Clinical trial results:
A Phase 2a, Randomized, Double-Blind, Placebo-Controlled, Multi-Dose, Cross-Over, Efficacy and Safety Study of IPI-145 in Mild Asthmatic Subjects Undergoing Allergen Challenge

Summary

EudraCT number	2012-001729-28
Trial protocol	GB DE
Global end of trial date	30 July 2014
Results information	
Result version number	v2 (current)
This version publication date	25 November 2023
First version publication date	16 August 2015
Version creation reason	• Correction of full data set Results contact info has changed.
Summary attachment (see zip file)	IPI-145-03_Clinical_Study_Report_Synopsis_FINAL_150720 (IPI-145-03_Clinical_Study_Report_Synopsis_FINAL_150720.pdf)

Trial information

Trial identification	
Sponsor protocol code	IPI-145-03
Additional study identifiers	
ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors	
Sponsor organisation name	Secura Bio, Inc.
Sponsor organisation address	1995 Village Center Circle, Suite 128, Las Vegas, NV, United States, 89134
Public contact	Beth Gregory, PharmD, MBA, Secura Bio, Inc., 1 702-254-0011, bgregory@securabio.com
Scientific contact	Beth Gregory, PharmD, MBA, Secura Bio, Inc., 1 702-254-0011, bgregory@securabio.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	24 September 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 July 2014
Global end of trial reached?	Yes
Global end of trial date	30 July 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Examine the effects of multi-dose regimens of different dose strengths of IPI-145 on lung function in asthmatic subjects following allergen challenge

Protection of trial subjects:

The Sponsor conducted internal safety reviews after Cohorts 1 and 2 and after the first 5 subjects were enrolled in Cohort 3 (prior to completing enrollment in this cohort). Teleconferences occurred between the Sponsor and Principal Investigators and their staff to discuss study conduct progress and any safety matters. The final study protocol and its amendments, including the final version of the informed consent form (ICF), was approved or given a favorable opinion in writing by an Independent Ethics Committee (IEC) at each clinical trial site. The Principal Investigator had to submit written approval to Infinity before he or she could enroll any subject into the study.
The Principal Investigator was responsible for informing the IEC of any amendment to the protocol. In addition, the IEC approved all advertising used to recruit subjects for the study.

Progress reports and notifications of serious adverse events (SAEs) were provided to the IEC according to regulations and guidelines.

The study was conducted in accordance with the principles of the Declaration of Helsinki in place at the time of study conduct. The study was conducted in compliance with the International Conference on Harmonisation (ICH) E6 Guideline for Good Clinical Practice (GCP) (Committee for Proprietary Medicinal Products [CPMP] guideline CPMP/ICH/135/95), and compliant with the European Union Clinical Trial Directive (EU CTD): Directive 2001/20/EC, and all applicable local regulatory requirements.
Written informed consent was obtained from all subjects prior to any study screening procedures and subsequent enrollment into the study. The information recorded for all consented subjects, regardless of their suitability for the study, was retained and archived.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	20 July 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 24
Country: Number of subjects enrolled	Germany: 26
Worldwide total number of subjects	50
EEA total number of subjects	50

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)	50
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment	
Recruitment details: -	
Pre-assignment	
Screening details: -	
Pre-assignment period milestones	
Number of subjects started	50
Number of subjects completed	49
Pre-assignment subject non-completion reasons	
Reason: Number of subjects	Subject discontinuted prior to first treatment: 1

Period 1	
Period 1 title	Treatment period 1
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor
Arms	
Are arms mutually exclusive?	Yes
Arm title	IPI-145+Placebo (Cohort 1)
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	IPI-145
Investigational medicinal product code	PR1
Other name	Duvelisib
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use
Dosage and administration details: 1 mg Q12h	
Arm title	IPI-145+Placebo (Cohort 2)
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	IPI-145
Investigational medicinal product code	PR2
Other name	Duvelisib
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use
Dosage and administration details: 5 mg Q12h	
Arm title	IPI-145+Placebo (Cohort 3)
Arm description: -	
Arm type	Experimental

Investigational medicinal product name	IPI-145
Investigational medicinal product code	PR3
Other name	Duvelisib
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

25 mg Q12h

Number of subjects in period 1[1]	IPI-145+Placebo (Cohort 1)	IPI-145+Placebo (Cohort 2)	IPI-145+Placebo (Cohort 3)
Started	13	18	18
Completed	11	18	18
Not completed	2	0	0
Physician decision	1	-	-
Adverse event, non-fatal	1	-	-

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: Baseline characteristics reported only for participants that received study treatment.

Period 2

Period 2 title	Treatment period 2
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	IPI-145+Placebo (Cohort 1)

Arm description: -

Arm type	Experimental
Investigational medicinal product name	IPI-145
Investigational medicinal product code	PR1
Other name	Duvelisib
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

1 mg Q12h

Arm title	IPI-145+Placebo (Cohort 2)

Arm description: -

Arm type	Experimental
Investigational medicinal product name	IPI-145
Investigational medicinal product code	PR2
Other name	Duvelisib
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:
5 mg Q12h

Arm title	IPI-145+Placebo (Cohort 3)
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	IPI-145
Investigational medicinal product code	PR3
Other name	Duvelisib
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:
25 mg Q12h

Number of subjects in period 2	IPI-145+Placebo (Cohort 1)	IPI-145+Placebo (Cohort 2)	IPI-145+Placebo (Cohort 3)
Started	11	18	18
Completed	11	18	18

Baseline characteristics

Reporting groups	
Reporting group title	Treatment period 1

Reporting group description: -

Reporting group values	Treatment period 1	Total	
Number of subjects	49	49	
Age categorical Units: Subjects			
18-29 years	19	19	
30-39 years	12	12	
40-49 years	13	13	
50-60 years	5	5	
Age continuous Units: years			
arithmetic mean	35.8		
full range (min-max)	21 to 59	-	
Gender categorical Units: Subjects			
Female	15	15	
Male	34	34	

Subject analysis sets	
Subject analysis set title	Full analysis set
Subject analysis set type	Full analysis

Subject analysis set description:

All subjects who received at least one dose of study drug (IPI-145 or matching placebo)

Subject analysis set title	IPI-145 cohort 1
Subject analysis set type	Per protocol

Subject analysis set description:

All Cohort 1 subjects in the full analysis set who completed allergen challenge in Treatment Period 1 and Treatment Period 2

Subject analysis set title	Placebo cohort 1
Subject analysis set type	Per protocol

Subject analysis set description:

All Cohort 1 subjects in the full analysis set who completed allergen challenge in Treatment Period 1 and Treatment Period 2

Subject analysis set title	IPI-145 cohort 2
Subject analysis set type	Per protocol

Subject analysis set description:

All Cohort 2 subjects in the full analysis set who completed allergen challenge in Treatment Period 1 and Treatment Period 2

Subject analysis set title	Placebo cohort 2
Subject analysis set type	Per protocol

Subject analysis set description:

All Cohort 2 subjects in the full analysis set who completed allergen challenge in Treatment Period 1 and Treatment Period 2

Subject analysis set title	IPI-145 cohort 3

Subject analysis set type	Per protocol

Subject analysis set description:

All Cohort 3 subjects in the full analysis set who completed allergen challenge in Treatment Period 1 and Treatment Period 2

Subject analysis set title	Placebo cohort 3
Subject analysis set type	Per protocol

Subject analysis set description:

All Cohort 3 subjects in the full analysis set who completed allergen challenge in Treatment Period 1 and Treatment Period 2

Subject analysis set title	Cohort 1 PK analysis
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Subjects with sufficient IPI-145 plasma concentrations

Subject analysis set title	Cohort 2 PK analysis
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Subjects with sufficient IPI-145 plasma concentrations

Subject analysis set title	Cohort 3 PK analysis
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Subjects with sufficient IPI-145 plasma concentrations

Reporting group values	Full analysis set	IPI-145 cohort 1	Placebo cohort 1
Number of subjects	49	10	10
Age categorical Units: Subjects			
18-29 years	19		
30-39 years	12		
40-49 years	13		
50-60 years	5		
Age continuous Units: years			
arithmetic mean	35.8		
full range (min-max)	21 to 59		
Gender categorical Units: Subjects			
Female	15		
Male	34		

Reporting group values	IPI-145 cohort 2	Placebo cohort 2	IPI-145 cohort 3
Number of subjects	17	17	16
Age categorical Units: Subjects			
18-29 years			
30-39 years			
40-49 years			
50-60 years			
Age continuous Units: years			
arithmetic mean			
full range (min-max)			

Gender categorical Units: Subjects			
Female Male			

Reporting group values	Placebo cohort 3	Cohort 1 PK analysis	Cohort 2 PK analysis
Number of subjects	16	12	18
Age categorical Units: Subjects			
18-29 years 30-39 years 40-49 years 50-60 years			
Age continuous Units: years arithmetic mean full range (min-max)			
Gender categorical Units: Subjects			
Female Male			

Reporting group values	Cohort 3 PK analysis		
Number of subjects	18		
Age categorical Units: Subjects			
18-29 years 30-39 years 40-49 years 50-60 years			
Age continuous Units: years arithmetic mean full range (min-max)			
Gender categorical Units: Subjects			
Female Male			

End points

End points reporting groups

Reporting group title	IPI-145+Placebo (Cohort 1)
Reporting group description: -	
Reporting group title	IPI-145+Placebo (Cohort 2)
Reporting group description: -	
Reporting group title	IPI-145+Placebo (Cohort 3)
Reporting group description: -	
Reporting group title	IPI-145+Placebo (Cohort 1)
Reporting group description: -	
Reporting group title	IPI-145+Placebo (Cohort 2)
Reporting group description: -	
Reporting group title	IPI-145+Placebo (Cohort 3)
Reporting group description: -	
Subject analysis set title	Full analysis set
Subject analysis set type	Full analysis
Subject analysis set description:	
All subjects who received at least one dose of study drug (IPI-145 or matching placebo)	
Subject analysis set title	IPI-145 cohort 1
Subject analysis set type	Per protocol
Subject analysis set description:	
All Cohort 1 subjects in the full analysis set who completed allergen challenge in Treatment Period 1 and Treatment Period 2	
Subject analysis set title	Placebo cohort 1
Subject analysis set type	Per protocol
Subject analysis set description:	
All Cohort 1 subjects in the full analysis set who completed allergen challenge in Treatment Period 1 and Treatment Period 2	
Subject analysis set title	IPI-145 cohort 2
Subject analysis set type	Per protocol
Subject analysis set description:	
All Cohort 2 subjects in the full analysis set who completed allergen challenge in Treatment Period 1 and Treatment Period 2	
Subject analysis set title	Placebo cohort 2
Subject analysis set type	Per protocol
Subject analysis set description:	
All Cohort 2 subjects in the full analysis set who completed allergen challenge in Treatment Period 1 and Treatment Period 2	
Subject analysis set title	IPI-145 cohort 3
Subject analysis set type	Per protocol
Subject analysis set description:	
All Cohort 3 subjects in the full analysis set who completed allergen challenge in Treatment Period 1 and Treatment Period 2	
Subject analysis set title	Placebo cohort 3
Subject analysis set type	Per protocol
Subject analysis set description:	
All Cohort 3 subjects in the full analysis set who completed allergen challenge in Treatment Period 1 and Treatment Period 2	
Subject analysis set title	Cohort 1 PK analysis
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Subjects with sufficient IPI-145 plasma concentrations

Subject analysis set title	Cohort 2 PK analysis
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Subjects with sufficient IPI-145 plasma concentrations

Subject analysis set title	Cohort 3 PK analysis
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Subjects with sufficient IPI-145 plasma concentrations

Primary: Maximal decrease from pre-allergen challenge in FEV1 following allergen challenge in the early asthmatic response [EAR]

End point title	Maximal decrease from pre-allergen challenge in FEV1 following allergen challenge in the early asthmatic response [EAR]

End point description:

End point type	Primary

End point timeframe:

Before and after each allergen challenge of each treatment period

End point values	IPI-145 cohort 1	Placebo cohort 1	IPI-145 cohort 2	Placebo cohort 2
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	10	10	17	17
Units: Liters				
least squares mean (standard error)	-0.885 (± 0.154)	-0.958 (± 0.154)	-0.938 (± 0.141)	-0.945 (± 0.141)

End point values	IPI-145 cohort 3	Placebo cohort 3		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	16	16		
Units: Liters				
least squares mean (standard error)	-0.993 (± 0.093)	-0.97 (± 0.093)		

Statistical analyses

Statistical analysis title	Mixed-effects model for a crossover design

Statistical analysis description:

The number of subjects included in this analysis are exactly half of the number of subjects reported below, because this is a cross-over design in which each subject receives both treatments (IPI-145 and placebo).

Comparison groups	IPI-145 cohort 1 v Placebo cohort 1

Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4571
Method	Mixed models analysis

Statistical analysis title	Mixed-effects model for a crossover design

Statistical analysis description:

The number of subjects included in this analysis are exactly half of the number of subjects reported below, because this is a cross-over design in which each subject receives both treatments (IPI-145 and placebo).

Comparison groups	IPI-145 cohort 2 v Placebo cohort 2
Number of subjects included in analysis	34
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.941
Method	Mixed models analysis

Statistical analysis title	Mixed-effects model for a crossover design

Statistical analysis description:

The number of subjects included in this analysis are exactly half of the number of subjects reported below, because this is a cross-over design in which each subject receives both treatments (IPI-145 and placebo).

Comparison groups	IPI-145 cohort 3 v Placebo cohort 3
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8021
Method	Mixed models analysis

Primary: Maximal decrease from pre-allergen challenge in FEV1 following allergen challenge in the late asthmatic response [LAR]

End point title	Maximal decrease from pre-allergen challenge in FEV1 following allergen challenge in the late asthmatic response [LAR]

End point description:

End point type	Primary

End point timeframe:

Day 14: post-allergen challenge LAR

End point values	IPI-145 cohort 1	Placebo cohort 1	IPI-145 cohort 2	Placebo cohort 2
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	10	10	17	17
Units: Liters				
least squares mean (standard error)	-1.054 (± 0.14)	-0.874 (± 0.14)	-1.094 (± 0.172)	-0.99 (± 0.172)

End point values	IPI-145 cohort 3	Placebo cohort 3		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	16	16		
Units: Liters				
least squares mean (standard error)	-0.597 (± 0.09)	-0.773 (± 0.09)		

Statistical analyses

Statistical analysis title	Mixed-effects model for a crossover design

Statistical analysis description:

The number of subjects included in this analysis are exactly half of the number of subjects reported below, because this is a cross-over design in which each subject receives both treatments (IPI-145 and placebo).

Comparison groups	IPI-145 cohort 1 v Placebo cohort 1
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1599
Method	Mixed models analysis

Statistical analysis title	Mixed-effects model for a crossover design

Statistical analysis description:

The number of subjects included in this analysis are exactly half of the number of subjects reported below, because this is a cross-over design in which each subject receives both treatments (IPI-145 and placebo).

Comparison groups	Placebo cohort 2 v IPI-145 cohort 2
Number of subjects included in analysis	34
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2497
Method	Mixed models analysis

Statistical analysis title	Mixed-effects model for a crossover design

Statistical analysis description:

The number of subjects included in this analysis are exactly half of the number of subjects reported below, because this is a cross-over design in which each subject receives both treatments (IPI-145 and placebo).

Comparison groups	IPI-145 cohort 3 v Placebo cohort 3
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0517
Method	Mixed models analysis

Secondary: AUC of FEV1 following allergen challenge

End point title	AUC of FEV1 following allergen challenge

End point description:

End point type	Secondary

End point timeframe:

From pre-challenge to 10 hours post-challenge in each treatment period

End point values	IPI-145 cohort 1	Placebo cohort 1	IPI-145 cohort 2	Placebo cohort 2
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	10	10	17	17
Units: Liters				
least squares mean (standard error)	-0.491 (± 0.083)	-0.361 (± 0.085)	-0.534 (± 0.054)	-0.524 (± 0.052)

End point values	IPI-145 cohort 3	Placebo cohort 3		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	16	16		
Units: Liters				
least squares mean (standard error)	-0.258 (± 0.05)	-0.456 (± 0.053)		

Statistical analyses

No statistical analyses for this end point

Secondary: Cmax

End point title	Cmax

End point description:

End point type	Secondary

End point timeframe:

From 0 to 12 hours post-dose (IPI-145)

End point values	Cohort 1 PK analysis	Cohort 2 PK analysis	Cohort 3 PK analysis	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	12	18	18	
Units: ng/ml				
arithmetic mean (standard deviation)	50.15 (± 15.978)	244.78 (± 90.169)	1347.33 (± 728.671)	

Statistical analyses

No statistical analyses for this end point

Secondary: AUC

End point title	AUC

End point description:

End point type	Secondary

End point timeframe:

From 0 to 12 hours post-dose (IPI-145)

End point values	Cohort 1 PK analysis	Cohort 2 PK analysis	Cohort 3 PK analysis	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	12	18	18	
Units: ng x h/ml				
arithmetic mean (standard deviation)	149.94 (± 41.396)	796.64 (± 253.6)	5663.91 (± 3262.805)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All AEs will be recorded from the time of informed consent until 21 days after the last dose of study drug. Subjects will be instructed to report all AEs and will be asked a general health status question at each study visit.

Adverse event reporting additional description:

AEs reported by at least 2 subjects while on any dose of IPI-145

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.1

Reporting groups

Reporting group title	IPI-145 (Cohort 1)
Reporting group description: -	
Reporting group title	IPI-145 (Cohort 2)
Reporting group description: -	
Reporting group title	IPI-145 (Cohort 3)
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Serious adverse events	IPI-145 (Cohort 1)	IPI-145 (Cohort 2)	IPI-145 (Cohort 3)
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 12 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			

Serious adverse events	Placebo		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 48 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			

Frequency threshold for reporting non-serious adverse events: 4 %

Non-serious adverse events	IPI-145 (Cohort 1)	IPI-145 (Cohort 2)	IPI-145 (Cohort 3)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 12 (75.00%)	12 / 18 (66.67%)	7 / 18 (38.89%)
General disorders and administration site conditions			
Headache			
subjects affected / exposed	4 / 12 (33.33%)	7 / 18 (38.89%)	4 / 18 (22.22%)
occurrences (all)	9	12	7
Nausea			
subjects affected / exposed	1 / 12 (8.33%)	3 / 18 (16.67%)	1 / 18 (5.56%)
occurrences (all)	9	12	7
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	0 / 12 (0.00%)	1 / 18 (5.56%)	1 / 18 (5.56%)
occurrences (all)	9	12	7
Dyspepsia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 18 (5.56%)	1 / 18 (5.56%)
occurrences (all)	9	12	7
Respiratory, thoracic and mediastinal disorders			
Nasopharyngitis			
subjects affected / exposed	5 / 12 (41.67%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	9	12	7
Cough			
subjects affected / exposed	1 / 12 (8.33%)	1 / 18 (5.56%)	0 / 18 (0.00%)
occurrences (all)	9	12	7

Non-serious adverse events	Placebo		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	29 / 48 (60.42%)		
General disorders and administration site conditions			
Headache			
subjects affected / exposed	17 / 48 (35.42%)		
occurrences (all)	29		
Nausea			
subjects affected / exposed	3 / 48 (6.25%)		
occurrences (all)	29		
Gastrointestinal disorders			

Abdominal pain upper subjects affected / exposed occurrences (all) Dyspepsia subjects affected / exposed occurrences (all)	1 / 48 (2.08%) 29 0 / 48 (0.00%) 29		
Respiratory, thoracic and mediastinal disorders Nasopharyngitis subjects affected / exposed occurrences (all) Cough subjects affected / exposed occurrences (all)	8 / 48 (16.67%) 29 1 / 48 (2.08%) 29		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 June 2012	Protocol Amendment 1 (UK only)
01 August 2012	Protocol Amendment 1 (Germany only)
10 October 2012	Protocol Amendment 2 (UK only)
29 January 2013	Protocol Amendment 3
22 January 2014	Protocol Amendment 4

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported