



## 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	v2 (current)
This version publication date	24 November 2023
First version publication date	25 May 2016
Version creation reason	<ul style="list-style-type: none"><li>• Correction of full data set</li><li>Results contact info has changed.</li></ul>
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
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##### **Additional study identifiers**

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

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	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  $\geq 15$  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	Ukraine: 57
Country: Number of subjects enrolled	Bulgaria: 17
Country: Number of subjects enrolled	Colombia: 16
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	Poland: 71
Country: Number of subjects enrolled	Romania: 1
Country: Number of subjects enrolled	Russian Federation: 39
Country: Number of subjects enrolled	Serbia: 15

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

Notes:

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**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
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Number of subjects completed	322
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### Period 1

Period 1 title	Baseline period (overall period)
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Is this the baseline period?	Yes
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Allocation method	Randomised - controlled
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Blinding used	Double blind
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Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor
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### Arms

Are arms mutually exclusive?	Yes
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<b>Arm title</b>	Cohort 1: duvelisib 0.5mg BID
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Arm description: -

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

BID dosing

<b>Arm title</b>	Cohort 2: duvelisib 1.0 mg BID
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Arm description: -

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

BID dosing

<b>Arm title</b>	Cohort 3: duvelisib 5.0 mg BID
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Arm description: -

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

BID dosing

<b>Arm title</b>	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.

<b>Number of subjects in period 1</b>	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	-

<b>Number of subjects in period 1</b>	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	-
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## 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	53.6	52.8	53.3
standard deviation	± 9.27	± 9.67	± 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	53.1	-	
standard deviation	± 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

<b>Reporting group values</b>	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
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	16.1
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### Reporting groups

Reporting group title	Total Duvelisib
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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 %

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

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

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

subjects affected / exposed occurrences (all)	1 / 242 (0.41%) 1		
Lymphocyte count decreased subjects affected / exposed occurrences (all)	1 / 242 (0.41%) 1		
Transaminases increased subjects affected / exposed occurrences (all)	1 / 242 (0.41%) 1		
Injury, poisoning and procedural complications			
Contusion subjects affected / exposed occurrences (all)	1 / 242 (0.41%) 1		
Fibula fracture subjects affected / exposed occurrences (all)	1 / 242 (0.41%) 1		
skin injury subjects affected / exposed occurrences (all)	1 / 242 (0.41%) 1		
Spinal fracture subjects affected / exposed occurrences (all)	1 / 242 (0.41%) 1		
Subcutaneous haematoma subjects affected / exposed occurrences (all)	1 / 242 (0.41%) 1		
Tibia fracture subjects affected / exposed occurrences (all)	1 / 242 (0.41%) 1		
Cardiac disorders			
Atrial fibrillation subjects affected / exposed occurrences (all)	1 / 242 (0.41%) 1		
Palpitations subjects affected / exposed occurrences (all)	1 / 242 (0.41%) 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		
<b>Blood and lymphatic system disorders</b>			
<b>Anaemia</b>			
subjects affected / exposed	14 / 242 (5.79%)		
occurrences (all)	14		
<b>Lymphopenia</b>			
subjects affected / exposed	11 / 242 (4.55%)		
occurrences (all)	11		
<b>Leukopenia</b>			
subjects affected / exposed	4 / 242 (1.65%)		
occurrences (all)	4		
<b>Neutropenia</b>			
subjects affected / exposed	2 / 242 (0.83%)		
occurrences (all)	2		
<b>Leukocytosis</b>			
subjects affected / exposed	1 / 242 (0.41%)		
occurrences (all)	1		
<b>Monocytopenia</b>			

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

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

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

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		
<b>Infections and infestations</b>			
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		
Herpes simplex			
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 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:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported