number of subjects included in analysis	124
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.278 [48]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.23
upper limit	3.25

Notes:

[48] - P-value for test of difference between ABT-981 200 mg dose group and Placebo at each postbaseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 4

Statistical analysis description:

Constant pain

Comparison groups	Placebo v ABT-981 25 mg
Number of subjects included in analysis	128
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.732 [49]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.42
upper limit	5.92

Notes:

[49] - P-value for test of difference between ABT-981 25 mg dose group and Placebo at each postbaseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 5

Statistical analysis description:	
Constant pain	
Comparison groups	Placebo v ABT-981 100 mg
Number of subjects included in analysis	124
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.216 [50]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-4.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.86
upper limit	2.69

Notes:

[50] - P-value for test of difference between ABT-981 100 mg dose group and Placebo at each postbaseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 6
Statistical analysis description:	
Constant pain	
Comparison groups	Placebo v ABT-981 200 mg
Number of subjects included in analysis	124
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.014 [51]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-9.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-16.42
upper limit	-1.88

Notes:

[51] - P-value for test of difference between ABT-981 200 mg dose group and Placebo at each postbaseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Secondary: Change From Baseline In Index Knee Pain Intensity at Week 16

End point title	Change From Baseline In Index Knee Pain Intensity at Week 16

End point description:

The index knee pain intensity was assessed in 3 different ways using an 11 -point NRS (0 to 10 points representing 'no pain' to 'worst possible pain'). Subjects were asked to enter: 1) average pain intensity during the past week (7-day recall period); 2) the worst pain during activity over the past 24 hours; 3) pain intensity before and after a 40 meter walk (performance pain, before and after). The 40 meter fast-paced walk test is a test of short distance walking activity, walking speed over short distances and changing direction during walking. Individuals taking the test should walk as quickly but as safely as possible, without running, along a walkway and then turn around, and repeat again for a total distance of 40 m (132 feet). The total time taken to walk the 40 meters is recorded.

Modified Intent to Treat population: all subjects who received at least 1 dose of study drug, observed cases.

End point type	Secondary

End point timeframe:

Baseline, Week 16

End point values	Placebo	ABT-981 25 mg	ABT-981 100 mg	ABT-981 200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	75	84	77	77
Units: units on a scale				
least squares mean (confidence interval 95%)				
7-Day Recall Period	-2.4 (-2.86 to -1.97)	-2.4 (-2.79 to -1.95)	-2.7 (-3.09 to -2.22)	-2.1 (-2.55 to -1.67)
Activity Pain	-2.3 (-2.85 to -1.82)	-2.4 (-2.85 to -1.87)	-2.7 (-3.19 to -2.17)	-2.1 (-2.59 to -1.56)
Performance Pain (Before)	-2.4 (-2.82 to -1.89)	-2.1 (-2.58 to -1.70)	-2.5 (-2.97 to -2.06)	-2.1 (-2.52 to -1.60)
Performance Pain (After)	-2.6 (-3.07 to -2.11)	-2.4 (-2.90 to -2.00)	-2.7 (-3.16 to -2.22)	-2.3 (-2.77 to -1.82)

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
7-day recall period	
Comparison groups	Placebo v ABT-981 25 mg
Number of subjects included in analysis	159
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.874 [52]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.56
upper limit	0.66

Notes:

[52] - P-value for test of difference between ABT-981 25 mg dose group and Placebo at each postbaseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 2
Statistical analysis description:	
7-day recall period	
Comparison groups	Placebo v ABT-981 100 mg

Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.451 [53]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.86
upper limit	0.38

Notes:

[53] - P-value for test of difference between ABT-981 100 mg dose group and Placebo at each postbaseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 3
Statistical analysis description:	
7-day recall period	
Comparison groups	Placebo v ABT-981 200 mg
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.331 [54]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.31
upper limit	0.93

Notes:

[54] - P-value for test of difference between ABT-981 200 mg dose group and Placebo at each postbaseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 4
Statistical analysis description:	
Activity pain	
Comparison groups	Placebo v ABT-981 25 mg
Number of subjects included in analysis	159
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.932 [55]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	0

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.73
upper limit	0.67

Notes:

[55] - P-value for test of difference between ABT-981 25 mg dose group and Placebo at each postbaseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 5

Statistical analysis description:

Activity pain

Comparison groups	ABT-981 100 mg v Placebo
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.344 [56]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.07
upper limit	0.37

Notes:

[56] - P-value for test of difference between ABT-981 100 mg dose group and Placebo at each postbaseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 6

Statistical analysis description:

Activity pain

Comparison groups	Placebo v ABT-981 200 mg
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.489 [57]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.47
upper limit	0.97

Notes:

[57] - P-value for test of difference between ABT-981 200 mg dose group and Placebo at each postbaseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 7

Statistical analysis description:	
Performance pain (before)	
Comparison groups	Placebo v ABT-981 25 mg
Number of subjects included in analysis	159
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.498 [58]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.42
upper limit	0.85

Notes:

[58] - P-value for test of difference between ABT-981 25 mg dose group and Placebo at each postbaseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 8
Statistical analysis description:	
Performance pain (before)	
Comparison groups	Placebo v ABT-981 100 mg
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.637 [59]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.8
upper limit	0.49

Notes:

[59] - P-value for test of difference between ABT-981 100 mg dose group and Placebo at each postbaseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 9
Statistical analysis description:	
Performance pain (before)	
Comparison groups	Placebo v ABT-981 200 mg
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.367 [60]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	0.3

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.35
upper limit	0.94

Notes:

[60] - P-value for test of difference between ABT-981 200 mg dose group and Placebo at each postbaseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 10
Statistical analysis description:	
Performance pain (after)	
Comparison groups	Placebo v ABT-981 25 mg
Number of subjects included in analysis	159
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.67 [61]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.51
upper limit	0.79

Notes:

[61] - P-value for test of difference between ABT-981 25 mg dose group and Placebo at each postbaseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 11
Statistical analysis description:	
Performance pain (after)	
Comparison groups	Placebo v ABT-981 100 mg
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.776 [62]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.76
upper limit	0.57

Notes:

[62] - P-value for test of difference between ABT-981 100 mg dose group and Placebo at each postbaseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 12

Statistical analysis description:	
Performance pain (after)	
Comparison groups	Placebo v ABT-981 200 mg
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.387 [63]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.37
upper limit	0.96

Notes:

[63] - P-value for test of difference between ABT-981 200 mg dose group and Placebo at each postbaseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Secondary: Change From Baseline In Index Knee Pain Intensity at Week 26

End point title	Change From Baseline In Index Knee Pain Intensity at Week 26

End point description:

The index knee pain intensity was assessed in 3 different ways using an 11 -point NRS (0 to 10 points representing 'no pain' to 'worst possible pain'). Subjects were asked to enter: 1) average pain intensity during the past week (7-day recall period); 2) the worst pain during activity over the past 24 hours; 3) pain intensity before and after a 40 meter walk (performance pain, before and after). The 40 meter fast-paced walk test is a test of short distance walking activity, walking speed over short distances and changing direction during walking. Individuals taking the test should walk as quickly but as safely as possible, without running, along a walkway and then turn around, and repeat again for a total distance of 40 m (132 feet). The total time taken to walk the 40 meters is recorded.

Modified Intent to Treat population: all subjects who received at least 1 dose of study drug, observed cases.

End point type	Secondary
End point timeframe:	
Baseline, Week 26	

End point values	Placebo	ABT-981 25 mg	ABT-981 100 mg	ABT-981 200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	68[64]	75	73[65]	73
Units: units on a scale				
least squares mean (confidence interval 95%)				
7-Day Recall Period	-2.2 (-2.76 to -1.73)	-2.4 (-2.89 to -1.91)	-2.8 (-3.29 to -2.31)	-2.5 (-2.98 to -1.99)
Activity Pain	-2.5 (-3.07 to -1.91)	-2.5 (-3.10 to -1.99)	-2.8 (-3.37 to -2.25)	-2.5 (-3.10 to -1.97)
Performance Pain (Before)	-2.2 (-2.72 to -1.70)	-2.2 (-2.68 to -1.71)	-2.6 (-3.13 to -2.16)	-2.7 (-3.15 to -2.17)
Performance Pain (After)	-2.5 (-3.01 to -1.98)	-2.4 (-2.90 to -1.92)	-3.0 (-3.53 to -2.54)	-2.6 (-3.13 to -2.13)

Notes:

[64] - n=67 for Performance Pain (After)

[65] - n=72 for Performance Pain (After)

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
7-day recall period	
Comparison groups	Placebo v ABT-981 25 mg
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.661 [66]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.86
upper limit	0.54

Notes:

[66] - P-value for test of difference between ABT-981 25 mg dose group and Placebo at each postbaseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 2
Statistical analysis description:	
7-day recall period	
Comparison groups	Placebo v ABT-981 100 mg
Number of subjects included in analysis	141
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.122 [67]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.26
upper limit	0.15

Notes:

[67] - P-value for test of difference between ABT-981 100 mg dose group and Placebo at each postbaseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 3
Statistical analysis description:	
7-day recall period	

Comparison groups	Placebo v ABT-981 200 mg
Number of subjects included in analysis	141
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.507 [68]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.94
upper limit	0.47

Notes:

[68] - P-value for test of difference between ABT-981 200 mg dose group and Placebo at each postbaseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 4

Statistical analysis description:

Activity pain

Comparison groups	Placebo v ABT-981 25 mg
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.892 [69]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.85
upper limit	0.74

Notes:

[69] - P-value for test of difference between ABT-981 25 mg dose group and Placebo at each postbaseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 5

Statistical analysis description:

Activity pain

Comparison groups	Placebo v ABT-981 100 mg
Number of subjects included in analysis	141
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.433 [70]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.3

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.12
upper limit	0.48

Notes:

[70] - P-value for test of difference between ABT-981 100 mg dose group and Placebo at each postbaseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 6

Statistical analysis description:

Activity pain

Comparison groups	Placebo v ABT-981 200 mg
Number of subjects included in analysis	141
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.92 [71]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.84
upper limit	0.76

Notes:

[71] - P-value for test of difference between ABT-981 200 mg dose group and Placebo at each postbaseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 7

Statistical analysis description:

Performance pain (before)

Comparison groups	Placebo v ABT-981 25 mg
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.957 [72]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.68
upper limit	0.71

Notes:

[72] - P-value for test of difference between ABT-981 25 mg dose group and Placebo at each postbaseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 8

Statistical analysis description:	
Performance pain (before)	
Comparison groups	Placebo v ABT-981 100 mg
Number of subjects included in analysis	141
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.222 [73]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.13
upper limit	0.26

Notes:

[73] - P-value for test of difference between ABT-981 100 mg dose group and Placebo at each postbaseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 9
Statistical analysis description:	
Performance pain (before)	
Comparison groups	Placebo v ABT-981 200 mg
Number of subjects included in analysis	141
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.209 [74]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.15
upper limit	0.25

Notes:

[74] - P-value for test of difference between ABT-981 200 mg dose group and Placebo at each postbaseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 10
Statistical analysis description:	
Performance pain (after); n=67 for placebo group (subjects in this analysis =142, not the auto-calculated 143)	
Comparison groups	Placebo v ABT-981 25 mg
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.813 [75]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	0.1

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.62
upper limit	0.79

Notes:

[75] - P-value for test of difference between ABT-981 25 mg dose group and Placebo at each postbaseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 11

Statistical analysis description:

Performance pain (after); n=67 for placebo group and n=72 for ABT-981 100 mg (subjects in this analysis =139, not the auto-calculated 141)

Comparison groups	Placebo v ABT-981 100 mg
Number of subjects included in analysis	141
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.135 [76]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.25
upper limit	0.17

Notes:

[76] - P-value for test of difference between ABT-981 100 mg dose group and Placebo at each postbaseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 12

Statistical analysis description:

Performance pain (after); n=67 for placebo group (subjects in this analysis =140, not the auto-calculated 141)

Comparison groups	Placebo v ABT-981 200 mg
Number of subjects included in analysis	141
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.697 [77]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.85
upper limit	0.57

Notes:

[77] - P-value for test of difference between ABT-981 200 mg dose group and Placebo at each postbaseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Secondary: Change From Baseline In Index Knee Pain Intensity at Week 52

End point title	Change From Baseline In Index Knee Pain Intensity at Week 52

End point description:

The index knee pain intensity was assessed in 3 different ways using an 11 -point NRS (0 to 10 points representing 'no pain' to 'worst possible pain'). Subjects were asked to enter: 1) average pain intensity during the past week (7-day recall period); 2) the worst pain during activity over the past 24 hours; 3) pain intensity before and after a 40 meter walk (performance pain, before and after). The 40 meter fast-paced walk test is a test of short distance walking activity, walking speed over short distances and changing direction during walking. Individuals taking the test should walk as quickly but as safely as possible, without running, along a walkway and then turn around, and repeat again for a total distance of 40 m (132 feet). The total time taken to walk the 40 meters is recorded.

Modified Intent to Treat population: all subjects who received at least 1 dose of study drug, observed cases.

End point type	Secondary

End point timeframe:

Baseline, Week 52

End point values	Placebo	ABT-981 25 mg	ABT-981 100 mg	ABT-981 200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	58	70	67	66
Units: units on a scale				
least squares mean (confidence interval 95%)				
7-Day Recall Period	-2.9 (-3.51 to -2.35)	-2.9 (-3.45 to -2.39)	-2.9 (-3.43 to -2.35)	-3.1 (-3.65 to -2.56)
Activity Pain	-2.8 (-3.48 to -2.16)	-3.0 (-3.64 to -2.43)	-3.2 (-3.77 to -2.55)	-3.0 (-3.65 to -2.40)
Performance Pain (Before)	-2.6 (-3.14 to -2.03)	-2.7 (-3.24 to -2.23)	-3.0 (-3.51 to -2.49)	-2.9 (-3.46 to -2.41)
Performance Pain (After)	-2.9 (-3.47 to -2.33)	-3.0 (-3.53 to -2.50)	-3.4 (-3.90 to -2.86)	-3.2 (-3.69 to -2.62)

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
7-day recall period	
Comparison groups	Placebo v ABT-981 25 mg
Number of subjects included in analysis	128
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.978 [78]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.76
upper limit	0.79

Notes:

[78] - P-value for test of difference between ABT-981 25 mg dose group and Placebo at each postbaseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 2
Statistical analysis description:	
7-day recall period	
Comparison groups	Placebo v ABT-981 100 mg
Number of subjects included in analysis	125
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.925 [79]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.75
upper limit	0.82

Notes:

[79] - P-value for test of difference between ABT-981 100 mg dose group and Placebo at each postbaseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 3
Statistical analysis description:	
7-day recall period	
Comparison groups	Placebo v ABT-981 200 mg
Number of subjects included in analysis	124
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.659 [80]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.96
upper limit	0.61

Notes:

[80] - P-value for test of difference between ABT-981 200 mg dose group and Placebo at each postbaseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 4
Statistical analysis description:	
Activity pain	
Comparison groups	Placebo v ABT-981 25 mg

Number of subjects included in analysis	128
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.633 [81]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	0.67

Notes:

[81] - P-value for test of difference between ABT-981 25 mg dose group and Placebo at each postbaseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 5
Statistical analysis description:	
Activity pain	
Comparison groups	Placebo v ABT-981 100 mg
Number of subjects included in analysis	125
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.46 [82]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.23
upper limit	0.56

Notes:

[82] - P-value for test of difference between ABT-981 100 mg dose group and Placebo at each postbaseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 6
Statistical analysis description:	
Activity pain	
Comparison groups	Placebo v ABT-981 200 mg
Number of subjects included in analysis	124
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.663 [83]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.2

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	0.7

Notes:

[83] - P-value for test of difference between ABT-981 200 mg dose group and Placebo at each postbaseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 7
Statistical analysis description:	
Performance pain (before)	
Comparison groups	Placebo v ABT-981 25 mg
Number of subjects included in analysis	128
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.696 [84]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.89
upper limit	0.59

Notes:

[84] - P-value for test of difference between ABT-981 25 mg dose group and Placebo at each postbaseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 8
Statistical analysis description:	
Performance pain (before)	
Comparison groups	ABT-981 100 mg v Placebo
Number of subjects included in analysis	125
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.278 [85]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.16
upper limit	0.34

Notes:

[85] - P-value for test of difference between ABT-981 100 mg dose group and Placebo at each postbaseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 9
Statistical analysis description:	
Performance pain (before)	
Comparison groups	Placebo v ABT-981 200 mg
Number of subjects included in analysis	124
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.357 [86]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	0.4

Notes:

[86] - P-value for test of difference between ABT-981 200 mg dose group and Placebo at each postbaseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 10
Statistical analysis description:	
Performance pain (after)	
Comparison groups	Placebo v ABT-981 25 mg
Number of subjects included in analysis	128
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.761 [87]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.87
upper limit	0.64

Notes:

[87] - P-value for test of difference between ABT-981 25 mg dose group and Placebo at each postbaseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 11
Statistical analysis description:	
Performance pain (after)	
Comparison groups	Placebo v ABT-981 100 mg

Number of subjects included in analysis	125
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.218 [88]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.25
upper limit	0.29

Notes:

[88] - P-value for test of difference between ABT-981 100 mg dose group and Placebo at each postbaseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 12
Statistical analysis description:	
Performance pain (after)	
Comparison groups	Placebo v ABT-981 200 mg
Number of subjects included in analysis	124
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.513 [89]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.02
upper limit	0.51

Notes:

[89] - P-value for test of difference between ABT-981 200 mg dose group and Placebo at each postbaseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Secondary: Change From Baseline in Patient Global Assessment (PGA) of Arthritis of the Index Knee at Week 16

End point title	Change From Baseline in Patient Global Assessment (PGA) of Arthritis of the Index Knee at Week 16

End point description:

The PGA is a single item for evaluating overall osteoarthritis disease activity. PGA is assessed using an 11-point NRS of 0 to 10 points (representing best to worst disease status, respectively), with a 7-day recall period.

Modified Intent to Treat population: all subjects who received at least 1 dose of study drug, observed cases.

End point type	Secondary

End point timeframe:

Baseline, Week 16

End point values	Placebo	ABT-981 25 mg	ABT-981 100 mg	ABT-981 200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	75	84	77	77
Units: units on a scale				
least squares mean (confidence interval 95%)	-2.5 (-2.94 to -2.01)	-2.4 (-2.80 to -1.92)	-2.9 (-3.34 to -2.42)	-2.6 (-3.08 to -2.15)

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	ABT-981 25 mg v Placebo
Number of subjects included in analysis	159
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.728 [90]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.52
upper limit	0.75

Notes:

[90] - P-value for test of difference between ABT-981 25 mg dose group and Placebo at each post-baseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v ABT-981 100 mg
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.219 [91]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.06
upper limit	0.24

Notes:

[91] - P-value for test of difference between ABT-981 100 mg dose group and Placebo at each post-baseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo v ABT-981 200 mg
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.673 [92]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.79
upper limit	0.51

Notes:

[92] - P-value for test of difference between ABT-981 200 mg dose group and Placebo at each post-baseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Secondary: Change From Baseline in PGA of Arthritis of the Index Knee at Week 26

End point title	Change From Baseline in PGA of Arthritis of the Index Knee at Week 26

End point description:

The PGA is a single item for evaluating overall osteoarthritis disease activity. PGA is assessed using an 11-point NRS of 0 to 10 points (representing best to worst disease status, respectively), with a 7-day recall period.

Modified Intent to Treat population: all subjects who received at least 1 dose of study drug, observed cases.

End point type	Secondary

End point timeframe:

Baseline, Week 26

End point values	Placebo	ABT-981 25 mg	ABT-981 100 mg	ABT-981 200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	68	75	73	73
Units: units on a scale				
least squares mean (confidence interval 95%)	-2.4 (-2.96 to -1.91)	-2.4 (-2.94 to -1.94)	-3.0 (-3.48 to -2.47)	-2.7 (-3.18 to -2.16)

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v ABT-981 25 mg

Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.984 [93]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.73
upper limit	0.71

Notes:

[93] - P-value for test of difference between ABT-981 25 mg dose group and Placebo at each postbaseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v ABT-981 100 mg
Number of subjects included in analysis	141
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.145 [94]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.26
upper limit	0.19

Notes:

[94] - P-value for test of difference between ABT-981 100 mg dose group and Placebo at each postbaseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo v ABT-981 200 mg
Number of subjects included in analysis	141
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.527 [95]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.96
upper limit	0.49

Notes:

[95] - P-value for test of difference between ABT-981 200 mg dose group and Placebo at each postbaseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Secondary: Change From Baseline in PGA of Arthritis of the Index Knee at Week 52	
End point title	Change From Baseline in PGA of Arthritis of the Index Knee at Week 52

End point description:

The PGA is a single item for evaluating overall osteoarthritis disease activity. PGA is assessed using an 11-point NRS of 0 to 10 points (representing best to worst disease status, respectively), with a 7-day recall period.

Modified Intent to Treat population: all subjects who received at least 1 dose of study drug, observed cases.

End point type	Secondary

End point timeframe:

Baseline, Week 52

End point values	Placebo	ABT-981 25 mg	ABT-981 100 mg	ABT-981 200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	58	70	67	66
Units: units on a scale				
least squares mean (confidence interval 95%)	-3.0 (-3.62 to -2.44)	-2.9 (-3.48 to -2.41)	-3.2 (-3.71 to -2.62)	-3.5 (-4.01 to -2.89)

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v ABT-981 25 mg
Number of subjects included in analysis	128
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.836 [96]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.71
upper limit	0.87

Notes:

[96] - P-value for test of difference between ABT-981 25 mg dose group and Placebo at each postbaseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v ABT-981 100 mg

Number of subjects included in analysis	125
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.738 [97]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.94
upper limit	0.66

Notes:

[97] - P-value for test of difference between ABT-981 100 mg dose group and Placebo at each postbaseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo v ABT-981 200 mg
Number of subjects included in analysis	124
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3 [98]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.22
upper limit	0.38

Notes:

[98] - P-value for test of difference between ABT-981 200 mg dose group and Placebo at each postbaseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Secondary: Change From Baseline in Cartilage Volume of the Index Knee at Week 26

End point title	Change From Baseline in Cartilage Volume of the Index Knee at Week 26

End point description:

Cartilage volume of the global knee, the medial central condyle + plateau, and the medial condyle + plateau was measured using MRI.

Modified Intent to Treat population: all subjects who received at least 1 dose of study drug, observed cases.

End point type	Secondary

End point timeframe:

Baseline, Week 26

End point values	Placebo	ABT-981 25 mg	ABT-981 100 mg	ABT-981 200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	58	65	53	66
Units: mm^3				
least squares mean (confidence interval 95%)				
Global knee	-326.0 (-400.83 to -251.13)	-325.5 (-397.10 to -253.83)	-322.4 (-400.20 to -244.61)	-359.0 (-429.72 to -288.35)
Medial central condyle + plateau	-59.1 (-83.12 to -35.10)	-54.9 (-77.83 to -31.90)	-50.1 (-75.13 to -25.07)	-57.5 (-80.12 to -34.88)
Medial condyle + plateau	-128.6 (-166.76 to -90.50)	-126.5 (-163.03 to -90.02)	-124.5 (-164.13 to -84.86)	-114.9 (-150.86 to -78.90)

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
Global knee	
Comparison groups	Placebo v ABT-981 25 mg
Number of subjects included in analysis	123
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.992 [99]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-101.59
upper limit	102.62

Notes:

[99] - P-value for test of difference between ABT-981 25 mg dose group and Placebo at each postbaseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 2
Statistical analysis description:	
Global knee	
Comparison groups	Placebo v ABT-981 100 mg
Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.948 [100]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	3.6

Confidence interval	
level	95 %
sides	2-sided
lower limit	-103.95
upper limit	111.1

Notes:

[100] - P-value for test of difference between ABT-981 100 mg dose group and Placebo at each postbaseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 3

Statistical analysis description:

Global knee

Comparison groups	Placebo v ABT-981 200 mg
Number of subjects included in analysis	124
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.523 [101]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-33.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-134.76
upper limit	68.65

Notes:

[101] - P-value for test of difference between ABT-981 200 mg dose group and Placebo at each postbaseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 4

Statistical analysis description:

Medial central condyle + plateau

Comparison groups	Placebo v ABT-981 25 mg
Number of subjects included in analysis	123
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.799 [102]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	4.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-28.47
upper limit	36.95

Notes:

[102] - P-value for test of difference between ABT-981 25 mg dose group and Placebo at each postbaseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 5

Statistical analysis description:	
Medial central condyle + plateau	
Comparison groups	Placebo v ABT-981 100 mg
Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.609 [103]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-25.62
upper limit	43.64

Notes:

[103] - P-value for test of difference between ABT-981 100 mg dose group and Placebo at each postbaseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 6
Statistical analysis description:	
Medial central condyle + plateau	
Comparison groups	Placebo v ABT-981 200 mg
Number of subjects included in analysis	124
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.923 [104]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	1.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-30.97
upper limit	34.19

Notes:

[104] - P-value for test of difference between ABT-981 200 mg dose group and Placebo at each postbaseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 7
Statistical analysis description:	
Medial condyle + plateau	
Comparison groups	Placebo v ABT-981 25 mg
Number of subjects included in analysis	123
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.937 [105]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	2.1

Confidence interval	
level	95 %
sides	2-sided
lower limit	-49.88
upper limit	54.08

Notes:

[105] - P-value for test of difference between ABT-981 25 mg dose group and Placebo at each postbaseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 8
Statistical analysis description:	
Medial condyle + plateau	
Comparison groups	Placebo v ABT-981 100 mg
Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.882 [106]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	4.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-50.68
upper limit	58.95

Notes:

[106] - P-value for test of difference between ABT-981 100 mg dose group and Placebo at each postbaseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 9
Statistical analysis description:	
Medial condyle + plateau	
Comparison groups	Placebo v ABT-981 200 mg
Number of subjects included in analysis	124
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.602 [107]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	13.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-38.05
upper limit	65.55

Notes:

[107] - P-value for test of difference between ABT-981 200 mg dose group and Placebo at each postbaseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Secondary: Change From Baseline in Cartilage Volume of the Index Knee at Week 52

End point title	Change From Baseline in Cartilage Volume of the Index Knee at

	Week 52

End point description:

Cartilage volume of the global knee, the medial central condyle + plateau, and the medial condyle + plateau was measured using MRI.

Modified Intent to Treat population: all subjects who received at least 1 dose of study drug, observed cases.

End point type	Secondary

End point timeframe:

Baseline, Week 52

End point values	Placebo	ABT-981 25 mg	ABT-981 100 mg	ABT-981 200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	49	57	50	56
Units: mm^3				
least squares mean (confidence interval 95%)				
Global knee	-557.0 (-659.86 to -454.10)	-598.7 (-694.66 to -502.76)	-554.3 (-654.92 to -453.60)	-583.1 (-678.88 to -487.23)
Medial central condyle + plateau	-101.2 (-134.56 to -67.79)	-126.3 (-157.5 to -95.09)	-90.1 (-122.89 to -57.29)	-113.0 (-144.08 to -81.84)
Medial condyle + plateau	-214.7 (-273.77 to -155.64)	-255.0 (-310.03 to -199.97)	-190.3 (-248.05 to -132.51)	-242.8 (-297.71 to -187.86)

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Global knee

Comparison groups	ABT-981 25 mg v Placebo
Number of subjects included in analysis	106
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.554 [108]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-41.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-180.49
upper limit	97.04

Notes:

[108] - P-value for test of difference between ABT-981 25 mg dose group and Placebo at each postbaseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 2
Statistical analysis description:	
Global knee	
Comparison groups	Placebo v ABT-981 100 mg
Number of subjects included in analysis	99
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.97 [109]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	2.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-140.86
upper limit	146.31

Notes:

[109] - P-value for test of difference between ABT-981 100 mg dose group and Placebo at each postbaseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 3
Statistical analysis description:	
Global knee	
Comparison groups	Placebo v ABT-981 200 mg
Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.713 [110]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-26.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-165.47
upper limit	113.32

Notes:

[110] - P-value for test of difference between ABT-981 200 mg dose group and Placebo at each postbaseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 4
Statistical analysis description:	
Medial central condyle + plateau	
Comparison groups	Placebo v ABT-981 25 mg
Number of subjects included in analysis	106
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.272 [111]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-25.1

Confidence interval	
level	95 %
sides	2-sided
lower limit	-70.12
upper limit	19.88

Notes:

[111] - P-value for test of difference between ABT-981 25 mg dose group and Placebo at each postbaseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 5
Statistical analysis description:	
Medial central condyle + plateau	
Comparison groups	Placebo v ABT-981 100 mg
Number of subjects included in analysis	99
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.64 [112]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	11.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-35.63
upper limit	57.8

Notes:

[112] - P-value for test of difference between ABT-981 100 mg dose group and Placebo at each postbaseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 6
Statistical analysis description:	
Medial central condyle + plateau	
Comparison groups	Placebo v ABT-981 200 mg
Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.608 [113]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-11.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-56.94
upper limit	33.38

Notes:

[113] - P-value for test of difference between ABT-981 200 mg dose group and Placebo at each postbaseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 7

Statistical analysis description:	
Medial condyle + plateau	
Comparison groups	Placebo v ABT-981 25 mg
Number of subjects included in analysis	106
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.319 [114]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-40.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-119.88
upper limit	39.3

Notes:

[114] - P-value for test of difference between ABT-981 25 mg dose group and Placebo at each postbaseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 8
Statistical analysis description:	
Medial condyle + plateau	
Comparison groups	Placebo v ABT-981 100 mg
Number of subjects included in analysis	99
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.56 [115]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	24.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-58.05
upper limit	106.91

Notes:

[115] - P-value for test of difference between ABT-981 100 mg dose group and Placebo at each postbaseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 9
Statistical analysis description:	
Medial condyle + plateau	
Comparison groups	Placebo v ABT-981 200 mg
Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.489 [116]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-28.1

Confidence interval	
level	95 %
sides	2-sided
lower limit	-107.97
upper limit	51.82

Notes:

[116] - P-value for test of difference between ABT-981 200 mg dose group and Placebo at each postbaseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Secondary: Change From Baseline in Cartilage Thickness of the Index Knee at Week 26

End point title	Change From Baseline in Cartilage Thickness of the Index Knee at Week 26

End point description:

Cartilage thickness of the global knee, the medial central condyle + plateau, and the medial condyle + plateau was measured using MRI.

Modified Intent to Treat population: all subjects who received at least 1 dose of study drug, observed cases.

End point type	Secondary

End point timeframe:

Baseline, Week 26

End point values	Placebo	ABT-981 25 mg	ABT-981 100 mg	ABT-981 200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	58	65	53	66
Units: mm				
least squares mean (confidence interval 95%)				
Global knee	-0.047 (-0.058 to -0.036)	-0.047 (-0.058 to -0.037)	-0.048 (-0.059 to -0.037)	-0.052 (-0.062 to -0.041)
Medial central condyle + plateau	-0.085 (-0.122 to -0.048)	-0.077 (-0.113 to -0.042)	-0.074 (-0.113 to -0.036)	-0.076 (-0.111 to -0.041)
Medial condyle + plateau	-0.046 (-0.060 to -0.031)	-0.045 (-0.059 to -0.031)	-0.047 (-0.062 to -0.032)	-0.044 (-0.058 to -0.031)

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Global knee

Comparison groups	Placebo v ABT-981 25 mg
Number of subjects included in analysis	123
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.972 [117]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	0

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.015
upper limit	0.015

Notes:

[117] - P-value for test of difference between ABT-981 25 mg dose group and Placebo at each postbaseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

Global knee

Comparison groups	Placebo v ABT-981 100 mg
Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.929 [118]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.001
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.017
upper limit	0.015

Notes:

[118] - P-value for test of difference between ABT-981 100 mg dose group and Placebo at each postbaseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 3

Statistical analysis description:

Global knee

Comparison groups	Placebo v ABT-981 200 mg
Number of subjects included in analysis	124
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.543 [119]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.005
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.02
upper limit	0.01

Notes:

[119] - P-value for test of difference between ABT-981 200 mg dose group and Placebo at each postbaseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 4

Statistical analysis description:	
Medial central condyle + plateau	
Comparison groups	Placebo v ABT-981 25 mg
Number of subjects included in analysis	123
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.752 [120]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	0.008
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.043
upper limit	0.059

Notes:

[120] - P-value for test of difference between ABT-981 25 mg dose group and Placebo at each postbaseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 5
Statistical analysis description:	
Medial central condyle + plateau	
Comparison groups	Placebo v ABT-981 100 mg
Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.691 [121]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	0.011
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.042
upper limit	0.064

Notes:

[121] - P-value for test of difference between ABT-981 100 mg dose group and Placebo at each postbaseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 6
Statistical analysis description:	
Medial central condyle + plateau	
Comparison groups	Placebo v ABT-981 200 mg
Number of subjects included in analysis	124
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.71 [122]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	0.01

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.041
upper limit	0.06

Notes:

[122] - P-value for test of difference between ABT-981 200 mg dose group and Placebo at each postbaseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 7
Statistical analysis description:	
Medial condyle + plateau	
Comparison groups	Placebo v ABT-981 25 mg
Number of subjects included in analysis	123
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.965 [123]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.019
upper limit	0.02

Notes:

[123] - P-value for test of difference between ABT-981 25 mg dose group and Placebo at each postbaseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 8
Statistical analysis description:	
Medial condyle + plateau	
Comparison groups	Placebo v ABT-981 100 mg
Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.885 [124]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.002
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.022
upper limit	0.019

Notes:

[124] - P-value for test of difference between ABT-981 100 mg dose group and Placebo at each postbaseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 9

Statistical analysis description:	
Medial condyle + plateau	
Comparison groups	Placebo v ABT-981 200 mg
Number of subjects included in analysis	124
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.887 [125]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	0.001
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.018
upper limit	0.021

Notes:

[125] - P-value for test of difference between ABT-981 200 mg dose group and Placebo at each postbaseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Secondary: Change From Baseline in Cartilage Thickness of the Index Knee at Week 52

End point title	Change From Baseline in Cartilage Thickness of the Index Knee at Week 52

End point description:

Cartilage thickness of the global knee, the medial central condyle + plateau, and the medial condyle + plateau was measured using MRI.

Modified Intent to Treat population: all subjects who received at least 1 dose of study drug, observed cases.

End point type	Secondary

End point timeframe:

Baseline, Week 52

End point values	Placebo	ABT-981 25 mg	ABT-981 100 mg	ABT-981 200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	49	57	50	56
Units: mm				
least squares mean (confidence interval 95%)				
Global knee	-0.081 (-0.095 to -0.066)	-0.085 (-0.099 to -0.072)	-0.081 (-0.095 to -0.067)	-0.083 (-0.097 to -0.070)
Medial central condyle + plateau	-0.136 (-0.187 to -0.084)	-0.176 (-0.224 to -0.127)	-0.113 (-0.163 to -0.062)	-0.141 (-0.190 to -0.093)
Medial condyle + plateau	-0.084 (-0.106 to -0.063)	-0.096 (-0.117 to -0.076)	-0.073 (-0.094 to -0.052)	-0.087 (-0.107 to -0.067)

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
Global knee	
Comparison groups	Placebo v ABT-981 25 mg
Number of subjects included in analysis	106
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.619 [126]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.005
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.024
upper limit	0.014

Notes:

[126] - P-value for test of difference between ABT-981 25 mg dose group and Placebo at each postbaseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 2
Statistical analysis description:	
Global knee	
Comparison groups	Placebo v ABT-981 100 mg
Number of subjects included in analysis	99
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.952 [127]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.001
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.02
upper limit	0.019

Notes:

[127] - P-value for test of difference between ABT-981 100 mg dose group and Placebo at each postbaseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 3
Statistical analysis description:	
Global knee	
Comparison groups	Placebo v ABT-981 200 mg
Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.765 [128]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.003

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.022
upper limit	0.016

Notes:

[128] - P-value for test of difference between ABT-981 200 mg dose group and Placebo at each postbaseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 4
Statistical analysis description:	
Medial central condyle + plateau	
Comparison groups	Placebo v ABT-981 25 mg
Number of subjects included in analysis	106
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.258 [129]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.11
upper limit	0.03

Notes:

[129] - P-value for test of difference between ABT-981 25 mg dose group and Placebo at each postbaseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 5
Statistical analysis description:	
Medial central condyle + plateau	
Comparison groups	Placebo v ABT-981 100 mg
Number of subjects included in analysis	99
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.535 [130]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	0.023
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.049
upper limit	0.094

Notes:

[130] - P-value for test of difference between ABT-981 100 mg dose group and Placebo at each postbaseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 6

Statistical analysis description:	
Medial central condyle + plateau	
Comparison groups	Placebo v ABT-981 200 mg
Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.866 [131]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.006
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.076
upper limit	0.064

Notes:

[131] - P-value for test of difference between ABT-981 200 mg dose group and Placebo at each postbaseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 7
Statistical analysis description:	
Medial condyle + plateau	
Comparison groups	Placebo v ABT-981 25 mg
Number of subjects included in analysis	106
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.413 [132]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.012
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.041
upper limit	0.017

Notes:

[132] - P-value for test of difference between ABT-981 25 mg dose group and Placebo at each postbaseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 8
Statistical analysis description:	
Medial condyle + plateau	
Comparison groups	Placebo v ABT-981 100 mg
Number of subjects included in analysis	99
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.445 [133]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	0.012

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.018
upper limit	0.042

Notes:

[133] - P-value for test of difference between ABT-981 100 mg dose group and Placebo at each postbaseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Statistical analysis title	Statistical Analysis 9

Statistical analysis description:

Medial condyle + plateau

Comparison groups	Placebo v ABT-981 200 mg
Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.835 [134]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.003
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.032
upper limit	0.026

Notes:

[134] - P-value for test of difference between ABT-981 200 mg dose group and Placebo at each postbaseline time point was from an ANCOVA model with treatment, age, and K-L grade as the main factors and baseline as a covariate.

Secondary: Outcome Measures in Rheumatology Clinical Trials/Osteoarthritis Research Society International (OMERACT/OARSI) Response Rate at Week 16

End point title	Outcome Measures in Rheumatology Clinical Trials/Osteoarthritis Research Society International (OMERACT/OARSI) Response Rate at Week 16

End point description:

Percentage of subjects classified as OMERACT-OARSI responders at Week 16. A subject was considered an OMERACT-OARSI responder if any of the following 3 criteria were met: 1. WOMAC Pain (in 0 – 100 scale) improvement ≥ 50% and absolute reduction ≥ 20 as compared to the baseline; or 2. WOMAC Function (in normalized 0 – 100 scale) improvement ≥ 50% and absolute reduction ≥ 20 as compared to the baseline; or 3. At least 2 of the following 3 are met: WOMAC Pain improvement ≥ 20% and absolute reduction (in normalized 0 – 100 scale) ≥ 10 as compared to the baseline; WOMAC Function improvement ≥ 20% and absolute reduction (in normalized 0 – 100 scale) ≥ 10 as compared to the baseline; PGA improvement ≥ 20% and absolute change (in normalized 0 – 100 scale) ≥ 10 as compared to the baseline. Response rate 95% confidence interval based on normal approximation.

Modified Intent to Treat population: all subjects who received at least 1 dose of study drug, LOCF.

End point type	Secondary

End point timeframe:

Week 16

End point values	Placebo	ABT-981 25 mg	ABT-981 100 mg	ABT-981 200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	85	88	84	87
Units: percentage of subjects				
number (confidence interval 95%)	60.0 (49.6 to 70.4)	67.0 (57.2 to 76.9)	72.6 (63.1 to 82.2)	65.5 (55.5 to 75.5)

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	ABT-981 25 mg v Placebo
Number of subjects included in analysis	173
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.311 [135]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Response Rate Difference
Point estimate	7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.3
upper limit	21.4

Notes:

[135] - P-value for test of difference between each ABT-981 dose group and Placebo was from a Cochran-Mantel-Haenszel test using age group and K-L grade as stratification factors.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v ABT-981 100 mg
Number of subjects included in analysis	169
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.08 [136]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Response Rate Difference
Point estimate	12.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.5
upper limit	26.7

Notes:

[136] - P-value for test of difference between each ABT-981 dose group and Placebo was from a Cochran-Mantel-Haenszel test using age group and K-L grade as stratification factors.

Statistical analysis title	Statistical Analysis 3
Comparison groups	ABT-981 200 mg v Placebo

Number of subjects included in analysis	172
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.435 [137]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Response Rate Difference
Point estimate	5.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.9
upper limit	19.9

Notes:

[137] - P-value for test of difference between each ABT-981 dose group and Placebo was from a Cochran-Mantel-Haenszel test using age group and K-L grade as stratification factors.

Secondary: OMERACT/OARSI Response Rate at Week 26

End point title	OMERACT/OARSI Response Rate at Week 26

End point description:

Percentage of subjects classified as OMERACT-OARSI responders at Week 26. A subject was considered an OMERACT-OARSI responder if any of the following 3 criteria were met: 1. WOMAC Pain (in 0 – 100 scale) improvement ≥ 50% and absolute reduction ≥ 20 as compared to the baseline; or 2. WOMAC Function (in normalized 0 – 100 scale) improvement ≥ 50% and absolute reduction ≥ 20 as compared to the baseline; or 3. At least 2 of the following 3 are met: WOMAC Pain improvement ≥ 20% and absolute reduction (in normalized 0 – 100 scale) ≥ 10 as compared to the baseline; WOMAC Function improvement ≥ 20% and absolute reduction (in normalized 0 – 100 scale) ≥ 10 as compared to the baseline; PGA improvement ≥ 20% and absolute change (in normalized 0 – 100 scale) ≥ 10 as compared to the baseline. Response rate 95% confidence interval based on normal approximation.

Modified Intent to Treat population: all subjects who received at least 1 dose of study drug, LOCF.

End point type	Secondary

End point timeframe:

Week 26

End point values	Placebo	ABT-981 25 mg	ABT-981 100 mg	ABT-981 200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	85	88	84	88
Units: percentage of subjects				
number (confidence interval 95%)	62.4 (52.1 to 72.7)	64.8 (54.8 to 74.8)	66.7 (56.6 to 76.7)	72.7 (63.4 to 82.0)

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v ABT-981 25 mg

Number of subjects included in analysis	173
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.744 [138]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Response Rate Difference
Point estimate	2.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.9
upper limit	16.8

Notes:

[138] - P-value for test of difference between each ABT-981 dose group and Placebo was from a Cochran-Mantel-Haenszel test using age group and K-L grade as stratification factors.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v ABT-981 100 mg
Number of subjects included in analysis	169
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.581 [139]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Response Rate Difference
Point estimate	4.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.1
upper limit	18.7

Notes:

[139] - P-value for test of difference between each ABT-981 dose group and Placebo was from a Cochran-Mantel-Haenszel test using age group and K-L grade as stratification factors.

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo v ABT-981 200 mg
Number of subjects included in analysis	173
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.146 [140]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Response Rate Difference
Point estimate	10.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.5
upper limit	24.3

Notes:

[140] - P-value for test of difference between each ABT-981 dose group and Placebo was from a Cochran-Mantel-Haenszel test using age group and K-L grade as stratification factors.

Secondary: OMERACT/OARSI Response Rate at Week 52

End point title	OMERACT/OARSI Response Rate at Week 52

End point description:

Percentage of subjects classified as OMERACT-OARSI responders at Week 52. A subject was considered an OMERACT-OARSI responder if any of the following 3 criteria were met: 1. WOMAC Pain (in 0 – 100 scale) improvement ≥ 50% and absolute reduction ≥ 20 as compared to the baseline; or 2. WOMAC Function (in normalized 0 – 100 scale) improvement ≥ 50% and absolute reduction ≥ 20 as compared to the baseline; or 3. At least 2 of the following 3 are met: WOMAC Pain improvement ≥ 20% and absolute reduction (in normalized 0 – 100 scale) ≥ 10 as compared to the baseline; WOMAC Function improvement ≥ 20% and absolute reduction (in normalized 0 – 100 scale) ≥ 10 as compared to the baseline; PGA improvement ≥ 20% and absolute change (in normalized 0 – 100 scale) ≥ 10 as compared to the baseline. Response rate 95% confidence interval based on normal approximation.

Modified Intent to Treat population: all subjects who received at least 1 dose of study drug, LOCF.

End point type	Secondary

End point timeframe:

Week 52

End point values	Placebo	ABT-981 25 mg	ABT-981 100 mg	ABT-981 200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	85	88	84	88
Units: percentage of subjects				
number (confidence interval 95%)	70.6 (60.9 to 80.3)	69.3 (59.7 to 79.0)	71.4 (61.8 to 81.1)	72.7 (63.4 to 82.0)

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	ABT-981 25 mg v Placebo
Number of subjects included in analysis	173
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.824 [141]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Response Rate Difference
Point estimate	-1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.9
upper limit	12.4

Notes:

[141] - P-value for test of difference between each ABT-981 dose group and Placebo was from a Cochran-Mantel-Haenszel test using age group and K-L grade as stratification factors.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v ABT-981 100 mg
Number of subjects included in analysis	169
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.964 [142]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Response Rate Difference
Point estimate	0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.8
upper limit	14.5

Notes:

[142] - P-value for test of difference between each ABT-981 dose group and Placebo was from a Cochran-Mantel-Haenszel test using age group and K-L grade as stratification factors.

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo v ABT-981 200 mg
Number of subjects included in analysis	173
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.763 [143]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Response Rate Difference
Point estimate	2.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.3
upper limit	15.6

Notes:

[143] - P-value for test of difference between each ABT-981 dose group and Placebo was from a Cochran-Mantel-Haenszel test using age group and K-L grade as stratification factors.

Adverse events

Adverse events information	
Timeframe for reporting adverse events: up to Week 52 (or last dose of study drug) plus 70 days	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	19.0
Reporting groups	
Reporting group title	Placebo
Reporting group description: Matching placebo subcutaneously (SC) every 2 weeks (E2W)	
Reporting group title	ABT-981 25 mg
Reporting group description: 25 mg ABT-981 SC E2W	
Reporting group title	ABT-981 100 mg
Reporting group description: 100 mg ABT-981 SC E2W	
Reporting group title	ABT-981 200 mg
Reporting group description: 200 mg ABT-981 SC E2W	

Serious adverse events	Placebo	ABT-981 25 mg	ABT-981 100 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 85 (9.41%)	11 / 89 (12.36%)	8 / 85 (9.41%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
BASAL CELL CARCINOMA	Additional description: In addition to this one subject with an SAE of basal cell carcinoma, two other subjects developed basal cell carcinomas that were considered AEs but not SAEs, by the site investigator.		
subjects affected / exposed	0 / 85 (0.00%)	1 / 89 (1.12%)	0 / 85 (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
COLON ADENOMA			
subjects affected / exposed	0 / 85 (0.00%)	1 / 89 (1.12%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INVASIVE DUCTAL BREAST CARCINOMA			

subjects affected / exposed	0 / 85 (0.00%)	0 / 89 (0.00%)	0 / 85 (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
LUNG CANCER METASTATIC			
subjects affected / exposed	0 / 85 (0.00%)	0 / 89 (0.00%)	0 / 85 (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
Injury, poisoning and procedural complications			
ANKLE FRACTURE			
subjects affected / exposed	1 / 85 (1.18%)	1 / 89 (1.12%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CERVICAL VERTEBRAL FRACTURE			
subjects affected / exposed	0 / 85 (0.00%)	0 / 89 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CONCUSSION			
subjects affected / exposed	0 / 85 (0.00%)	1 / 89 (1.12%)	0 / 85 (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
FALL			
subjects affected / exposed	2 / 85 (2.35%)	0 / 89 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HIP FRACTURE			
subjects affected / exposed	0 / 85 (0.00%)	0 / 89 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HUMERUS FRACTURE			
subjects affected / exposed	1 / 85 (1.18%)	0 / 89 (0.00%)	0 / 85 (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
JOINT INJURY			

subjects affected / exposed	0 / 85 (0.00%)	0 / 89 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LACERATION			
subjects affected / exposed	0 / 85 (0.00%)	0 / 89 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PROCEDURAL INTESTINAL PERFORATION			
subjects affected / exposed	0 / 85 (0.00%)	1 / 89 (1.12%)	0 / 85 (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
RADIUS FRACTURE			
subjects affected / exposed	1 / 85 (1.18%)	0 / 89 (0.00%)	0 / 85 (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
ROAD TRAFFIC ACCIDENT			
subjects affected / exposed	1 / 85 (1.18%)	0 / 89 (0.00%)	0 / 85 (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
SKULL FRACTURE			
subjects affected / exposed	1 / 85 (1.18%)	0 / 89 (0.00%)	0 / 85 (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
TIBIA FRACTURE			
subjects affected / exposed	1 / 85 (1.18%)	0 / 89 (0.00%)	0 / 85 (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
UPPER LIMB FRACTURE			
subjects affected / exposed	1 / 85 (1.18%)	0 / 89 (0.00%)	0 / 85 (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
Vascular disorders			
HYPERTENSION			

subjects affected / exposed	0 / 85 (0.00%)	1 / 89 (1.12%)	0 / 85 (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
Nervous system disorders			
AQUEDUCTAL STENOSIS			
subjects affected / exposed	0 / 85 (0.00%)	0 / 89 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BRAIN OEDEMA			
subjects affected / exposed	0 / 85 (0.00%)	0 / 89 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CEREBRAL HAEMORRHAGE			
subjects affected / exposed	0 / 85 (0.00%)	1 / 89 (1.12%)	0 / 85 (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
HYDROCEPHALUS			
subjects affected / exposed	0 / 85 (0.00%)	0 / 89 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PARKINSON'S DISEASE			
subjects affected / exposed	0 / 85 (0.00%)	0 / 89 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SEIZURE			
subjects affected / exposed	0 / 85 (0.00%)	1 / 89 (1.12%)	0 / 85 (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
SYNCOPE			
subjects affected / exposed	0 / 85 (0.00%)	0 / 89 (0.00%)	0 / 85 (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
Gastrointestinal disorders			

COLITIS			
subjects affected / exposed	0 / 85 (0.00%)	1 / 89 (1.12%)	0 / 85 (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
ENTERITIS			
subjects affected / exposed	0 / 85 (0.00%)	1 / 89 (1.12%)	0 / 85 (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
ENTEROCOLITIS			
subjects affected / exposed	1 / 85 (1.18%)	0 / 89 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PANCREATITIS			
subjects affected / exposed	0 / 85 (0.00%)	0 / 89 (0.00%)	0 / 85 (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
SMALL INTESTINAL OBSTRUCTION			
subjects affected / exposed	1 / 85 (1.18%)	0 / 89 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
CHOLECYSTITIS			
subjects affected / exposed	0 / 85 (0.00%)	1 / 89 (1.12%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LIVER DISORDER			
subjects affected / exposed	1 / 85 (1.18%)	0 / 89 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
ALVEOLITIS ALLERGIC			
subjects affected / exposed	0 / 85 (0.00%)	0 / 89 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

ASTHMA			
subjects affected / exposed	0 / 85 (0.00%)	0 / 89 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DYSPNOEA			
subjects affected / exposed	0 / 85 (0.00%)	0 / 89 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
NEPHROLITHIASIS			
subjects affected / exposed	0 / 85 (0.00%)	1 / 89 (1.12%)	0 / 85 (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
Endocrine disorders			
ADRENAL HAEMORRHAGE			
subjects affected / exposed	0 / 85 (0.00%)	1 / 89 (1.12%)	0 / 85 (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
Musculoskeletal and connective tissue disorders			
BACK PAIN			
subjects affected / exposed	0 / 85 (0.00%)	1 / 89 (1.12%)	0 / 85 (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
OSTEOARTHRITIS			
subjects affected / exposed	0 / 85 (0.00%)	0 / 89 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
APPENDICITIS			
subjects affected / exposed	0 / 85 (0.00%)	1 / 89 (1.12%)	0 / 85 (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
DIVERTICULITIS			

subjects affected / exposed	1 / 85 (1.18%)	0 / 89 (0.00%)	0 / 85 (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
PERITONITIS			
subjects affected / exposed	0 / 85 (0.00%)	1 / 89 (1.12%)	0 / 85 (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
PNEUMONIA			
subjects affected / exposed	0 / 85 (0.00%)	0 / 89 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
URINARY TRACT INFECTION			
subjects affected / exposed	1 / 85 (1.18%)	0 / 89 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	ABT-981 200 mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 88 (4.55%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
BASAL CELL CARCINOMA	Additional description: In addition to this one subject with an SAE of basal cell carcinoma, two other subjects developed basal cell carcinomas that were considered AEs but not SAEs, by the site investigator.		
subjects affected / exposed	0 / 88 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
COLON ADENOMA			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
INVASIVE DUCTAL BREAST CARCINOMA			

subjects affected / exposed	1 / 88 (1.14%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
LUNG CANCER METASTATIC				
subjects affected / exposed	1 / 88 (1.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
ANKLE FRACTURE				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
CERVICAL VERTEBRAL FRACTURE				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
CONCUSSION				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
FALL				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
HIP FRACTURE				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
HUMERUS FRACTURE				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
JOINT INJURY				

subjects affected / exposed	0 / 88 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
LACERATION				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
PROCEDURAL INTESTINAL PERFORATION				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
RADIUS FRACTURE				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
ROAD TRAFFIC ACCIDENT				
subjects affected / exposed	1 / 88 (1.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
SKULL FRACTURE				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
TIBIA FRACTURE				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
UPPER LIMB FRACTURE				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vascular disorders				
HYPERTENSION				

subjects affected / exposed	0 / 88 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
AQUEDUCTAL STENOSIS			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
BRAIN OEDEMA			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
CEREBRAL HAEMORRHAGE			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
HYDROCEPHALUS			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
PARKINSON'S DISEASE			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
SEIZURE			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
SYNCOPE			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			

COLITIS				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
ENTERITIS				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
ENTEROCOLITIS				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
PANCREATITIS				
subjects affected / exposed	1 / 88 (1.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
SMALL INTESTINAL OBSTRUCTION				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
CHOLECYSTITIS				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
LIVER DISORDER				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
ALVEOLITIS ALLERGIC				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

ASTHMA			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
DYSPNOEA			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
NEPHROLITHIASIS			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			
ADRENAL HAEMORRHAGE			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
BACK PAIN			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
OSTEOARTHRITIS			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
APPENDICITIS			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
DIVERTICULITIS			

subjects affected / exposed	0 / 88 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
PERITONITIS			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
PNEUMONIA			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
URINARY TRACT INFECTION			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Placebo	ABT-981 25 mg	ABT-981 100 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	66 / 85 (77.65%)	63 / 89 (70.79%)	65 / 85 (76.47%)
Investigations			
NEUTROPHIL COUNT DECREASED			
subjects affected / exposed	1 / 85 (1.18%)	3 / 89 (3.37%)	13 / 85 (15.29%)
occurrences (all)	2	12	53
Injury, poisoning and procedural complications			
CONTUSION			
subjects affected / exposed	3 / 85 (3.53%)	9 / 89 (10.11%)	2 / 85 (2.35%)
occurrences (all)	3	9	2
FALL			
subjects affected / exposed	3 / 85 (3.53%)	5 / 89 (5.62%)	3 / 85 (3.53%)
occurrences (all)	3	6	4
LIGAMENT SPRAIN			

subjects affected / exposed	3 / 85 (3.53%)	6 / 89 (6.74%)	2 / 85 (2.35%)
occurrences (all)	3	6	2
Vascular disorders			
HYPERTENSION			
subjects affected / exposed	6 / 85 (7.06%)	7 / 89 (7.87%)	5 / 85 (5.88%)
occurrences (all)	9	8	7
Nervous system disorders			
DIZZINESS			
subjects affected / exposed	1 / 85 (1.18%)	3 / 89 (3.37%)	6 / 85 (7.06%)
occurrences (all)	1	3	8
HEADACHE			
subjects affected / exposed	22 / 85 (25.88%)	14 / 89 (15.73%)	14 / 85 (16.47%)
occurrences (all)	48	37	29
Blood and lymphatic system disorders			
NEUTROPENIA			
subjects affected / exposed	1 / 85 (1.18%)	12 / 89 (13.48%)	12 / 85 (14.12%)
occurrences (all)	1	22	21
General disorders and administration site conditions			
FATIGUE			
subjects affected / exposed	12 / 85 (14.12%)	4 / 89 (4.49%)	5 / 85 (5.88%)
occurrences (all)	15	4	5
INJECTION SITE ERYTHEMA			
subjects affected / exposed	1 / 85 (1.18%)	4 / 89 (4.49%)	7 / 85 (8.24%)
occurrences (all)	1	11	36
INJECTION SITE PAIN			
subjects affected / exposed	7 / 85 (8.24%)	2 / 89 (2.25%)	2 / 85 (2.35%)
occurrences (all)	15	2	3
INJECTION SITE RASH			
subjects affected / exposed	3 / 85 (3.53%)	3 / 89 (3.37%)	7 / 85 (8.24%)
occurrences (all)	28	26	24
INJECTION SITE REACTION			
subjects affected / exposed	0 / 85 (0.00%)	6 / 89 (6.74%)	8 / 85 (9.41%)
occurrences (all)	0	15	10
PAIN			
subjects affected / exposed	6 / 85 (7.06%)	3 / 89 (3.37%)	4 / 85 (4.71%)
occurrences (all)	8	3	7

Gastrointestinal disorders			
DIARRHOEA			
subjects affected / exposed	7 / 85 (8.24%)	6 / 89 (6.74%)	5 / 85 (5.88%)
occurrences (all)	9	7	5
NAUSEA			
subjects affected / exposed	3 / 85 (3.53%)	4 / 89 (4.49%)	6 / 85 (7.06%)
occurrences (all)	3	7	6
Respiratory, thoracic and mediastinal disorders			
COUGH			
subjects affected / exposed	5 / 85 (5.88%)	7 / 89 (7.87%)	5 / 85 (5.88%)
occurrences (all)	6	7	5
OROPHARYNGEAL PAIN			
subjects affected / exposed	2 / 85 (2.35%)	4 / 89 (4.49%)	5 / 85 (5.88%)
occurrences (all)	2	7	5
Skin and subcutaneous tissue disorders			
PRURITUS			
subjects affected / exposed	0 / 85 (0.00%)	6 / 89 (6.74%)	5 / 85 (5.88%)
occurrences (all)	0	7	6
RASH			
subjects affected / exposed	3 / 85 (3.53%)	2 / 89 (2.25%)	6 / 85 (7.06%)
occurrences (all)	3	2	7
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	16 / 85 (18.82%)	16 / 89 (17.98%)	19 / 85 (22.35%)
occurrences (all)	20	24	37
BACK PAIN			
subjects affected / exposed	14 / 85 (16.47%)	8 / 89 (8.99%)	11 / 85 (12.94%)
occurrences (all)	15	9	16
MUSCULOSKELETAL PAIN			
subjects affected / exposed	5 / 85 (5.88%)	5 / 89 (5.62%)	4 / 85 (4.71%)
occurrences (all)	7	6	6
MYALGIA			
subjects affected / exposed	1 / 85 (1.18%)	2 / 89 (2.25%)	3 / 85 (3.53%)
occurrences (all)	1	2	4
PAIN IN EXTREMITY			

subjects affected / exposed	6 / 85 (7.06%)	5 / 89 (5.62%)	7 / 85 (8.24%)
occurrences (all)	8	14	7
Infections and infestations			
BRONCHITIS			
subjects affected / exposed	2 / 85 (2.35%)	5 / 89 (5.62%)	1 / 85 (1.18%)
occurrences (all)	2	6	1
INFLUENZA			
subjects affected / exposed	10 / 85 (11.76%)	2 / 89 (2.25%)	5 / 85 (5.88%)
occurrences (all)	17	2	5
NASOPHARYNGITIS			
subjects affected / exposed	16 / 85 (18.82%)	9 / 89 (10.11%)	13 / 85 (15.29%)
occurrences (all)	18	10	16
SINUSITIS			
subjects affected / exposed	1 / 85 (1.18%)	5 / 89 (5.62%)	3 / 85 (3.53%)
occurrences (all)	1	5	5
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	8 / 85 (9.41%)	8 / 89 (8.99%)	7 / 85 (8.24%)
occurrences (all)	12	8	8
URINARY TRACT INFECTION			
subjects affected / exposed	4 / 85 (4.71%)	3 / 89 (3.37%)	5 / 85 (5.88%)
occurrences (all)	5	3	5

Non-serious adverse events	ABT-981 200 mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	75 / 88 (85.23%)		
Investigations			
NEUTROPHIL COUNT DECREASED			
subjects affected / exposed	13 / 88 (14.77%)		
occurrences (all)	43		
Injury, poisoning and procedural complications			
CONTUSION			
subjects affected / exposed	5 / 88 (5.68%)		
occurrences (all)	8		
FALL			
subjects affected / exposed	8 / 88 (9.09%)		
occurrences (all)	9		

LIGAMENT SPRAIN subjects affected / exposed occurrences (all)	2 / 88 (2.27%) 2		
Vascular disorders HYPERTENSION subjects affected / exposed occurrences (all)	1 / 88 (1.14%) 1		
Nervous system disorders DIZZINESS subjects affected / exposed occurrences (all) HEADACHE subjects affected / exposed occurrences (all)	3 / 88 (3.41%) 3 21 / 88 (23.86%) 34		
Blood and lymphatic system disorders NEUTROPENIA subjects affected / exposed occurrences (all)	21 / 88 (23.86%) 41		
General disorders and administration site conditions FATIGUE subjects affected / exposed occurrences (all) INJECTION SITE ERYTHEMA subjects affected / exposed occurrences (all) INJECTION SITE PAIN subjects affected / exposed occurrences (all) INJECTION SITE RASH subjects affected / exposed occurrences (all) INJECTION SITE REACTION subjects affected / exposed occurrences (all) PAIN	7 / 88 (7.95%) 8 5 / 88 (5.68%) 12 1 / 88 (1.14%) 1 8 / 88 (9.09%) 86 12 / 88 (13.64%) 30		

subjects affected / exposed occurrences (all)	4 / 88 (4.55%) 4		
Gastrointestinal disorders DIARRHOEA subjects affected / exposed occurrences (all) NAUSEA subjects affected / exposed occurrences (all)	 9 / 88 (10.23%) 12 6 / 88 (6.82%) 6		
Respiratory, thoracic and mediastinal disorders COUGH subjects affected / exposed occurrences (all) OROPHARYNGEAL PAIN subjects affected / exposed occurrences (all)	 5 / 88 (5.68%) 5 7 / 88 (7.95%) 8		
Skin and subcutaneous tissue disorders PRURITUS subjects affected / exposed occurrences (all) RASH subjects affected / exposed occurrences (all)	 4 / 88 (4.55%) 5 4 / 88 (4.55%) 4		
Musculoskeletal and connective tissue disorders ARTHRALGIA subjects affected / exposed occurrences (all) BACK PAIN subjects affected / exposed occurrences (all) MUSCULOSKELETAL PAIN subjects affected / exposed occurrences (all) MYALGIA subjects affected / exposed occurrences (all)	 14 / 88 (15.91%) 26 14 / 88 (15.91%) 17 4 / 88 (4.55%) 4 9 / 88 (10.23%) 11		

PAIN IN EXTREMITY			
subjects affected / exposed	5 / 88 (5.68%)		
occurrences (all)	7		
Infections and infestations			
BRONCHITIS			
subjects affected / exposed	4 / 88 (4.55%)		
occurrences (all)	4		
INFLUENZA			
subjects affected / exposed	4 / 88 (4.55%)		
occurrences (all)	5		
NASOPHARYNGITIS			
subjects affected / exposed	17 / 88 (19.32%)		
occurrences (all)	22		
SINUSITIS			
subjects affected / exposed	3 / 88 (3.41%)		
occurrences (all)	3		
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	12 / 88 (13.64%)		
occurrences (all)	16		
URINARY TRACT INFECTION			
subjects affected / exposed	8 / 88 (9.09%)		
occurrences (all)	9		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 October 2013	Added secondary objective of safety and tolerability.
28 January 2014	Added additional questions to increase sensitivity of knee pain intensity measure and changed AE grading to CTCAE grading scale.
01 April 2014	Extended minimal post-dosing observational period to 1 hour, extended the assessment period of knee pain intensity prior to screening to 14 days to enhance selection of appropriate subjects, allowed for the use of low dose ibuprofen as an add-on rescue medication, and added subject discontinuation criteria due to lack of efficacy based on the subject's assessment of knee pain intensity scores.
02 October 2014	Expanded screening and washout periods to accommodate scheduling/assessment of screening imaging procedures, gave sites the option to use ultrasound or MRI imaging to detect synovitis during screening, clarified pregnancy testing requirements, included previous exposure to drugs of an immunosuppressive nature as exclusion criterion, allowed subjects with widened degree of moderate knee mal-alignment to be enrolled, further defined several abnormal laboratory values which were considered exclusionary, revised knee pain intensity to provide instructions for 40 meter fast-paced walk test, modified section for the collection and handling of PK and ADA samples, and added Appendix D to list various TB test scenarios.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported