Clinical trial results:
A Phase 2a, multicenter, randomized, double-blind, placebo-controlled study comparing the safety and efficacy of ABT-981 to placebo in subjects with erosive hand osteoarthritis

Summary

EudraCT number	2014-001096-31
Trial protocol	DK BE NL
Global end of trial date	13 July 2016

Results information

Result version number	v1 (current)
This version publication date	29 July 2017
First version publication date	29 July 2017

Trial information

Trial identification

Sponsor protocol code	M14-171

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02384538
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	Global Medical Services, Abbvie, 001 800-633-9110,
Scientific contact	Marc C. Levesque, MD, PhD, Abbvie, 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 July 2016
Is this the analysis of the primary completion data?	No

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

Notes:

General information about the trial

Main objective of the trial:

This is a multicenter, randomized, double-blind, placebo-controlled study to compare the safety and efficacy of ABT-981 to placebo in subjects with erosive hand osteoarthritis.

Protection of trial subjects:

Subject read and understood the information provided about the study and gave written permission.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 March 2015
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	Netherlands: 4
Country: Number of subjects enrolled	Belgium: 20
Country: Number of subjects enrolled	Denmark: 27
Country: Number of subjects enrolled	France: 3
Country: Number of subjects enrolled	Switzerland: 2
Country: Number of subjects enrolled	United States: 76
Worldwide total number of subjects	132
EEA total number of subjects	54

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)	56

From 65 to 84 years	76
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 132 subjects were randomized and included in the intent-to-treat (ITT) population; 1 subject who was randomized to the ABT-981 treatment group did not receive a dose of study drug and was excluded from the analyses, for a total of 131 subjects in the modified intent-to-treat population (mITT).

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Placebo for ABT-981 every two weeks (Q2W) for 24 weeks.

Arm type	Placebo
Investigational medicinal product name	Placebo for ABT-981
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection/infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

Placebo for ABT-981 administered by subcutaneous injection.

Arm title	ABT-981

Arm description:

ABT-981 200 mg every two weeks (Q2W) for 24 weeks.

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

Dosage and administration details:

ABT-981 administered by subcutaneous injection.

Number of subjects in period 1[1]	Placebo	ABT-981
Started	67	64
Completed	61	49
Not completed	6	15
Not specified	1	3
Adverse event	1	4
Withdrew consent	-	4
Lack of efficacy	4	4

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: A total of 132 subjects were randomized; 1 subject who was randomized to the ABT-981 treatment group did not receive a dose of study drug and was excluded from the analyses, for a total of 131 subjects in the modified intent-to-treat population (mITT).

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Placebo for ABT-981 every two weeks (Q2W) for 24 weeks.	
Reporting group title	ABT-981
Reporting group description:	
ABT-981 200 mg every two weeks (Q2W) for 24 weeks.	

Reporting group values	Placebo	ABT-981	Total
Number of subjects	67	64	131
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	65.8	65.7	
standard deviation	± 7.325	± 8.132	-
Gender categorical Units: Subjects			
Female	58	53	111
Male	9	11	20

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Placebo for ABT-981 every two weeks (Q2W) for 24 weeks.	
Reporting group title	ABT-981
Reporting group description:	
ABT-981 200 mg every two weeks (Q2W) for 24 weeks.	

Primary: Australian/Canadian Hand Osteoarthritis Index (AUSCAN NR3.1) Pain Subdomain Score: Change From Baseline to Week 16

End point title	Australian/Canadian Hand Osteoarthritis Index (AUSCAN NR3.1) Pain Subdomain Score: Change From Baseline to Week
End point description:	
The AUSCAN NR3.1 is a self-report measure composed of a battery of 15 questions assessing the three dimensions of pain (5 questions), joint stiffness (1 question) and physical function (9 questions) using an 11-box Numerical Rating Scale (NRS-11) from 0 (low) to 10 (high). The pain subdomain score ranges from 0 to 50; lower scores indicate better status. A decrease in the pain subdomain score represents improvement in status. Last Observation Carried Forward (LOCF): Missing responses were imputed by calculation based on the last nonmissing postbaseline component values.	
End point type	Primary
End point timeframe:	
Week 0 (Baseline), Week 16	

End point values	Placebo	ABT-981		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	65[1]	64[2]		
Units: units on a scale				
least squares mean (confidence interval 95%)	-10.74 (-15.433 to -6.045)	-9.22 (-13.798 to -4.645)		

Notes:

[1] - mITT population: all randomized subjects who received at least 1 dose of study drug.

[2] - mITT population: all randomized subjects who received at least 1 dose of study drug.

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v ABT-981
Number of subjects included in analysis	129
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.386 [3]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	1.52

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.944
upper limit	4.99

Notes:

[3] - P-value for test of difference in change from baseline between ABT-981 dose group and placebo is from an ANCOVA model with treatment group and country as the main factors and baseline as a covariate.

Secondary: Australian/Canadian Hand Osteoarthritis Index (AUSCAN NR3.1) Pain Subdomain Score: Change From Baseline to Each Visit

End point title	Australian/Canadian Hand Osteoarthritis Index (AUSCAN NR3.1) Pain Subdomain Score: Change From Baseline to Each

End point description:

The AUSCAN NR3.1 is a self-report measure composed of a battery of 15 questions assessing the three dimensions of pain (5 questions), joint stiffness (1 question) and physical function (9 questions) using an 11-box Numerical Rating Scale (NRS-11) from 0 (low) to 10 (high). The pain subdomain score ranges from 0 to 50; lower scores indicate better status. A decrease in the pain subdomain score represents improvement in status. LOCF: Missing responses were imputed by calculation based on the last nonmissing postbaseline component values. n=number of subjects with evaluable data at given time point.

End point type	Secondary

End point timeframe:

Week 0 (Baseline) and Weeks 2, 4, 8, 12, 16, 20, and 26

End point values	Placebo	ABT-981		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	67[4]	64[5]		
Units: units on a scale				
least squares mean (confidence interval 95%)				
Week 2 (n=65,62)	-3.25 (-7.058 to 0.55)	-3.27 (-6.983 to 0.438)		
Week 4 (n=65,64)	-5.01 (-9.144 to -0.885)	-4.26 (-8.28 to -0.237)		
Week 8 (n=65,64)	-8.9 (-13.065 to -4.744)	-6.44 (-10.488 to -2.384)		
Week 12 (n=65,64)	-8.31 (-12.593 to -4.03)	-5.64 (-9.809 to -1.469)		
Week 16 (n=65,64)	-10.74 (-15.443 to -6.045)	-9.22 (-13.798 to -4.645)		
Week 20 (n=65,64)	-7.28 (-11.969 to -2.591)	-8.37 (-12.941 to -3.807)		
Week 26 (n=65,64)	-8.76 (-13.782 to -3.737)	-10.37 (-15.264 to -5.481)		

Notes:

[4] - All subjects in the mITT population.

[5] - All subjects in the mITT population.

Statistical analyses

No statistical analyses for this end point

Secondary: Australian/Canadian Hand Osteoarthritis Index (AUSCAN NR3.1) Physical Function Subdomain Score: Change From Baseline to Each Visit

End point title	Australian/Canadian Hand Osteoarthritis Index (AUSCAN NR3.1) Physical Function Subdomain Score: Change From Baseline to Each Visit

End point description:

The AUSCAN NR3.1 is a self-report measure composed of a battery of 15 questions assessing the three dimensions of pain (5 questions), joint stiffness (1 question) and physical function (9 questions) using an 11-box Numerical Rating Scale (NRS-11) from 0 (low) to 10 (high). The physical function subdomain score ranges from 0 to 90; lower scores indicate better status. A decrease in the physical function subdomain score represents improvement in status. LOCF: Missing responses were imputed by calculation based on the last nonmissing postbaseline component values. n=number of subjects with evaluable data at given time point.

End point type	Secondary

End point timeframe:

Week 0 (Baseline) and Weeks 2, 4, 8, 12, 16, 20, and 26

End point values	Placebo	ABT-981		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	67[6]	64[7]		
Units: units on a scale				
least squares mean (confidence interval 95%)				
Week 2 (n=65,62)	-6.23 (-13.098 to 0.63)	-4.79 (-11.44 to 1.861)		
Week 4 (n=65,64)	-8.43 (-15.879 to -0.974)	-7.04 (-14.249 to 0.177)		
Week 8 (n=65,64)	-14.25 (-21.729 to -6.763)	-8.97 (-16.211 to -1.725)		
Week 12 (n=65,64)	-12.54 (-20.14 to -4.947)	-8.53 (-15.887 to -1.182)		
Week 16 (n=65,64)	-17.18 (-24.938 to -9.431)	-14.64 (-22.142 to -7.133)		
Week 20 (n=65,64)	-11.5 (-19.415 to -3.584)	-12.53 (-20.189 to -4.867)		
Week 26 (n=65,64)	-14.25 (-22.523 to -5.978)	-16.39 (-24.402 to -8.388)		

Notes:

[6] - All subjects in the mITT population.

[7] - All subjects in the mITT population.

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Week 16

Comparison groups	Placebo v ABT-981

Number of subjects included in analysis	131
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.383 [8]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	2.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.214
upper limit	8.308

Notes:

[8] - P-value for test of difference in change from baseline between ABT-981 dose group and placebo is from an ANCOVA model with treatment group and country as the main factors and baseline as a covariate.

Secondary: Australian/Canadian Hand Osteoarthritis Index (AUSCAN NR3.1) Stiffness Subdomain Score: Change From Baseline to Each Visit

End point title	Australian/Canadian Hand Osteoarthritis Index (AUSCAN NR3.1) Stiffness Subdomain Score: Change From Baseline to Each Visit

End point description:

The AUSCAN NR3.1 is a self-report measure composed of a battery of 15 questions assessing the three dimensions of pain (5 questions), joint stiffness (1 question) and physical function (9 questions) using an 11-box Numerical Rating Scale (NRS-11) from 0 (low) to 10 (high). The stiffness subdomain score ranges from 0 to 10; lower scores indicate better status. A decrease in the stiffness subdomain score represents improvement in status. LOCF: Missing responses were imputed by calculation based on the last nonmissing postbaseline component values. n=number of subjects with evaluable data at given time point.

End point type	Secondary

End point timeframe:

Week 0 (Baseline) and Weeks 2, 4, 8, 12, 16, 20, and 26

End point values	Placebo	ABT-981		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	67[9]	64[10]		
Units: units on a scale				
least squares mean (confidence interval 95%)				
Week 2 (n=65,62)	-0.74 (-1.692 to 0.215)	-0.96 (-1.877 to -0.036)		
Week 4 (n=65,64)	-0.98 (-1.937 to -0.028)	-1.24 (-2.163 to -0.321)		
Week 8 (n=65,64)	-1.51 (-2.535 to -0.493)	-1.43 (-2.412 to -0.441)		
Week 12 (n=65,64)	-1.65 (-2.706 to -0.599)	-1.23 (-2.244 to -0.211)		
Week 16 (n=65,64)	-1.76 (-2.885 to -0.633)	-1.61 (-2.695 to -0.522)		
Week 20 (n=65,64)	-1.34 (-2.515 to -0.169)	-1.85 (-2.986 to -0.722)		
Week 26 (n=65,64)	-1.94 (-3.017 to -0.859)	-2.45 (-3.492 to -1.41)		

Notes:

[9] - All subjects in the mITT population.

[10] - All subjects in the mITT population.

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
Week 16	
Comparison groups	Placebo v ABT-981
Number of subjects included in analysis	131
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.719 [11]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	0.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.677
upper limit	0.979

Notes:

[11] - P-value for test of difference in change from baseline between ABT-981 dose group and placebo is from an ANCOVA model with treatment group and country as the main factors and baseline as a covariate.

Secondary: Australian/Canadian Hand Osteoarthritis Index (AUSCAN NR3.1) Total Score: Change From Baseline to Each Visit

End point title	Australian/Canadian Hand Osteoarthritis Index (AUSCAN NR3.1) Total Score: Change From Baseline to Each Visit

End point description:

The AUSCAN NR3.1 is a self-report measure composed of a battery of 15 questions assessing the three dimensions of pain (5 questions), joint stiffness (1 question) and physical function (9 questions) using an 11-box Numerical Rating Scale (NRS-11) from 0 (low) to 10 (high). The total score ranges from 0 to 150; lower scores indicate better status. A decrease in the total score represents improvement in status. LOCF: Missing responses were imputed by calculation based on the last nonmissing postbaseline component values. n=number of subjects with evaluable data at given time point.

End point type	Secondary

End point timeframe:

Week 0 (Baseline) and Weeks 2, 4, 8, 12, 16, 20, and 26

End point values	Placebo	ABT-981		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	67[12]	64[13]		
Units: units on a scale				
least squares mean (confidence interval 95%)				

Week 2 (n=65,62)	-10.01 (-21.037 to 1.019)	-8.85 (-19.545 to 1.835)		
Week 4 (n=65,64)	-14.06 (-26.185 to -1.93)	-12.18 (-23.928 to -0.439)		
Week 8 (n=65,64)	-24.52 (-36.66 to -12.373)	-16.65 (-28.406 to -4.886)		
Week 12 (n=65,64)	-22.29 (-34.714 to -9.873)	-15.15 (-27.181 to -3.124)		
Week 16 (n=65,64)	-29.37 (-42.469 to -16.264)	-25.12 (-37.808 to -12.429)		
Week 20 (n=65,64)	-19.68 (-32.894 to -6.458)	-22.33 (-35.128 to -9.526)		
Week 26 (n=65,64)	-24.73 (-38.636 to -10.82)	-28.99 (-42.461 to -15.523)		

Notes:

[12] - All subjects in the mITT population.

[13] - All subjects in the mITT population.

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
Week 16	
Comparison groups	Placebo v ABT-981
Number of subjects included in analysis	131
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.387 [14]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	4.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.448
upper limit	13.945

Notes:

[14] - P-value for test of difference in change from baseline between ABT-981 dose group and placebo is from an ANCOVA model with treatment group and country as the main factors and baseline as a covariate.

Secondary: Subject Assessment of Index Hand Pain Intensity Using Numeric Rating Scale (NRS-11): Change From Baseline to Each Visit

End point title	Subject Assessment of Index Hand Pain Intensity Using Numeric Rating Scale (NRS-11): Change From Baseline to Each Visit

End point description:

Subjects rated the pain intensity of each hand during the previous 48 hours using an 11-point scale (NRS-11). The change from baseline to each visit in NRS-11 in the index hand (the hand with the most disease) are presented. Scores range from 0 to 10 points, with higher scores indicating greater pain intensity. A decrease in the NRS-11 score represents a decrease in pain intensity. n=number of subjects with evaluable data at given time point.

End point type	Secondary

End point timeframe:

Week 0 (Baseline) and Weeks 2, 4, 8, 12, 16, 20, and 26

End point values	Placebo	ABT-981		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	67[15]	64[16]		
Units: units on a scale				
least squares mean (confidence interval 95%)				
Week 2 (n=65,62)	-0.62 (-1.55 to 0.32)	-0.69 (-1.613 to 0.228)		
Week 4 (n=65,63)	-1.18 (-2.163 to -0.195)	-1.06 (-2.025 to -0.088)		
Week 8 (n=63,58)	-2.4 (-3.339 to -1.465)	-1.74 (-2.66 to -0.814)		
Week 12 (n=61,53)	-1.65 (-2.434 to -0.875)	-0.81 (-1.629 to 0.01)		
Week 16 (n=61,51)	-2.05 (-3.085 to -1.017)	-1.6 (-2.626 to -0.578)		
Week 20 (n=57,49)	-1.61 (-2.749 to -0.477)	-1.75 (-2.892 to -0.612)		
Week 26 (n=60,50)	-2.02 (-3.132 to -0.901)	-2.52 (-3.62 to -1.415)		

Notes:

[15] - All subjects in the mITT population.

[16] - All subjects in the mITT population.

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Week 16

Comparison groups	Placebo v ABT-981
Number of subjects included in analysis	131
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.281 [17]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	0.45
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.373
upper limit	1.272

Notes:

[17] - P-value for test of difference in change from baseline between ABT-981 dose group and placebo is from an ANCOVA model with treatment group and country as the main factors and baseline as a covariate.

Secondary: Patient Global Assessment of Hand Osteoarthritis (OA) Status by NRS-11: Change From Baseline to Each Visit

End point title	Patient Global Assessment of Hand Osteoarthritis (OA) Status by NRS-11: Change From Baseline to Each Visit

End point description:

Subjects were asked how much they were affected by hand OA by responding to the question "Considering all the ways your hand OA affects you, how have you been during the last 48 hours?" using an 11-point scale (NRS-11). Scores range from 0 to 10 points, with higher scores indicating greater effect of hand OA on the subject. A decrease in the NRS-11 score represents an improvement the effect of hand OA on the subject. n=number of subjects with evaluable data at given time point.

End point type	Secondary

End point timeframe:

Week 0 (Baseline) and Weeks 2, 4, 8, 12, 16, 20, and 26

End point values	Placebo	ABT-981		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	67[18]	64[19]		
Units: units on a scale				
least squares mean (confidence interval 95%)				
Week 2 (n=65,62)	-0.52 (-1.399 to 0.351)	-0.54 (-1.403 to 0.316)		
Week 4 (n=65,63)	-1.31 (-2.277 to -0.335)	-1.13 (-2.083 to -0.176)		
Week 8 (n=63,58)	-1.85 (-2.74 to -0.952)	-1.2 (-2.08 to -0.324)		
Week 12 (n=61,53)	-1.78 (-2.567 to -0.993)	-1.17 (-1.997 to -0.348)		
Week 16 (n=61,51)	-2.2 (-3.225 to -1.185)	-1.69 (-2.697 to -0.677)		
Week 20 (n=57,49)	-1.73 (-3.225 to -1.185)	-1.77 (-2.879 to -0.666)		
Week 26 (n=60,50)	-2 (-3.133 to -0.874)	-2.35 (-3.465 to -1.236)		

Notes:

[18] - All subjects in the mITT population.

[19] - All subjects in the mITT population.

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Week 16

Comparison groups	Placebo v ABT-981
Number of subjects included in analysis	131
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.212 [20]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	0.52

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.3
upper limit	1.336

Notes:

[20] - P-value for test of difference in change from baseline between ABT-981 dose group and placebo is from an ANCOVA model with treatment group and country as the main factors and baseline as a covariate.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Treatment-emergent adverse events (TEAEs) and serious adverse events (TESAEs) were collected from first dose of study drug until 70 days after the last dose of study drug (up to 34 weeks).

Adverse event reporting additional description:

TEAEs and TESAEs are defined as any AE or SAE that begins on or after the first dose of study drug, up to 70 days after the last dose of study drug.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups

Reporting group title	Placebo

Reporting group description:

Placebo for ABT-981 every two weeks (Q2W) for 24 weeks.

Reporting group title	ABT-981

Reporting group description:

ABT-981 200 mg every two weeks (Q2W) for 24 weeks.

Serious adverse events	Placebo	ABT-981	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 67 (2.99%)	2 / 64 (3.13%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Investigations			
Haemoglobin decreased			
subjects affected / exposed	0 / 67 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Invasive breast carcinoma			
subjects affected / exposed	1 / 67 (1.49%)	0 / 64 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute coronary syndrome			

subjects affected / exposed	1 / 67 (1.49%)	0 / 64 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Faeces discoloured			
subjects affected / exposed	0 / 67 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 67 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Placebo	ABT-981	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	45 / 67 (67.16%)	49 / 64 (76.56%)	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	3 / 67 (4.48%)	4 / 64 (6.25%)	
occurrences (all)	3	4	
Nervous system disorders			
Dizziness			
subjects affected / exposed	4 / 67 (5.97%)	4 / 64 (6.25%)	
occurrences (all)	10	9	
Headache			
subjects affected / exposed	17 / 67 (25.37%)	10 / 64 (15.63%)	
occurrences (all)	35	22	
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	0 / 67 (0.00%)	6 / 64 (9.38%)	
occurrences (all)	0	12	
General disorders and administration			

site conditions			
Fatigue			
subjects affected / exposed	0 / 67 (0.00%)	4 / 64 (6.25%)	
occurrences (all)	0	4	
Injection site erythema			
subjects affected / exposed	0 / 67 (0.00%)	7 / 64 (10.94%)	
occurrences (all)	0	10	
Injection site rash			
subjects affected / exposed	3 / 67 (4.48%)	7 / 64 (10.94%)	
occurrences (all)	6	44	
Injection site reaction			
subjects affected / exposed	3 / 67 (4.48%)	7 / 64 (10.94%)	
occurrences (all)	3	18	
Pain			
subjects affected / exposed	4 / 67 (5.97%)	0 / 64 (0.00%)	
occurrences (all)	4	0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	6 / 67 (8.96%)	4 / 64 (6.25%)	
occurrences (all)	6	4	
Nausea			
subjects affected / exposed	2 / 67 (2.99%)	8 / 64 (12.50%)	
occurrences (all)	2	11	
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	5 / 67 (7.46%)	4 / 64 (6.25%)	
occurrences (all)	5	4	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	6 / 67 (8.96%)	4 / 64 (6.25%)	
occurrences (all)	12	4	
Back pain			
subjects affected / exposed	11 / 67 (16.42%)	3 / 64 (4.69%)	
occurrences (all)	16	5	
Pain in extremity			

subjects affected / exposed	4 / 67 (5.97%)	3 / 64 (4.69%)	
occurrences (all)	5	3	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	17 / 67 (25.37%)	13 / 64 (20.31%)	
occurrences (all)	23	18	
Upper respiratory tract infection			
subjects affected / exposed	4 / 67 (5.97%)	4 / 64 (6.25%)	
occurrences (all)	4	4	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
22 October 2015	The main purpose of this amendments was to remove the Patient Global Assessment Questionnaire from Inclusion criteria and clarify patient reported outcome collection method.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported