



Clinical trial results:

Phase 2 Study of Single-Agent PF-03084014 in Patients With Advanced Triple-Negative Breast Cancer With or Without Genomic Alterations in Notch Receptors

Summary

EudraCT number	2014-002286-30
Trial protocol	GB IT BE ES DE HU
Global end of trial date	26 January 2016

Results information

Result version number	v1 (current)
This version publication date	04 December 2016
First version publication date	04 December 2016

Trial information

Trial identification

Sponsor protocol code	A8641020
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Pfizer, Inc.
Sponsor organisation address	235 E 42nd Street, New York, United States, NY 10017
Public contact	Pfizer ClinicalTrials.gov Call Center, Pfizer, Inc., +1 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer, Inc., +1 8007181021, ClinicalTrials.gov_Inquiries@pfizer.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	31 May 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	26 January 2016
Global end of trial reached?	Yes
Global end of trial date	26 January 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To estimate the objective response rate (ORR) of PF-03084014 when given as a single agent in the treatment of patients with advanced triple receptor-negative breast cancer (mTNBC) harboring activating genomic alterations in Notch receptors (NA+).

Protection of trial subjects:

This study was conducted in compliance with the ethical principles originating in or derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. In addition, all local regulatory requirements were followed, in particular, those affording greater protection to the safety of trial subjects.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 February 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	Italy: 5
Country: Number of subjects enrolled	Poland: 1
Country: Number of subjects enrolled	Spain: 4
Country: Number of subjects enrolled	United Kingdom: 3
Country: Number of subjects enrolled	United States: 6
Worldwide total number of subjects	19
EEA total number of subjects	13

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)	15
From 65 to 84 years	4
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 30 subjects were planned to be enrolled in the study: 15 subjects each with NA+ mTNBC and NA-mTNBC.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	PF-03084014
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Arm description:

PF-03084014 at the starting dose of 150 mg twice daily (BID) (in the form of one 100-mg and one 50-mg tablet) was administered orally BID continuously in 21-day cycles until disease progression, unacceptable toxicity, patient refusal of further treatment, patient withdrawal of consent or death, whichever occurred first.

Arm type	Experimental
Investigational medicinal product name	PF-03084014
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

PF-03084014 at the starting dose of 150 mg BID (in the form of one 100 mg and one 50-mg tablet) was to be administered orally BID continuously in 21-day cycles.

Number of subjects in period 1	PF-03084014
Started	19
Completed	0
Not completed	19
Adverse event, serious fatal	1
Consent withdrawn by subject	2
Global deterioration of health status	1
Adverse event, non-fatal	2
Unspecified	3
Objective progression or relapse	10

Baseline characteristics

Reporting groups

Reporting group title	PF-03084014
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Reporting group description:

PF-03084014 at the starting dose of 150 mg twice daily (BID) (in the form of one 100-mg and one 50-mg tablet) was administered orally BID continuously in 21-day cycles until disease progression, unacceptable toxicity, patient refusal of further treatment, patient withdrawal of consent or death, whichever occurred first.

Reporting group values	PF-03084014	Total	
Number of subjects	19	19	
Age categorical			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	15	15	
From 65-84 years	4	4	
85 years and over	0	0	
Age Continuous			
Units: years			
arithmetic mean	57.4		
standard deviation	± 12.1	-	
Gender, Male/Female			
Units: Participants			
Male	0	0	
Female	19	19	

End points

End points reporting groups

Reporting group title	PF-03084014
Reporting group description: PF-03084014 at the starting dose of 150 mg twice daily (BID) (in the form of one 100-mg and one 50-mg tablet) was administered orally BID continuously in 21-day cycles until disease progression, unacceptable toxicity, patient refusal of further treatment, patient withdrawal of consent or death, whichever occurred first.	

Primary: Objective Response (OR) Rate in Subjects With Advanced Triple Receptor-Negative Breast Cancer (mTNBC) Harboring Activating Genomic Alterations in Notch Receptors (NA+)

End point title	Objective Response (OR) Rate in Subjects With Advanced Triple Receptor-Negative Breast Cancer (mTNBC) Harboring Activating Genomic Alterations in Notch Receptors (NA+) ^[1]
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End point description:

OR status based on assessment of confirmed complete remission (CR) or confirmed partial remission (PR) according to Response Evaluation Criteria in Solid Tumors (RECIST 1.1). CR: Complete disappearance of all target lesions with the exception of nodal disease and all target nodes decreased to normal size (short axis less than [$<$]10 millimeter [mm]). PR: Greater than or equal to (\geq)30% decrease under baseline of the sum of diameters of all target measurable lesions.

End point type	Primary
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End point timeframe:

Every 6 weeks

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Data for this outcome measure was not collected due to early termination of this study.

End point values	PF-03084014			
Subject group type	Reporting group			
Number of subjects analysed	0 ^[2]			
Units: percentage of subjects				
number (confidence interval 95%)	(to)			

Notes:

[2] - Data for this outcome measure was not collected due to early termination of this study.

Statistical analyses

No statistical analyses for this end point

Secondary: OR Rate in Subjects With mTNBC Whose Tumors Tested Negative for Genomic Alterations in Notch Receptor (NA-)

End point title	OR Rate in Subjects With mTNBC Whose Tumors Tested Negative for Genomic Alterations in Notch Receptor (NA-)
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End point description:

OR status based on assessment of confirmed CR or confirmed PR according to RECIST version 1.1. CR: Complete disappearance of all target lesions with the exception of nodal disease and all target nodes decreased to normal size (short axis $<$ 10 millimeter [mm]). PR: \geq 30% decrease under baseline of the sum of diameters of all target measurable lesions.

End point type	Secondary
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End point timeframe:

Every 6 weeks

End point values	PF-03084014			
Subject group type	Reporting group			
Number of subjects analysed	0 ^[3]			
Units: percentage of subjects				
number (confidence interval 95%)	(to)			

Notes:

[3] - Data for this outcome measure was not collected due to early termination of this study.

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-Free Survival (PFS) in Subjects With NA+ or NA mTNBC

End point title	Progression-Free Survival (PFS) in Subjects With NA+ or NA mTNBC
End point description:	The period from study entry until disease progression, death, whichever occurs first.
End point type	Secondary
End point timeframe:	2 years

End point values	PF-03084014			
Subject group type	Reporting group			
Number of subjects analysed	0 ^[4]			
Units: months				
median (confidence interval 95%)	(to)			

Notes:

[4] - Data for this outcome measure was not collected due to early termination of this study.

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DR) in Participants With NA+ or NA mTNBC

End point title	Duration of Response (DR) in Participants With NA+ or NA mTNBC
End point description:	Time from the first documentation of objective tumor response to objective tumor progression or death due to any cause. DR was calculated for the subgroup of patients with a confirmed objective tumor response.
End point type	Secondary

End point timeframe:

2 years

End point values	PF-03084014			
Subject group type	Reporting group			
Number of subjects analysed	0 ^[5]			
Units: months				
median (confidence interval 95%)	(to)			

Notes:

[5] - Data for this outcome measure was not collected due to early termination of this study.

Statistical analyses

No statistical analyses for this end point

Secondary: One-Year Survival Probability in Subjects With NA+ or NA mTNBC

End point title	One-Year Survival Probability in Subjects With NA+ or NA mTNBC
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End point description:

Overall survival (OS) status (alive or not) at 1 year after study entry. The 1-year OS probability was summarized as a product limit estimator based on the Kaplan-Meier method to account for censored events.

End point type	Secondary
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End point timeframe:

1 year

End point values	PF-03084014			
Subject group type	Reporting group			
Number of subjects analysed	0 ^[6]			
Units: percent chance of survival				
number (confidence interval 95%)	(to)			

Notes:

[6] - Data for this outcome measure was not collected due to early termination of this study.

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS) in Subjects With NA+ or NA mTNBC

End point title	Overall Survival (OS) in Subjects With NA+ or NA mTNBC
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End point description:

OS was the duration from enrollment to death. For participants who are alive, overall survival was censored at the last contact.

End point type	Secondary
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End point timeframe:

2 years

End point values	PF-03084014			
Subject group type	Reporting group			
Number of subjects analysed	0 ^[7]			
Units: subjects				
median (confidence interval 95%)	(to)			

Notes:

[7] - Data for this outcome measure was not collected due to early termination of this study.

Statistical analyses

No statistical analyses for this end point

Secondary: Type and Number of Notch Genomic Alterations in Subjects With NA+ mTNBC

End point title	Type and Number of Notch Genomic Alterations in Subjects With NA+ mTNBC
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End point description:

Type and number of notch genomic alterations identified by NGS assay in patients with NA+ mTNBC

End point type	Secondary
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End point timeframe:

2 years

End point values	PF-03084014			
Subject group type	Reporting group			
Number of subjects analysed	0 ^[8]			
Units: subjects				
number (not applicable)				

Notes:

[8] - Data for this outcome measure was not collected due to early termination of this study.

Statistical analyses

No statistical analyses for this end point

Secondary: Pre-dose Serum Concentration (Ctough) for PF-03084014

End point title	Pre-dose Serum Concentration (Ctough) for PF-03084014
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End point description:

End point type	Secondary
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End point timeframe:

Day 1 of Cycle 1, 2, 3, and 5

End point values	PF-03084014			
Subject group type	Reporting group			
Number of subjects analysed	0 ^[9]			
Units: ng/mL				
geometric mean (geometric coefficient of variation)	()			

Notes:

[9] - Due to study termination, no PK analyses were performed for this study.

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacodynamic (PD) Effects of PF03084014 in Tumor Specimens and Peripheral Blood

End point title	Pharmacodynamic (PD) Effects of PF03084014 in Tumor Specimens and Peripheral Blood
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End point description:

Original diagnostic tumor tissue or the most recent metastatic tumor (archival or de novo biopsy), plasma, and peripheral blood samples were collected for biomarker assessments of circulating analytes, immunohistochemistry for notch receptors expression, expression of notch pathway components and modulators, mutational analysis of pathway and disease associated genes.

End point type	Secondary
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End point timeframe:

Day 1 of Cycle 1, 2, 3, and 5

End point values	PF-03084014			
Subject group type	Reporting group			
Number of subjects analysed	0 ^[10]			
Units: subjects				
number (not applicable)				

Notes:

[10] - Due to study termination, no PD analyses were performed for this study.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Treatment-Emergent Adverse Events (AEs) or Serious Adverse Events (SAEs)

End point title	Number of Subjects with Treatment-Emergent Adverse Events (AEs) or Serious Adverse Events (SAEs)
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End point description:

An AE was any untoward medical occurrence without regard to causality in a subject who received study drug. An SAE was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life-threatening experience (immediate risk

of dying)); persistent or significant disability/incapacity; congenital anomaly.

End point type	Secondary
End point timeframe:	
2 years	

End point values	PF-03084014			
Subject group type	Reporting group			
Number of subjects analysed	19			
Units: subjects				
Number of Participants with AEs	18			
Number of Participants with SAEs	6			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Treatment-Emergent AEs by CTCAE Grade

End point title	Number of Subjects with Treatment-Emergent AEs by CTCAE Grade
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End point description:

An AE was any untoward medical occurrence without regard to causality in a subject who received study drug. AEs were defined according to Common Terminology Criteria for Adverse Events (CTCAE) version 4.03.

End point type	Secondary
End point timeframe:	
2 years	

End point values	PF-03084014			
Subject group type	Reporting group			
Number of subjects analysed	19			
Units: subjects				
Any AEs, Grade 1	1			
Any AEs, Grade 2	5			
Any AEs, Grade 3	9			
Any AEs, Grade 4	1			
Any AEs, Grade 5	2			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Laboratory Test (Hematology) Abnormalities

End point title	Number of Subjects with Laboratory Test (Hematology) Abnormalities
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End point description:

Number of subjects with CTCAE version 4.03 grade 1 to 4 hematological test abnormalities.

End point type	Secondary
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End point timeframe:

Day 1 of Cycles 1, 2, 3, 4, 5, and subsequent cycles.

End point values	PF-03084014			
Subject group type	Reporting group			
Number of subjects analysed	19			
Units: subjects				
Anemia	12			
Lymphocyte count increased	0			
Lymphopenia	11			
Neutrophils (absolute)	0			
Platelets	3			
White blood cells	4			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Laboratory Test (Chemistry) Abnormalities

End point title	Number of Subjects with Laboratory Test (Chemistry) Abnormalities
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End point description:

Number of subjects with CTCAE version 4.03 grade 1 to 4 chemistry test abnormalities

End point type	Secondary
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End point timeframe:

Day 1 and Day 15 of Cycles 1, 2, 3, 4, 5, and subsequent cycles up to Cycle 8 and Day 8 of Cycle 1

End point values	PF-03084014			
Subject group type	Reporting group			
Number of subjects analysed	19			
Units: Number of subjects				
Alanine aminotransferase	5			
Alkaline phosphatase	6			
Aspartate aminotransferase	9			
Bilirubin (total)	1			
Creatine kinase	1			
Creatinine	13			

Gamma glutamyl transferase	1			
Hypercalcemia	3			
Hyperglycemia	13			
Hyperkalemia	3			
Hypermagnesemia	1			
Hypernatremia	0			
Hypoalbuminemia	8			
Hypocalcemia	4			
Hypoglycemia	1			
Hypokalemia	5			
Hypomagnesemia	3			
Hyponatremia	6			
Hypophosphatemia	14			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Laboratory Test (Urinalysis) Abnormalities

End point title	Number of Subjects with Laboratory Test (Urinalysis) Abnormalities
End point description:	
Number of subjects with CTCAE version 4.03 grade 1 to 4 urinalysis test abnormalities for urine protein.	
End point type	Secondary
End point timeframe:	
Day 1 of Cycle 1	

End point values	PF-03084014			
Subject group type	Reporting group			
Number of subjects analysed	19			
Units: Number of subjects	2			

Statistical analyses

No statistical analyses for this end point

Post-hoc: Alterations in Genes, Proteins, and RNAs Relevant to the Notch Signaling Pathway, to TNBC Biology, and to Sensitivity/Resistance to PF-03084014 in Tumor Specimens and Peripheral Blood.

End point title	Alterations in Genes, Proteins, and RNAs Relevant to the Notch Signaling Pathway, to TNBC Biology, and to Sensitivity/Resistance to PF-03084014 in Tumor Specimens and Peripheral Blood.
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End point description:

Original diagnostic tumor tissue or the most recent metastatic tumor (archival or de novo biopsy),

plasma, and peripheral blood samples were collected for biomarker assessments of circulating analytes, immunohistochemistry for notch receptors expression, expression of notch pathway components and modulators, mutational analysis of pathway and disease associated genes.

End point type	Post-hoc
End point timeframe:	
Day 1 of Cycle 1, 2, 3, and 5	

End point values	PF-03084014			
Subject group type	Reporting group			
Number of subjects analysed	0 ^[11]			
Units: subjects				
number (not applicable)				

Notes:

[11] - Due to study termination, no PD analyses were performed for the study.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

2 years

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	18.1
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Reporting groups

Reporting group title	PF-03084014
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Reporting group description:

PF-03084014 at the starting dose of 150 mg twice daily (BID) (in the form of one 100 mg and one 50-mg tablet) was administered orally BID continuously in 21-day cycles.

Serious adverse events	PF-03084014		
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 19 (31.58%)		
number of deaths (all causes)	2		
number of deaths resulting from adverse events	2		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Transitional cell carcinoma			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Disease progression			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	1 / 1		
Pyrexia			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			

subjects affected / exposed	1 / 19 (5.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	1 / 1		
Psychiatric disorders			
Confusional state			
subjects affected / exposed	2 / 19 (10.53%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Lung infection			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Hypophosphataemia			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	PF-03084014		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	18 / 19 (94.74%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour exudation			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Tumour haemorrhage			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Tumour pain			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	2		
General disorders and administration site conditions			

<p>Asthenia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Chest pain</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Fatigue</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Mucosal inflammation</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Oedema peripheral</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Pyrexia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 19 (5.26%)</p> <p>1</p>		
	<p>2 / 19 (10.53%)</p> <p>2</p>		
	<p>8 / 19 (42.11%)</p> <p>10</p>		
	<p>3 / 19 (15.79%)</p> <p>5</p>		
	<p>1 / 19 (5.26%)</p> <p>1</p>		
	<p>5 / 19 (26.32%)</p> <p>8</p>		
<p>Respiratory, thoracic and mediastinal disorders</p> <p>Cough</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Nasal congestion</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Productive cough</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Upper respiratory tract inflammation</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>5 / 19 (26.32%)</p> <p>7</p>		
	<p>1 / 19 (5.26%)</p> <p>1</p>		
	<p>1 / 19 (5.26%)</p> <p>1</p>		
	<p>1 / 19 (5.26%)</p> <p>1</p>		
<p>Psychiatric disorders</p> <p>Anxiety</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Depression</p>	<p>1 / 19 (5.26%)</p> <p>1</p>		

subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	2		
Aspartate aminotransferase increased			
subjects affected / exposed	3 / 19 (15.79%)		
occurrences (all)	5		
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Blood chloride decreased			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Blood creatinine increased			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Carbon dioxide increased			
subjects affected / exposed	2 / 19 (10.53%)		
occurrences (all)	2		
Glomerular filtration rate decreased			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Electrocardiogram QT prolonged			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Protein total increased			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Transaminases increased			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Weight decreased			

subjects affected / exposed occurrences (all)	2 / 19 (10.53%) 2		
Cardiac disorders Angina pectoris subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1		
Nervous system disorders Balance disorder subjects affected / exposed occurrences (all) Dizziness subjects affected / exposed occurrences (all) Dysgeusia subjects affected / exposed occurrences (all) Headache subjects affected / exposed occurrences (all) Lethargy subjects affected / exposed occurrences (all) Peripheral motor neuropathy subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1 1 / 19 (5.26%) 1 2 / 19 (10.53%) 2 1 / 19 (5.26%) 1 2 / 19 (10.53%) 3 1 / 19 (5.26%) 1		
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 5		
Ear and labyrinth disorders Vertigo subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1		
Eye disorders Eye discharge subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 2		

Photopsia			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Vitreous floaters			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Abdominal pain			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Diarrhoea			
subjects affected / exposed	11 / 19 (57.89%)		
occurrences (all)	16		
Dry mouth			
subjects affected / exposed	2 / 19 (10.53%)		
occurrences (all)	2		
Dyspepsia			
subjects affected / exposed	3 / 19 (15.79%)		
occurrences (all)	3		
Nausea			
subjects affected / exposed	8 / 19 (42.11%)		
occurrences (all)	13		
Oral pain			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Stomatitis			
subjects affected / exposed	2 / 19 (10.53%)		
occurrences (all)	2		
Vomiting			
subjects affected / exposed	7 / 19 (36.84%)		
occurrences (all)	13		
Skin and subcutaneous tissue disorders			

Nail dystrophy			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Rash			
subjects affected / exposed	3 / 19 (15.79%)		
occurrences (all)	7		
Rash macular			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Urticaria			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	2		
Musculoskeletal and connective tissue disorders			
Bone pain			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Flank pain			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	3		
Muscular weakness			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Musculoskeletal chest pain			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Myalgia			
subjects affected / exposed	2 / 19 (10.53%)		
occurrences (all)	2		
Neck pain			

subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Pain in extremity			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Infections and infestations			
Conjunctivitis			
subjects affected / exposed	3 / 19 (15.79%)		
occurrences (all)	3		
Gastroenteritis viral			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Nasopharyngitis			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Pharyngitis			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Respiratory tract infection			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	2		
Urinary tract infection			
subjects affected / exposed	2 / 19 (10.53%)		
occurrences (all)	2		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	2 / 19 (10.53%)		
occurrences (all)	2		
Hypercalcaemia			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Hyperglycaemia			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Hypoalbuminaemia			

subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Hypocalcaemia			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Hypokalaemia			
subjects affected / exposed	3 / 19 (15.79%)		
occurrences (all)	8		
Hypophosphataemia			
subjects affected / exposed	7 / 19 (36.84%)		
occurrences (all)	21		
Hypouricaemia			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 September 2014	Protocol Amendment 1
16 February 2015	Protocol Amendment 2
20 April 2015	Protocol Amendment 3

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

This study was terminated prematurely based on project re-prioritization by the Sponsor and was not due to any safety concerns or regulatory actions.

Notes: