Clinical trial results:
A multicenter randomised study comparing the efficacy of pegylated interferon-alfa-2a plus placebo vs. pegylated interfeorn-alfa-2a plus tenofovir for the treatment of chronic delta hepatitis- The Hep-Net International Delta hepatits 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
Arm title	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

Arm title	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.

Number of subjects in period 1	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: -

Serious adverse events	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	
Surgical and medical procedures			
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	
Pregnancy, puerperium and perinatal conditions			
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	
Psychiatric disorders			
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	
Dysphagia			
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	
Gastritis			
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	
Gastrointestinal haemorrhage			
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	
Varices oesophageal			
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	
Hepatobiliary disorders			
Hepatomegaly			
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	
Skin and subcutaneous tissue disorders			
Skin infection			
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 and urinary disorders			
Ureterolithiasis			
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 %

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

subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)	
occurrences (all)	1	0	
Renal stone removal			
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)	
occurrences (all)	0	1	
Tooth extraction			
subjects affected / exposed	0 / 36 (0.00%)	2 / 34 (5.88%)	
occurrences (all)	0	2	
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)	
occurrences (all)	0	1	
Pregnancy			
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	8 / 36 (22.22%)	2 / 34 (5.88%)	
occurrences (all)	8	2	
Chest discomfort			
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)	
occurrences (all)	0	1	
Chest pain			
subjects affected / exposed	1 / 36 (2.78%)	3 / 34 (8.82%)	
occurrences (all)	1	4	
Chills			
subjects affected / exposed	4 / 36 (11.11%)	4 / 34 (11.76%)	
occurrences (all)	5	4	
Exercise tolerance decreased			
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)	
occurrences (all)	1	0	
Fatigue			
subjects affected / exposed	13 / 36 (36.11%)	15 / 34 (44.12%)	
occurrences (all)	15	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	0 / 36 (0.00%)	1 / 34 (2.94%)	
occurrences (all)	0	1	
Seasonal allergy			
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)	
occurrences (all)	1	0	
Reproductive system and breast disorders			
Erectile dysfunction			
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)	
occurrences (all)	0	1	
Menorrhagia			
subjects affected / exposed	1 / 36 (2.78%)	2 / 34 (5.88%)	
occurrences (all)	1	2	
Ovarian cyst ruptured			
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)	
occurrences (all)	0	1	
Prostatitis			
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)	
occurrences (all)	1	0	
Testicular swelling			
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	4 / 36 (11.11%)	0 / 34 (0.00%)	
occurrences (all)	4	0	
Dyspnoea			
subjects affected / exposed	2 / 36 (5.56%)	1 / 34 (2.94%)	
occurrences (all)	3	1	
Epistaxis			
subjects affected / exposed	2 / 36 (5.56%)	5 / 34 (14.71%)	
occurrences (all)	3	9	
Nasal dryness			
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)	
occurrences (all)	0	1	
Oropharyngeal pain			

subjects affected / exposed	4 / 36 (11.11%)	3 / 34 (8.82%)	
occurrences (all)	4	3	
Rhinitis allergic			
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)	
occurrences (all)	0	1	
Sputum increased			
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			
Affect lability			
subjects affected / exposed	3 / 36 (8.33%)	1 / 34 (2.94%)	
occurrences (all)	4	1	
Aggression			
subjects affected / exposed	2 / 36 (5.56%)	3 / 34 (8.82%)	
occurrences (all)	2	3	
Conversion disorder			
subjects affected / exposed	0 / 36 (0.00%)	2 / 34 (5.88%)	
occurrences (all)	0	2	
Depressed mood			
subjects affected / exposed	5 / 36 (13.89%)	2 / 34 (5.88%)	
occurrences (all)	5	2	
Depression			
subjects affected / exposed	5 / 36 (13.89%)	2 / 34 (5.88%)	
occurrences (all)	5	2	
Insomnia			
subjects affected / exposed	2 / 36 (5.56%)	0 / 34 (0.00%)	
occurrences (all)	2	0	
Irritability			
subjects affected / exposed	1 / 36 (2.78%)	1 / 34 (2.94%)	
occurrences (all)	1	1	
Listless			
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)	
occurrences (all)	1	0	
Loss of libido			
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)	
occurrences (all)	0	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	1 / 36 (2.78%)	1 / 34 (2.94%)	
occurrences (all)	1	1	
International normalised ratio increased			
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)	
occurrences (all)	1	0	
Platelet count decreased			
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)	
occurrences (all)	1	0	
Transaminases increased			
subjects affected / exposed	1 / 36 (2.78%)	5 / 34 (14.71%)	
occurrences (all)	1	5	
Weight decreased			
subjects affected / exposed	2 / 36 (5.56%)	3 / 34 (8.82%)	
occurrences (all)	2	3	
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 36 (2.78%)	1 / 34 (2.94%)	
occurrences (all)	1	1	
Nasal injury			
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)	
occurrences (all)	1	0	
Radius fracture			
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)	
occurrences (all)	1	0	
Rib fracture			
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)	
occurrences (all)	1	0	
Vaccination complication			
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)	
occurrences (all)	0	1	
Cardiac disorders			
Cardiac failure			
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)	
occurrences (all)	1	0	
Cardiovascular disorder			

subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)	
occurrences (all)	1	0	
Chordae tendinae rupture			
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Ageusia			
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)	
occurrences (all)	0	1	
Disturbance in attention			
subjects affected / exposed	2 / 36 (5.56%)	2 / 34 (5.88%)	
occurrences (all)	2	2	
Dizziness			
subjects affected / exposed	5 / 36 (13.89%)	4 / 34 (11.76%)	
occurrences (all)	6	4	
Dysgeusia			
subjects affected / exposed	1 / 36 (2.78%)	3 / 34 (8.82%)	
occurrences (all)	1	4	
Encephalopathy			
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)	
occurrences (all)	0	1	
Headache			
subjects affected / exposed	9 / 36 (25.00%)	11 / 34 (32.35%)	
occurrences (all)	11	13	
Hypertonia			
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)	
occurrences (all)	0	2	
Hypoaesthesia			
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)	
occurrences (all)	0	1	
Lumbar radiculopathy			
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)	
occurrences (all)	0	1	
Memory impairment			
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)	
occurrences (all)	1	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	1 / 36 (2.78%)	1 / 34 (2.94%)	
occurrences (all)	1	1	
Lip dry			
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)	
occurrences (all)	1	0	
Nausea			
subjects affected / exposed	5 / 36 (13.89%)	8 / 34 (23.53%)	
occurrences (all)	6	11	
Stomatitis			
subjects affected / exposed	2 / 36 (5.56%)	1 / 34 (2.94%)	
occurrences (all)	2	1	
Toothache			
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)	
occurrences (all)	1	0	
Varices oesophageal			
subjects affected / exposed	3 / 36 (8.33%)	3 / 34 (8.82%)	
occurrences (all)	3	4	
Vomiting			
subjects affected / exposed	2 / 36 (5.56%)	2 / 34 (5.88%)	
occurrences (all)	2	2	
Hepatobiliary disorders			
Chronic hepatic failure			
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)	
occurrences (all)	0	1	
Hepatic cirrhosis			
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)	
occurrences (all)	1	0	
Hepatic failure			
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)	
occurrences (all)	0	1	
Hepatitis			
subjects affected / exposed	2 / 36 (5.56%)	0 / 34 (0.00%)	
occurrences (all)	2	0	
Hepatomegaly			
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)	
occurrences (all)	0	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	0 / 36 (0.00%)	2 / 34 (5.88%)	
occurrences (all)	0	2	
Pruritus			
subjects affected / exposed	9 / 36 (25.00%)	8 / 34 (23.53%)	
occurrences (all)	10	9	
Pruritus generalised			
subjects affected / exposed	1 / 36 (2.78%)	1 / 34 (2.94%)	
occurrences (all)	1	1	
Rash			
subjects affected / exposed	0 / 36 (0.00%)	5 / 34 (14.71%)	
occurrences (all)	0	5	
Rash erythematous			
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)	
occurrences (all)	2	0	
Skin burning sensation			
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)	
occurrences (all)	1	0	
Skin infection			
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)	
occurrences (all)	1	0	
Spider naevus			
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)	
occurrences (all)	1	0	
Swelling face			
subjects affected / exposed	1 / 36 (2.78%)	0 / 34 (0.00%)	
occurrences (all)	1	0	
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	2 / 36 (5.56%)	0 / 34 (0.00%)	
occurrences (all)	3	0	
Pollakiuria			
subjects affected / exposed	1 / 36 (2.78%)	1 / 34 (2.94%)	
occurrences (all)	1	1	
Renal pain			
subjects affected / exposed	0 / 36 (0.00%)	1 / 34 (2.94%)	
occurrences (all)	0	2	

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

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