



## Clinical trial results:

**A multicenter randomised study comparing the efficacy of pegylated interferon-alfa-2a plus placebo vs. pegylated interferon-alfa-2a plus tenofovir for the treatment of chronic delta hepatitis- The Hep-Net International Delta hepatitis Interventional Trial II (HIDIT-II)**

### Summary

EudraCT number	2008-005560-13
Trial protocol	DE GR
Global end of trial date	02 August 2017

### Results information

Result version number	v1 (current)
This version publication date	09 August 2022
First version publication date	09 August 2022

### Trial information

#### Trial identification

Sponsor protocol code	Hep-Net-HIDIT-2
-----------------------	-----------------

#### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00932971
WHO universal trial number (UTN)	-

Notes:

### Sponsors

Sponsor organisation name	Hannover Medical School
Sponsor organisation address	Carl-Neuberg-Str. 1, Hannover, Germany, 30625
Public contact	Zentrum für Klinische Studien, Hannover Medical School, EudraCT@mh-hannover.de
Scientific contact	Zentrum für Klinische Studien, Hannover Medical School, EudraCT@mh-hannover.de

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	22 October 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	02 August 2017
Global end of trial reached?	Yes
Global end of trial date	02 August 2017
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

To compare the virological efficacy (HDV-RNA) and safety of 96 weeks of therapy with PEG-IFN-2a plus tenofovir to 96 weeks of therapy with PEG-IFN-2a plus placebo for the treatment of patients with chronic delta hepatitis virus.

Protection of trial subjects:

The clinical trial was conducted in accordance with the ethical principles that have their origins in the Declaration of Helsinki and with the standards of International Conference on Harmonisation (ICH) Good Clinical Practice (GCP).

A continuous risk assessment was performed during the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	23 July 2009
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	Germany: 46
Country: Number of subjects enrolled	Romania: 19
Country: Number of subjects enrolled	Greece: 5
Worldwide total number of subjects	70
EEA total number of subjects	70

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)	70

From 65 to 84 years	0
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

71 subjects were enrolled over a period of 20 months. The first patient was enrolled on 23.07.2009 and the last patient was completed on 02.08.2017 (study period: 2009 - 2017). The clinical trial was not prematurely terminated and not temporarily halted.

### Pre-assignment

Screening details:

This was a clinical trial with a 1:1 randomization ratio for arm A:B. Patients were randomly assigned to one of the two study arms. After successful screening and approval of patient's eligibility by the investigator, the patient was randomized.

### Period 1

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

Blinding implementation details:

Pegylated interferon-alfa-2a will be provided by Roche. Placebo and tenofovir verum medication will be provided by Gilead Sciences GmbH. The code for each vial containing either tenofovir or placebo will be known only by the Hep-Net central randomization unit in Munich (provided by the Hep-Net CIO Dr. Müller, Munich, Germany) and by NextPharma Göttingen for blinded labeling of study medication.

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Arm A - PEG-Interferon + Tenofovir

Arm description:

PEG-Interferon alpha-2a 180µg oiw +  
Tenofovir disoproxilfumarat 245mg daily

Arm type	Experimental
Investigational medicinal product name	PEGASYS® (Pegylated Interferon-alfa-2a)
Investigational medicinal product code	
Other name	Pegylated Interferon-alfa-2a
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Pegylated interferon-alfa-2a: 180 mg/0.5mL; 0.5 mL solution in 0.5 mL refilled syringe for single dose sc injection and one needle. Storage: Refrigerate at 2° - 8° C (36° - 46° F).  
once weekly. Specific guidelines for adjusting the dose of pegylated interferon-alfa-2a are provided in Section 8.4. All pegylated interferon-alfa-2a administrations will be via the sc route utilizing sterile technique.

Study drug may be self-administered by the patients. Before providing the patient with study medication, the investigator or a qualified staff member will instruct the patient on the proper methods of storage of the medication, self-injection, and management and disposal of needles and syringes.

Investigational medicinal product name	VIREAD® (Tenofovir)
Investigational medicinal product code	
Other name	Tenofovir
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

245 mg tablets. Each film-coated tablet contains 245 mg of tenofovir disoproxil, equivalent to 300 mg of tenofovir disoproxil fumarate, or 136 mg of tenofovir. This medicinal product does not require any special storage conditions.

Tablets should be stored at room temperature

<b>Arm title</b>	Arm B - Peg + Placebo
Arm description: PEG-Interferon alpha-2a 180µg oiw + Placebo daily	
Arm type	Placebo
Investigational medicinal product name	PEGASYS® (Pegylated Interferon-alfa-2a)
Investigational medicinal product code	
Other name	Pegylated Interferon-alfa-2a
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Pegylated interferon-alfa-2a: 180 mg/0.5mL; 0.5 mL solution in 0.5 mL refilled syringe for single dose sc injection and one needle. Storage: Refrigerate at 2° - 8° C (36° - 46° F). once weekly. Specific guidelines for adjusting the dose of pegylated interferon-alfa-2a are provided in Section 8.4. All pegylated interferon-alfa-2a administrations will be via the sc route utilizing sterile technique.

Study drug may be self-administered by the patients. Before providing the patient with study medication, the investigator or a qualified staff member will instruct the patient on the proper methods of storage of the medication, self-injection, and management and disposal of needles and syringes.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

The placebo is available as a film-coated tablet which contains sugar or starch, additional excipients and taste corrigents. This medicinal product does not require any special storage conditions. Tablets should be stored at room temperature.

<b>Number of subjects in period 1</b>	Arm A - PEG-Interferon + Tenofovir	Arm B - Peg + Placebo
Started	34	36
Completed	34	36

## Baseline characteristics

### Reporting groups

Reporting group title	Arm A - PEG-Interferon + Tenofovir
Reporting group description:	
PEG-Interferon alpha-2a 180µg oiw + Tenofovir disoproxilfumarat 245mg daily	
Reporting group title	Arm B - Peg + Placebo
Reporting group description:	
PEG-Interferon alpha-2a 180µg oiw + Placebo daily	

Reporting group values	Arm A - PEG-Interferon + Tenofovir	Arm B - Peg + Placebo	Total
Number of subjects	34	36	70
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	34	36	70
From 65-84 years	0	0	0
85 years and over	0	0	0
Gender categorical			
Units: Subjects			
Female	12	12	24
Male	22	24	46
HDV RNA			
Units: Subjects			
missing	0	1	1
>=100000 IU/ml	16	19	35
<100000 IU/ml	18	16	34
HBV DNA			
Units: Subjects			
missing	3	7	10
>=100 IU/ml	15	17	32
<100 IU/ml	16	12	28
ALT			
Units: Subjects			
missing	0	1	1
>5xULN	4	3	7
<5xULN	30	32	62
Previously treated with interferon			
Units: Subjects			
no	21	21	42
yes	13	15	28



## End points

### End points reporting groups

Reporting group title	Arm A - PEG-Interferon + Tenofovir
Reporting group description:	
PEG-Interferon alpha-2a 180µg oiw + Tenofovir disoproxilfumarat 245mg daily	
Reporting group title	Arm B - Peg + Placebo
Reporting group description:	
PEG-Interferon alpha-2a 180µg oiw + Placebo daily	

### Primary: Negativation of HDV-RNA

End point title	Negativation of HDV-RNA
End point description:	
Negativation of HDV-RNA at the end of therapy (week 96) To compare the virological efficacy (HDV-RNA) and safety of 96 weeks of therapy with pegylated interferon-alfa-2a plus tenofovir to 96 weeks of therapy with pegylated interferon-alfa-2a plus placebo for the treatment of patients with chronic delta hepatitis virus.	
End point type	Primary
End point timeframe:	
96 weeks	

End point values	Arm A - PEG-Interferon + Tenofovir	Arm B - Peg + Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	34	36		
Units: percent	50	33		

### Statistical analyses

Statistical analysis title	Efficacy Results
Statistical analysis description:	
At the end of therapy (treatment week 96), 12/36 (33.3%) placebo-treated patients and 17/34 (50.0%) tenofovir treated patients had undetectable HDV RNA (Odds Ratio 1.980, 95%-CI: 0.739 – 5.310, P = 0.1745).	
Comparison groups	Arm A - PEG-Interferon + Tenofovir v Arm B - Peg + Placebo
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.05
Method	Fisher exact
Parameter estimate	Odds ratio (OR)

---

Confidence interval	
level	95 %
sides	2-sided
lower limit	20
upper limit	30

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Adverse Events were collected throughout the study up to the Post-Treatment Week 356 Visit.

Adverse event reporting additional description:

Numbers in the non-serious adverse events section reflect all adverse events occurring during the study (non-serious and serious).

Assessment type	Systematic
-----------------	------------

### Dictionary used

Dictionary name	MedDRA
-----------------	--------

Dictionary version	20.1
--------------------	------

### Reporting groups

Reporting group title	Placebo
-----------------------	---------

Reporting group description: -

Reporting group title	Verum
-----------------------	-------

Reporting group description: -

<b>Serious adverse events</b>	Placebo	Verum	
Total subjects affected by serious adverse events			
subjects affected / exposed	14 / 36 (38.89%)	12 / 34 (35.29%)	
number of deaths (all causes)	1	0	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic neoplasm			
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatocellular carcinoma			
subjects affected / exposed	3 / 36 (8.33%)	1 / 34 (2.94%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Thrombosis			

subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Surgical and medical procedures</b>			
Bursa removal			
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatectomy			
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nasal septal operation			
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal stone removal			
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Pregnancy, puerperium and perinatal conditions</b>			
Abortion spontaneous			
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy			
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Psychiatric disorders</b>			
Depression			
subjects affected / exposed	2 / 36 (5.56%)	0 / 34 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Investigations			
Transaminases increased			
subjects affected / exposed	1 / 36 (2.78%)	3 / 34 (8.82%)	
occurrences causally related to treatment / all	1 / 1	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac failure			
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Chordae tendinae rupture			
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Nervous system disorders			
Encephalopathy			
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	0 / 36 (0.00%)	3 / 34 (8.82%)	
occurrences causally related to treatment / all	0 / 0	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Diplopia			
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Anal ulcer			
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ascites			

subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Dysphagia</b>			
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Gastritis</b>			
subjects affected / exposed	1 / 36 (2.78%)	1 / 34 (2.94%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Gastrointestinal haemorrhage</b>			
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Varices oesophageal</b>			
subjects affected / exposed	1 / 36 (2.78%)	1 / 34 (2.94%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Hepatobiliary disorders</b>			
<b>Hepatomegaly</b>			
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Skin and subcutaneous tissue disorders</b>			
<b>Skin infection</b>			
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Renal and urinary disorders</b>			
<b>Ureterolithiasis</b>			
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Urinary retention			
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bursitis			
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abscess limb			
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess sweat gland			
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute sinusitis			
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Gastrointestinal infection			
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Plasmodium falciparum infection			
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 36 (0.00%)	2 / 34 (5.88%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Scrotal abscess			
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0 %

<b>Non-serious adverse events</b>	Placebo	Verum	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	35 / 36 (97.22%)	32 / 34 (94.12%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)	
occurrences (all)	1	0	
Haemangioma			
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)	
occurrences (all)	0	1	
Hepatic neoplasm			
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)	
occurrences (all)	1	0	
Hepatocellular carcinoma			

subjects affected / exposed occurrences (all)	4 / 36 (11.11%) 5	1 / 34 (2.94%) 1	
Lipoma subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	0 / 34 (0.00%) 0	
Pyogenic granuloma subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	0 / 34 (0.00%) 0	
Vascular disorders			
Hot flush subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	1 / 34 (2.94%) 1	
Hypertension subjects affected / exposed occurrences (all)	3 / 36 (8.33%) 3	1 / 34 (2.94%) 1	
Raynaud's phenomenon subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	1 / 34 (2.94%) 1	
Thrombosis subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	1 / 34 (2.94%) 1	
Surgical and medical procedures			
Bursa removal subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	0 / 34 (0.00%) 0	
Hepatectomy subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	0 / 34 (0.00%) 0	
High frequency ablation subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	0 / 34 (0.00%) 0	
Knee operation subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	1 / 34 (2.94%) 1	
Nasal septal operation			

subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	0 / 34 (0.00%) 0	
Renal stone removal subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	1 / 34 (2.94%) 1	
Tooth extraction subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	2 / 34 (5.88%) 2	
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	1 / 34 (2.94%) 1	
Pregnancy subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	1 / 34 (2.94%) 1	
General disorders and administration site conditions			
Asthenia subjects affected / exposed occurrences (all)	8 / 36 (22.22%) 8	2 / 34 (5.88%) 2	
Chest discomfort subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	1 / 34 (2.94%) 1	
Chest pain subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	3 / 34 (8.82%) 4	
Chills subjects affected / exposed occurrences (all)	4 / 36 (11.11%) 5	4 / 34 (11.76%) 4	
Exercise tolerance decreased subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	0 / 34 (0.00%) 0	
Fatigue subjects affected / exposed occurrences (all)	13 / 36 (36.11%) 15	15 / 34 (44.12%) 17	
Feeling cold			

subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)
occurrences (all)	0	1
Feeling hot		
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)
occurrences (all)	0	2
Influenza like illness		
subjects affected / exposed	22 / 36 (61.11%)	18 / 34 (52.94%)
occurrences (all)	23	18
Infusion site erythema		
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)
occurrences (all)	1	0
Injection site erythema		
subjects affected / exposed	2 / 36 (5.56%)	2 / 34 (5.88%)
occurrences (all)	2	2
Injection site paraesthesia		
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)
occurrences (all)	0	1
Injection site pruritus		
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)
occurrences (all)	1	0
Injection site reaction		
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)
occurrences (all)	0	1
Mucosal dryness		
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)
occurrences (all)	0	1
Oedema peripheral		
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)
occurrences (all)	1	0
Pain		
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)
occurrences (all)	0	1
Pyrexia		
subjects affected / exposed	7 / 36 (19.44%)	8 / 34 (23.53%)
occurrences (all)	13	9
Immune system disorders		

Dust allergy subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	1 / 34 (2.94%) 1	
Seasonal allergy subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	0 / 34 (0.00%) 0	
Reproductive system and breast disorders			
Erectile dysfunction subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	1 / 34 (2.94%) 1	
Menorrhagia subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	2 / 34 (5.88%) 2	
Ovarian cyst ruptured subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	1 / 34 (2.94%) 1	
Prostatitis subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	0 / 34 (0.00%) 0	
Testicular swelling subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	0 / 34 (0.00%) 0	
Respiratory, thoracic and mediastinal disorders			
Cough subjects affected / exposed occurrences (all)	4 / 36 (11.11%) 4	0 / 34 (0.00%) 0	
Dyspnoea subjects affected / exposed occurrences (all)	2 / 36 (5.56%) 3	1 / 34 (2.94%) 1	
Epistaxis subjects affected / exposed occurrences (all)	2 / 36 (5.56%) 3	5 / 34 (14.71%) 9	
Nasal dryness subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	1 / 34 (2.94%) 1	
Oropharyngeal pain			

subjects affected / exposed occurrences (all)	4 / 36 (11.11%) 4	3 / 34 (8.82%) 3	
Rhinitis allergic subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	1 / 34 (2.94%) 1	
Sputum increased subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	0 / 34 (0.00%) 0	
Psychiatric disorders			
Affect lability subjects affected / exposed occurrences (all)	3 / 36 (8.33%) 4	1 / 34 (2.94%) 1	
Aggression subjects affected / exposed occurrences (all)	2 / 36 (5.56%) 2	3 / 34 (8.82%) 3	
Conversion disorder subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	2 / 34 (5.88%) 2	
Depressed mood subjects affected / exposed occurrences (all)	5 / 36 (13.89%) 5	2 / 34 (5.88%) 2	
Depression subjects affected / exposed occurrences (all)	5 / 36 (13.89%) 5	2 / 34 (5.88%) 2	
Insomnia subjects affected / exposed occurrences (all)	2 / 36 (5.56%) 2	0 / 34 (0.00%) 0	
Irritability subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	1 / 34 (2.94%) 1	
Listless subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	0 / 34 (0.00%) 0	
Loss of libido subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	1 / 34 (2.94%) 1	

Mental disorder			
subjects affected / exposed	3 / 36 (8.33%)	0 / 34 (0.00%)	
occurrences (all)	3	0	
Mood swings			
subjects affected / exposed	1 / 36 (2.78%)	1 / 34 (2.94%)	
occurrences (all)	1	1	
Nervousness			
subjects affected / exposed	1 / 36 (2.78%)	2 / 34 (5.88%)	
occurrences (all)	1	2	
Sleep disorder			
subjects affected / exposed	5 / 36 (13.89%)	4 / 34 (11.76%)	
occurrences (all)	6	6	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	4 / 36 (11.11%)	2 / 34 (5.88%)	
occurrences (all)	4	3	
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)	
occurrences (all)	0	1	
Biopsy liver			
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)	
occurrences (all)	1	0	
Blood bilirubin increased			
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)	
occurrences (all)	0	1	
Blood triglycerides increased			
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)	
occurrences (all)	0	1	
Cardiac murmur			
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)	
occurrences (all)	0	1	
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 36 (2.78%)	2 / 34 (5.88%)	
occurrences (all)	1	2	
Hepatitis B DNA increased			

subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	1 / 34 (2.94%) 1	
International normalised ratio increased			
subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	0 / 34 (0.00%) 0	
Platelet count decreased			
subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	0 / 34 (0.00%) 0	
Transaminases increased			
subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	5 / 34 (14.71%) 5	
Weight decreased			
subjects affected / exposed occurrences (all)	2 / 36 (5.56%) 2	3 / 34 (8.82%) 3	
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	1 / 34 (2.94%) 1	
Nasal injury			
subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	0 / 34 (0.00%) 0	
Radius fracture			
subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	0 / 34 (0.00%) 0	
Rib fracture			
subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	0 / 34 (0.00%) 0	
Vaccination complication			
subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	1 / 34 (2.94%) 1	
Cardiac disorders			
Cardiac failure			
subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	0 / 34 (0.00%) 0	
Cardiovascular disorder			

subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	0 / 34 (0.00%) 0	
Chordae tendinae rupture subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	0 / 34 (0.00%) 0	
<b>Nervous system disorders</b>			
Ageusia subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	1 / 34 (2.94%) 1	
Disturbance in attention subjects affected / exposed occurrences (all)	2 / 36 (5.56%) 2	2 / 34 (5.88%) 2	
Dizziness subjects affected / exposed occurrences (all)	5 / 36 (13.89%) 6	4 / 34 (11.76%) 4	
Dysgeusia subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	3 / 34 (8.82%) 4	
Encephalopathy subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	1 / 34 (2.94%) 1	
Headache subjects affected / exposed occurrences (all)	9 / 36 (25.00%) 11	11 / 34 (32.35%) 13	
Hypertonia subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	1 / 34 (2.94%) 2	
Hypoaesthesia subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	1 / 34 (2.94%) 1	
Lumbar radiculopathy subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	1 / 34 (2.94%) 1	
Memory impairment subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	0 / 34 (0.00%) 0	

Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 36 (5.56%)	2 / 34 (5.88%)	
occurrences (all)	2	2	
Leukopenia			
subjects affected / exposed	5 / 36 (13.89%)	2 / 34 (5.88%)	
occurrences (all)	7	3	
Lymphocytosis			
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)	
occurrences (all)	0	1	
Lymphopenia			
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)	
occurrences (all)	0	2	
Neutropenia			
subjects affected / exposed	4 / 36 (11.11%)	4 / 34 (11.76%)	
occurrences (all)	6	6	
Neutrophilia			
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)	
occurrences (all)	0	1	
Splenomegaly			
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)	
occurrences (all)	0	2	
Thrombocytopenia			
subjects affected / exposed	4 / 36 (11.11%)	7 / 34 (20.59%)	
occurrences (all)	5	8	
Ear and labyrinth disorders			
Hypoacusis			
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)	
occurrences (all)	0	1	
Tinnitus			
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)	
occurrences (all)	1	0	
Vertigo			
subjects affected / exposed	2 / 36 (5.56%)	1 / 34 (2.94%)	
occurrences (all)	2	1	
Eye disorders			

Diplopia		
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)
occurrences (all)	2	0
Dry eye		
subjects affected / exposed	1 / 36 (2.78%)	1 / 34 (2.94%)
occurrences (all)	1	1
Extraocular muscle disorder		
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)
occurrences (all)	1	0
Eye allergy		
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)
occurrences (all)	1	0
Eye irritation		
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)
occurrences (all)	1	0
Eye pain		
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)
occurrences (all)	0	1
Eyelid oedema		
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)
occurrences (all)	1	0
Ocular discomfort		
subjects affected / exposed	2 / 36 (5.56%)	0 / 34 (0.00%)
occurrences (all)	2	0
Ocular hyperaemia		
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)
occurrences (all)	1	0
Vision blurred		
subjects affected / exposed	2 / 36 (5.56%)	0 / 34 (0.00%)
occurrences (all)	2	0
Visual acuity reduced		
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)
occurrences (all)	0	1
Visual impairment		
subjects affected / exposed	2 / 36 (5.56%)	2 / 34 (5.88%)
occurrences (all)	2	3

Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	1 / 36 (2.78%)	1 / 34 (2.94%)	
occurrences (all)	1	1	
Abdominal distension			
subjects affected / exposed	1 / 36 (2.78%)	1 / 34 (2.94%)	
occurrences (all)	1	1	
Abdominal pain			
subjects affected / exposed	4 / 36 (11.11%)	8 / 34 (23.53%)	
occurrences (all)	4	12	
Abdominal pain lower			
subjects affected / exposed	1 / 36 (2.78%)	1 / 34 (2.94%)	
occurrences (all)	1	1	
Abdominal pain upper			
subjects affected / exposed	6 / 36 (16.67%)	5 / 34 (14.71%)	
occurrences (all)	6	6	
Anal ulcer			
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)	
occurrences (all)	0	1	
Ascites			
subjects affected / exposed	1 / 36 (2.78%)	1 / 34 (2.94%)	
occurrences (all)	1	1	
Breath odour			
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)	
occurrences (all)	0	1	
Chronic gastritis			
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)	
occurrences (all)	0	1	
Constipation			
subjects affected / exposed	1 / 36 (2.78%)	2 / 34 (5.88%)	
occurrences (all)	1	2	
Diarrhoea			
subjects affected / exposed	5 / 36 (13.89%)	5 / 34 (14.71%)	
occurrences (all)	5	7	
Dry mouth			

subjects affected / exposed	4 / 36 (11.11%)	2 / 34 (5.88%)
occurrences (all)	4	2
Dyspepsia		
subjects affected / exposed	1 / 36 (2.78%)	3 / 34 (8.82%)
occurrences (all)	1	3
Dysphagia		
subjects affected / exposed	1 / 36 (2.78%)	1 / 34 (2.94%)
occurrences (all)	1	1
Epigastric discomfort		
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)
occurrences (all)	0	1
Flatulence		
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)
occurrences (all)	1	0
Gastric ulcer		
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)
occurrences (all)	0	1
Gastritis		
subjects affected / exposed	2 / 36 (5.56%)	3 / 34 (8.82%)
occurrences (all)	2	3
Gastrointestinal disorder		
subjects affected / exposed	0 / 36 (0.00%)	2 / 34 (5.88%)
occurrences (all)	0	2
Gastrointestinal haemorrhage		
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)
occurrences (all)	0	2
Gastrooesophageal reflux disease		
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)
occurrences (all)	1	0
Gingival bleeding		
subjects affected / exposed	2 / 36 (5.56%)	1 / 34 (2.94%)
occurrences (all)	2	1
Haematochezia		
subjects affected / exposed	2 / 36 (5.56%)	1 / 34 (2.94%)
occurrences (all)	2	1
Haemorrhoids		

subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	1 / 34 (2.94%) 1	
Lip dry subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	0 / 34 (0.00%) 0	
Nausea subjects affected / exposed occurrences (all)	5 / 36 (13.89%) 6	8 / 34 (23.53%) 11	
Stomatitis subjects affected / exposed occurrences (all)	2 / 36 (5.56%) 2	1 / 34 (2.94%) 1	
Toothache subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	0 / 34 (0.00%) 0	
Varices oesophageal subjects affected / exposed occurrences (all)	3 / 36 (8.33%) 3	3 / 34 (8.82%) 4	
Vomiting subjects affected / exposed occurrences (all)	2 / 36 (5.56%) 2	2 / 34 (5.88%) 2	
Hepatobiliary disorders			
Chronic hepatic failure subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	1 / 34 (2.94%) 1	
Hepatic cirrhosis subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	0 / 34 (0.00%) 0	
Hepatic failure subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	1 / 34 (2.94%) 1	
Hepatitis subjects affected / exposed occurrences (all)	2 / 36 (5.56%) 2	0 / 34 (0.00%) 0	
Hepatomegaly subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	1 / 34 (2.94%) 1	

Jaundice			
subjects affected / exposed	1 / 36 (2.78%)	2 / 34 (5.88%)	
occurrences (all)	1	2	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	7 / 36 (19.44%)	5 / 34 (14.71%)	
occurrences (all)	8	6	
Dermatitis			
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)	
occurrences (all)	1	0	
Dry skin			
subjects affected / exposed	3 / 36 (8.33%)	3 / 34 (8.82%)	
occurrences (all)	3	3	
Eczema			
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)	
occurrences (all)	0	1	
Eczema nummular			
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)	
occurrences (all)	1	0	
Hyperhidrosis			
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)	
occurrences (all)	1	0	
Erythema			
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)	
occurrences (all)	0	2	
Night sweats			
subjects affected / exposed	1 / 36 (2.78%)	1 / 34 (2.94%)	
occurrences (all)	1	1	
Hyperkeratosis			
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)	
occurrences (all)	1	0	
Pain of skin			
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)	
occurrences (all)	0	1	
Papule			

subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	2 / 34 (5.88%) 2	
Pruritus			
subjects affected / exposed occurrences (all)	9 / 36 (25.00%) 10	8 / 34 (23.53%) 9	
Pruritus generalised			
subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	1 / 34 (2.94%) 1	
Rash			
subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	5 / 34 (14.71%) 5	
Rash erythematous			
subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 2	0 / 34 (0.00%) 0	
Skin burning sensation			
subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	0 / 34 (0.00%) 0	
Skin infection			
subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	0 / 34 (0.00%) 0	
Spider naevus			
subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	0 / 34 (0.00%) 0	
Swelling face			
subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	0 / 34 (0.00%) 0	
Renal and urinary disorders			
Dysuria			
subjects affected / exposed occurrences (all)	2 / 36 (5.56%) 3	0 / 34 (0.00%) 0	
Pollakiuria			
subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	1 / 34 (2.94%) 1	
Renal pain			
subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	1 / 34 (2.94%) 2	

Ureterolithiasis subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	0 / 34 (0.00%) 0	
Urinary retention subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	0 / 34 (0.00%) 0	
Urine odour abnormal subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	1 / 34 (2.94%) 1	
Endocrine disorders Hypothyroidism subjects affected / exposed occurrences (all)	3 / 36 (8.33%) 3	1 / 34 (2.94%) 1	
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	10 / 36 (27.78%) 14	8 / 34 (23.53%) 10	
Arthropathy subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	0 / 34 (0.00%) 0	
Back pain subjects affected / exposed occurrences (all)	5 / 36 (13.89%) 7	3 / 34 (8.82%) 3	
Bursitis subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	0 / 34 (0.00%) 0	
Flank pain subjects affected / exposed occurrences (all)	3 / 36 (8.33%) 3	0 / 34 (0.00%) 0	
Groin pain subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	1 / 34 (2.94%) 1	
Intervertebral disc protrusion subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	0 / 34 (0.00%) 0	
Kyphosis			

subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	0 / 34 (0.00%) 0	
Muscle spasms subjects affected / exposed occurrences (all)	3 / 36 (8.33%) 5	2 / 34 (5.88%) 2	
Muscle tightness subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	1 / 34 (2.94%) 1	
Musculoskeletal chest pain subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	1 / 34 (2.94%) 1	
Musculoskeletal pain subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	0 / 34 (0.00%) 0	
Myalgia subjects affected / exposed occurrences (all)	4 / 36 (11.11%) 4	8 / 34 (23.53%) 8	
Osteoarthritis subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	0 / 34 (0.00%) 0	
Osteoporosis subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	0 / 34 (0.00%) 0	
Pain in extremity subjects affected / exposed occurrences (all)	3 / 36 (8.33%) 3	6 / 34 (17.65%) 6	
Synovial cyst subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	0 / 34 (0.00%) 0	
<b>Infections and infestations</b>			
Abscess subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	0 / 34 (0.00%) 0	
Abscess limb subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 2	0 / 34 (0.00%) 0	

Abscess sweat gland		
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)
occurrences (all)	0	1
Acute haemorrhagic conjunctivitis		
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)
occurrences (all)	1	0
Acute sinusitis		
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)
occurrences (all)	1	0
Appendicitis		
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)
occurrences (all)	1	0
Breast abscess		
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)
occurrences (all)	0	1
Bronchitis		
subjects affected / exposed	3 / 36 (8.33%)	3 / 34 (8.82%)
occurrences (all)	4	3
Conjunctivitis		
subjects affected / exposed	2 / 36 (5.56%)	0 / 34 (0.00%)
occurrences (all)	2	0
Cystitis		
subjects affected / exposed	1 / 36 (2.78%)	2 / 34 (5.88%)
occurrences (all)	1	2
Diverticulitis		
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)
occurrences (all)	0	1
Febrile infection		
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)
occurrences (all)	0	1
Fungal infection		
subjects affected / exposed	1 / 36 (2.78%)	2 / 34 (5.88%)
occurrences (all)	1	2
Gastroenteritis		
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)
occurrences (all)	1	0

Gastrointestinal infection		
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)
occurrences (all)	0	1
Gingivitis		
subjects affected / exposed	3 / 36 (8.33%)	1 / 34 (2.94%)
occurrences (all)	3	1
Helicobacter gastritis		
subjects affected / exposed	2 / 36 (5.56%)	1 / 34 (2.94%)
occurrences (all)	2	1
Hepatitis D		
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)
occurrences (all)	0	1
Herpes zoster		
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)
occurrences (all)	1	0
Influenza		
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)
occurrences (all)	1	0
Latent tuberculosis		
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)
occurrences (all)	1	0
Nasopharyngitis		
subjects affected / exposed	5 / 36 (13.89%)	4 / 34 (11.76%)
occurrences (all)	6	6
Onychomycosis		
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)
occurrences (all)	1	0
Oral herpes		
subjects affected / exposed	2 / 36 (5.56%)	0 / 34 (0.00%)
occurrences (all)	2	0
Otitis media		
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)
occurrences (all)	1	0
Plasmodium falciparum infection		
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)
occurrences (all)	0	1

Pneumonia			
subjects affected / exposed	0 / 36 (0.00%)	2 / 34 (5.88%)	
occurrences (all)	0	2	
Pulpitis dental			
subjects affected / exposed	0 / 36 (0.00%)	2 / 34 (5.88%)	
occurrences (all)	0	2	
Puncture site abscess			
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)	
occurrences (all)	0	1	
Respiratory tract infection			
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)	
occurrences (all)	0	1	
Scrotal abscess			
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)	
occurrences (all)	0	1	
Sinusitis			
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)	
occurrences (all)	1	0	
Tonsillitis			
subjects affected / exposed	2 / 36 (5.56%)	1 / 34 (2.94%)	
occurrences (all)	2	1	
Upper respiratory tract infection			
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)	
occurrences (all)	1	0	
Urinary tract infection			
subjects affected / exposed	2 / 36 (5.56%)	2 / 34 (5.88%)	
occurrences (all)	4	4	
Vaginal infection			
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)	
occurrences (all)	1	0	
Vulvovaginal mycotic infection			
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)	
occurrences (all)	0	2	
Metabolism and nutrition disorders			
Decreased appetite			

subjects affected / exposed	12 / 36 (33.33%)	12 / 34 (35.29%)
occurrences (all)	16	14
Diabetes mellitus		
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)
occurrences (all)	1	0
Food intolerance		
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)
occurrences (all)	1	0
Vitamin D deficiency		
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)
occurrences (all)	0	1
Zinc deficiency		
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)
occurrences (all)	1	0

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 November 2010	modification concomitant medication

Notes:

---

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported

---

### Online references

<http://www.ncbi.nlm.nih.gov/pubmed/30833068>

<http://www.ncbi.nlm.nih.gov/pubmed/29888837>