Clinical trial results:
A Phase 2, Double-Blind, Parallel, Placebo-Controlled, Randomized Study to Evaluate Multiple Dose Levels of IPI- 145 with Background Methotrexate in Subjects with Active Rheumatoid Arthritis and an Inadequate Response to Methotrexate Alone

Summary

EudraCT number	2012-003724-20
Trial protocol	HU DE BG RO
Global end of trial date	23 December 2014

Results information

Result version number	v1
This version publication date	25 May 2016
First version publication date	25 May 2016
Summary attachment (see zip file)	IPI-145-04 CSR Synopsis (ipi-145-04-CSR-synopsis.pdf)

Trial information

Trial identification

Sponsor protocol code	IPI-145-04

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01851707
WHO universal trial number (UTN)	U1111-1138-8603

Notes:

Sponsors

Sponsor organisation name	Infinity Pharmaceuticals, Inc.
Sponsor organisation address	784 Memorial Drive, Cambridge, United States, 02139
Public contact	Shannon Devens, Infinity Pharmaceuticals, Inc, 001 6174531340,
Scientific contact	Claudio Dansky Ulmann, Infinity Pharmaceuticals, Inc, 001 6174531338,

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	24 September 2014
Global end of trial reached?	Yes
Global end of trial date	23 December 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Evaluate the efficacy of multiple dose levels of IPI 145 compared to placebo in subjects with moderate-to-severe active rheumatoid arthritis (RA) taking a stable dose of methotrexate (MTX)

Protection of trial subjects:

The final study protocol and its amendments, including the final version of the informed consent form (ICF), were approved or given a favorable opinion in writing by an Independent Ethics Committee (IEC) at each clinical trial site. The Principal Investigator had to provide evidence of IEC approval to Infinity before he or she could enroll any subject into the study. The Principal Investigator was responsible for informing the IRB/IEC of any amendment to the protocol. In addition, the IRB/IEC approved all advertising used to recruit subjects for the study. The protocol was re-approved by the IRB/IEC annually. Progress reports and notifications of serious adverse events (SAEs) were provided to the IRB/IEC according to regulations and guidelines.

Background therapy:

Methotrexate (MTX): Study subjects must have taken MTX for at least 3 months prior to Screening, with a stable dose and route (between 7.5 and 25.0 mg once per week) from at least 6 weeks prior to dosing (Day 1) to be eligible for inclusion.
Once on study, subjects must remain on a stable dose and route of MTX (between 7.5 and 25.0 mg once per week) from Screening through the last study visit (final Follow-up Visit).
If the weekly MTX dose is less than 15 mg, then subjects must have a documented history of intolerance or toxicity at doses ≥15 mg per week.

Evidence for comparator: -

Actual start date of recruitment	30 April 2013
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Romania: 1
Country: Number of subjects enrolled	Bulgaria: 17
Country: Number of subjects enrolled	Germany: 3
Country: Number of subjects enrolled	Hungary: 22
Country: Number of subjects enrolled	Mexico: 74
Country: Number of subjects enrolled	New Zealand: 7
Country: Number of subjects enrolled	Russian Federation: 39
Country: Number of subjects enrolled	Serbia: 15
Country: Number of subjects enrolled	Ukraine: 57
Country: Number of subjects enrolled	Colombia: 16
Country: Number of subjects enrolled	Poland: 71

Worldwide total number of subjects	322
EEA total number of subjects	114

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)	319
From 65 to 84 years	3
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details: -

Pre-assignment period milestones

Number of subjects started	322
Number of subjects completed	322

Period 1

Period 1 title	Baseline period (overall period)
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	Cohort 1: duvelisib 0.5mg BID

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	duvelisib
Investigational medicinal product code	IPI-145
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:
BID dosing

Arm title	Cohort 2: duvelisib 1.0 mg BID

Arm description: -

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

Dosage and administration details:
BID dosing

Arm title	Cohort 3: duvelisib 5.0 mg BID

Arm description: -

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

Dosage and administration details:

BID dosing

Arm title	Cohort 4: placebo BID
Arm description: -	
Arm type	Placebo
Investigational medicinal product name	placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

IPI-145 placebo will be supplied in capsule form and consists of capsules filled with silicified microcrystalline cellulose. The IPI-145 placebo capsules are supplied as size 2, white opaque hard gelatin capsules to match the 0.5 and 1 mg IPI-145 drug product capsules and as size 2 orange opaque hard gelatin capsules to match the 5 mg IPI-145 drug product capsule.

Number of subjects in period 1	Cohort 1: duvelisib 0.5mg BID	Cohort 2: duvelisib 1.0 mg BID	Cohort 3: duvelisib 5.0 mg BID
Started	81	80	81
Baseline	81	80	81
End of Treatment	70	75	58
Completed	70	75	58
Not completed	11	5	23
Consent withdrawn by subject	3	-	5
Adverse event, non-fatal	5	3	14
other	-	-	1
Lost to follow-up	-	-	2
Lack of efficacy	3	1	1
Protocol deviation	-	1	-

Number of subjects in period 1	Cohort 4: placebo BID
Started	80
Baseline	80
End of Treatment	71
Completed	71
Not completed	9
Consent withdrawn by subject	4
Adverse event, non-fatal	2
other	-
Lost to follow-up	1
Lack of efficacy	2

Protocol deviation	-

Baseline characteristics

Reporting groups	
Reporting group title	Cohort 1: duvelisib 0.5mg BID
Reporting group description: -	
Reporting group title	Cohort 2: duvelisib 1.0 mg BID
Reporting group description: -	
Reporting group title	Cohort 3: duvelisib 5.0 mg BID
Reporting group description: -	
Reporting group title	Cohort 4: placebo BID
Reporting group description: -	

Reporting group values	Cohort 1: duvelisib 0.5mg BID	Cohort 2: duvelisib 1.0 mg BID	Cohort 3: duvelisib 5.0 mg BID
Number of subjects	81	80	81
Age categorical Units: Subjects			
Adults (18-64 years)	81	80	78
From 65-84 years	0	0	3
Age continuous			
Age at baseline			
Units: years arithmetic mean standard deviation	 53.6 ± 9.27	 52.8 ± 9.67	 53.3 ± 11.8
Gender categorical Units: Subjects			
Female	72	66	70
Male	9	14	11

Reporting group values	Cohort 4: placebo BID	Total	
Number of subjects	80	322	
Age categorical Units: Subjects			
Adults (18-64 years)	80	319	
From 65-84 years	0	3	
Age continuous			
Age at baseline			
Units: years arithmetic mean standard deviation	 53.1 ± 9.56	 -	
Gender categorical Units: Subjects			
Female	60	268	
Male	20	54	

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

Subject analysis set description:
All subjects dosed

Reporting group values	Full Analysis		
Number of subjects	322		
Age categorical Units: Subjects			
Adults (18-64 years)	319		
From 65-84 years	3		
Age continuous			
Age at baseline			
Units: years			
arithmetic mean	53.2		
standard deviation	± 10.08		
Gender categorical Units: Subjects			
Female	268		
Male	54		

End points

End points reporting groups

Reporting group title	Cohort 1: duvelisib 0.5mg BID
Reporting group description: -	
Reporting group title	Cohort 2: duvelisib 1.0 mg BID
Reporting group description: -	
Reporting group title	Cohort 3: duvelisib 5.0 mg BID
Reporting group description: -	
Reporting group title	Cohort 4: placebo BID
Reporting group description: -	
Subject analysis set title	Full Analysis
Subject analysis set type	Full analysis
Subject analysis set description: All subjects dosed	

Primary: ACR20

End point title	ACR20
End point description: American College of Rheumatology 20% improvement	
End point type	Primary
End point timeframe: Week 12	

End point values	Cohort 1: duvelisib 0.5mg BID	Cohort 2: duvelisib 1.0 mg BID	Cohort 3: duvelisib 5.0 mg BID	Cohort 4: placebo BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	81	80	81	80
Units: subjects	42	36	35	37

End point values	Full Analysis			
Subject group type	Subject analysis set			
Number of subjects analysed	322			
Units: subjects	150			

Statistical analyses

Statistical analysis title	Primary Analyses of ACR20 Response at Week 12
Statistical analysis description: Primary Analyses of ACR20 Response at Week 12	
Comparison groups	Cohort 4: placebo BID v Cohort 3: duvelisib 5.0 mg BID v Cohort 2: duvelisib 1.0 mg BID v Cohort 1: duvelisib 0.5mg

	BID
Number of subjects included in analysis	322
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.73
upper limit	2.16
Variability estimate	Standard deviation

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Treatment period plus 21 day follow-up	
Assessment type	Non-systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	16.1
Reporting groups	
Reporting group title	Total Duvelisib

Reporting group description: -

Serious adverse events	Total Duvelisib		
Total subjects affected by serious adverse events			
subjects affected / exposed	10 / 242 (4.13%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Nervous system disorders			
Cerebral infarction			
subjects affected / exposed	1 / 242 (0.41%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Guillain-Barre syndrome			
subjects affected / exposed	1 / 242 (0.41%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ear and labyrinth disorders			
vertigo			
subjects affected / exposed	1 / 242 (0.41%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Dermatitis exfoliative			
subjects affected / exposed	1 / 242 (0.41%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

Neurodermatitis			
subjects affected / exposed	1 / 242 (0.41%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
foot deformity			
subjects affected / exposed	1 / 242 (0.41%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Rheumatoid arthritis			
subjects affected / exposed	1 / 242 (0.41%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
arcodermatitis			
subjects affected / exposed	1 / 242 (0.41%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
urinary tract infection			
subjects affected / exposed	1 / 242 (0.41%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Impetigo			
subjects affected / exposed	1 / 242 (0.41%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 0.1 %

Non-serious adverse events	Total Duvelisib		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	117 / 242 (48.35%)		
Vascular disorders			

Hypertension			
subjects affected / exposed	5 / 242 (2.07%)		
occurrences (all)	5		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	3 / 242 (1.24%)		
occurrences (all)	3		
Influenza like illness			
subjects affected / exposed	1 / 242 (0.41%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	2 / 242 (0.83%)		
occurrences (all)	2		
Allergic pharyngitis			
subjects affected / exposed	1 / 242 (0.41%)		
occurrences (all)	1		
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 242 (0.41%)		
occurrences (all)	1		
Cough			
subjects affected / exposed	1 / 242 (0.41%)		
occurrences (all)	1		
Psychiatric disorders			
Sleep disorder			
subjects affected / exposed	3 / 242 (1.24%)		
occurrences (all)	3		
Depression			
subjects affected / exposed	2 / 242 (0.83%)		
occurrences (all)	2		
Anhedonia			
subjects affected / exposed	1 / 242 (0.41%)		
occurrences (all)	1		
anxiety disorder			

subjects affected / exposed	1 / 242 (0.41%)		
occurrences (all)	1		
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	13 / 242 (5.37%)		
occurrences (all)	13		
Alanine aminotransferase increased			
subjects affected / exposed	12 / 242 (4.96%)		
occurrences (all)	12		
Lipase increased			
subjects affected / exposed	4 / 242 (1.65%)		
occurrences (all)	4		
Blood creatine phosphokinase increased			
subjects affected / exposed	3 / 242 (1.24%)		
occurrences (all)	3		
Blood creatinine increased			
subjects affected / exposed	2 / 242 (0.83%)		
occurrences (all)	2		
Blood pressure increased			
subjects affected / exposed	2 / 242 (0.83%)		
occurrences (all)	2		
Amylase increased			
subjects affected / exposed	1 / 242 (0.41%)		
occurrences (all)	1		
Blood calcium increased			
subjects affected / exposed	1 / 242 (0.41%)		
occurrences (all)	1		
Blood immunoglobulin E increased			
subjects affected / exposed	1 / 242 (0.41%)		
occurrences (all)	1		
Blood magnesium decreased			
subjects affected / exposed	1 / 242 (0.41%)		
occurrences (all)	1		
Blood urea increased			

subjects affected / exposed	1 / 242 (0.41%)		
occurrences (all)	1		
Lymphocyte count decreased			
subjects affected / exposed	1 / 242 (0.41%)		
occurrences (all)	1		
Transaminases increased			
subjects affected / exposed	1 / 242 (0.41%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 242 (0.41%)		
occurrences (all)	1		
Fibula fracture			
subjects affected / exposed	1 / 242 (0.41%)		
occurrences (all)	1		
skin injury			
subjects affected / exposed	1 / 242 (0.41%)		
occurrences (all)	1		
Spinal fracture			
subjects affected / exposed	1 / 242 (0.41%)		
occurrences (all)	1		
Subcutaneous haematoma			
subjects affected / exposed	1 / 242 (0.41%)		
occurrences (all)	1		
Tibia fracture			
subjects affected / exposed	1 / 242 (0.41%)		
occurrences (all)	1		
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 242 (0.41%)		
occurrences (all)	1		
Palpitations			
subjects affected / exposed	1 / 242 (0.41%)		
occurrences (all)	1		
Nervous system disorders			

Headache			
subjects affected / exposed	6 / 242 (2.48%)		
occurrences (all)	6		
Dizziness			
subjects affected / exposed	4 / 242 (1.65%)		
occurrences (all)	4		
Cerebral infarction			
subjects affected / exposed	1 / 242 (0.41%)		
occurrences (all)	1		
Guillain-Barre syndrome			
subjects affected / exposed	1 / 242 (0.41%)		
occurrences (all)	1		
Somnolence			
subjects affected / exposed	1 / 242 (0.41%)		
occurrences (all)	1		
Tremor			
subjects affected / exposed	1 / 242 (0.41%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	14 / 242 (5.79%)		
occurrences (all)	14		
Lymphopenia			
subjects affected / exposed	11 / 242 (4.55%)		
occurrences (all)	11		
Leukopenia			
subjects affected / exposed	4 / 242 (1.65%)		
occurrences (all)	4		
Neutropenia			
subjects affected / exposed	2 / 242 (0.83%)		
occurrences (all)	2		
Leukocytosis			
subjects affected / exposed	1 / 242 (0.41%)		
occurrences (all)	1		
Monocytopenia			

subjects affected / exposed	1 / 242 (0.41%)		
occurrences (all)	1		
Neutrophilia			
subjects affected / exposed	1 / 242 (0.41%)		
occurrences (all)	1		
Thrombocytosis			
subjects affected / exposed	1 / 242 (0.41%)		
occurrences (all)	1		
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 242 (0.41%)		
occurrences (all)	1		
Eye disorders			
Blepharitis			
subjects affected / exposed	1 / 242 (0.41%)		
occurrences (all)	1		
conjuntival haemorrhage			
subjects affected / exposed	1 / 242 (0.41%)		
occurrences (all)	1		
Scleritis			
subjects affected / exposed	1 / 242 (0.41%)		
occurrences (all)	1		
Vitreous floaters			
subjects affected / exposed	1 / 242 (0.41%)		
occurrences (all)	1		
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	7 / 242 (2.89%)		
occurrences (all)	7		
Dyspepsia			
subjects affected / exposed	5 / 242 (2.07%)		
occurrences (all)	5		
Diarrhoea			
subjects affected / exposed	4 / 242 (1.65%)		
occurrences (all)	4		
Gastritis			

subjects affected / exposed	3 / 242 (1.24%)		
occurrences (all)	3		
Vomiting			
subjects affected / exposed	2 / 242 (0.83%)		
occurrences (all)	2		
Abdominal pain			
subjects affected / exposed	1 / 242 (0.41%)		
occurrences (all)	1		
Abdominal pain upper			
subjects affected / exposed	1 / 242 (0.41%)		
occurrences (all)	1		
Anal fissure			
subjects affected / exposed	1 / 242 (0.41%)		
occurrences (all)	1		
Constipation			
subjects affected / exposed	1 / 242 (0.41%)		
occurrences (all)	1		
Dry mouth			
subjects affected / exposed	1 / 242 (0.41%)		
occurrences (all)	1		
Epigastric discomfort			
subjects affected / exposed	1 / 242 (0.41%)		
occurrences (all)	1		
Food poisoning			
subjects affected / exposed	1 / 242 (0.41%)		
occurrences (all)	1		
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 242 (0.41%)		
occurrences (all)	1		
Impaired gastric emptying			
subjects affected / exposed	1 / 242 (0.41%)		
occurrences (all)	1		
Pancreatitis			
subjects affected / exposed	1 / 242 (0.41%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			

Dermatitis exfoliative			
subjects affected / exposed	1 / 242 (0.41%)		
occurrences (all)	1		
Erythema			
subjects affected / exposed	1 / 242 (0.41%)		
occurrences (all)	1		
Neurodermatitis			
subjects affected / exposed	1 / 242 (0.41%)		
occurrences (all)	1		
Pruritus			
subjects affected / exposed	1 / 242 (0.41%)		
occurrences (all)	1		
Rash			
subjects affected / exposed	1 / 242 (0.41%)		
occurrences (all)	1		
Rash erythematous			
subjects affected / exposed	1 / 242 (0.41%)		
occurrences (all)	1		
Rash pruritic			
subjects affected / exposed	1 / 242 (0.41%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	5 / 242 (2.07%)		
occurrences (all)	5		
Back pain			
subjects affected / exposed	3 / 242 (1.24%)		
occurrences (all)	3		
Joint swelling			
subjects affected / exposed	3 / 242 (1.24%)		
occurrences (all)	3		
Fibromyalgia			
subjects affected / exposed	2 / 242 (0.83%)		
occurrences (all)	2		
muscle contracture			

subjects affected / exposed	2 / 242 (0.83%)		
occurrences (all)	2		
Musculoskeletal stiffness			
subjects affected / exposed	2 / 242 (0.83%)		
occurrences (all)	2		
Rheumatoid arthritis			
subjects affected / exposed	2 / 242 (0.83%)		
occurrences (all)	2		
foot deformity			
subjects affected / exposed	1 / 242 (0.41%)		
occurrences (all)	1		
Myalgia			
subjects affected / exposed	1 / 242 (0.41%)		
occurrences (all)	1		
Rotator cuff syndrome			
subjects affected / exposed	1 / 242 (0.41%)		
occurrences (all)	1		
Spinal osteoarthritis			
subjects affected / exposed	1 / 242 (0.41%)		
occurrences (all)	1		
Spinal pain			
subjects affected / exposed	1 / 242 (0.41%)		
occurrences (all)	1		
Tenosynovitis			
subjects affected / exposed	1 / 242 (0.41%)		
occurrences (all)	1		
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	6 / 242 (2.48%)		
occurrences (all)	6		
Pharyngitis			
subjects affected / exposed	3 / 242 (1.24%)		
occurrences (all)	3		
Upper respiratory tract infection			
subjects affected / exposed	3 / 242 (1.24%)		
occurrences (all)	3		

Bronchitis				
subjects affected / exposed	2 / 242 (0.83%)			
occurrences (all)	2			
Gastroenteritis				
subjects affected / exposed	2 / 242 (0.83%)			
occurrences (all)	2			
Urinary tract infection				
subjects affected / exposed	2 / 242 (0.83%)			
occurrences (all)	2			
Acarodermatitis				
subjects affected / exposed	1 / 242 (0.41%)			
occurrences (all)	1			
Cystitis				
subjects affected / exposed	1 / 242 (0.41%)			
occurrences (all)	1			
Escherichia urinary tract infection				
subjects affected / exposed	1 / 242 (0.41%)			
occurrences (all)	1			
Herpes simplex				
subjects affected / exposed	1 / 242 (0.41%)			
occurrences (all)	1			
Herpes zoster				
subjects affected / exposed	1 / 242 (0.41%)			
occurrences (all)	1			
Impetigo				
subjects affected / exposed	1 / 242 (0.41%)			
occurrences (all)	1			
Influenza				
subjects affected / exposed	1 / 242 (0.41%)			
occurrences (all)	1			
Oral herpes				
subjects affected / exposed	1 / 242 (0.41%)			
occurrences (all)	1			
Orchitis				
subjects affected / exposed	1 / 242 (0.41%)			
occurrences (all)	1			

Otitis media			
subjects affected / exposed	1 / 242 (0.41%)		
occurrences (all)	1		
Parasitic gastroenteritis			
subjects affected / exposed	1 / 242 (0.41%)		
occurrences (all)	1		
pharyngitis bacterial			
subjects affected / exposed	1 / 242 (0.41%)		
occurrences (all)	1		
Pneumonia			
subjects affected / exposed	1 / 242 (0.41%)		
occurrences (all)	1		
Sinusitis			
subjects affected / exposed	1 / 242 (0.41%)		
occurrences (all)	1		
Tonsillitis			
subjects affected / exposed	1 / 242 (0.41%)		
occurrences (all)	1		
Tooth abscess			
subjects affected / exposed	1 / 242 (0.41%)		
occurrences (all)	1		
Varicella			
subjects affected / exposed	1 / 242 (0.41%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	2 / 242 (0.83%)		
occurrences (all)	2		
decreased appetite			
subjects affected / exposed	1 / 242 (0.41%)		
occurrences (all)	1		
Diabetes mellitus			
subjects affected / exposed	1 / 242 (0.41%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 November 2012	Amendment 1
18 January 2013	Amendment 2
20 March 2014	Amendment 3

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported