Clinical trial results:
A Phase 2a, Randomised, Double-blind, Placebo-controlled Assessment of the Safety and Protective Efficacy of Flufirvitide-3 (FF-3) Dry Powder Administered by Nasal Inhalation for 5 Days to Healthy Adult Subjects who are Experimentally Infected with a Challenge Strain of Influenza A Virus

Summary

EudraCT number	2015-001103-31
Trial protocol	GB
Global end of trial date	16 June 2016

Results information

Result version number	v1 (current)
This version publication date	07 June 2017
First version publication date	07 June 2017

Trial information

Trial identification

Sponsor protocol code	AIT02-2001/DMID 14-0052

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02423577
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Autoimmune Technologies, LLC
Sponsor organisation address	830 Union Street, Suite 200, New Orleans, Louisiana, United States, 70112
Public contact	Russell B. Wilson, PhD, Autoimmune Technologies, LLC, +1 504-896-2789,
Scientific contact	Russell B. Wilson, PhD, Autoimmune Technologies, LLC, +1 504-896-2789,

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	16 June 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	16 June 2016
Global end of trial reached?	Yes
Global end of trial date	16 June 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine the effect of prophylaxis with FF-3 (i.e. protective efficacy) in comparison to placebo on the frequencies of viral shedding, infectivity, and sero-conversion in subjects who are experimentally inoculated with a live, wild-type A/California/H1N1 2009 challenge strain of influenza A virus.

Protection of trial subjects:

The study was conducted in accordance with Good Clinical Practice as required by the International Council on Harmonization guidelines and in accordance with the ethical principles of the Declaration of Helsinki.

Background therapy:

Subjects received live, wild-type A/California/H1N1 2009 challenge strain of influenza A virus. The challenge virus was administered by intranasal inoculation approximately 4 hours after the subject had received their first dose of either FF-3 or placebo.

Evidence for comparator: -

Actual start date of recruitment	14 September 2015
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	United Kingdom: 79
Worldwide total number of subjects	79
EEA total number of subjects	79

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)	79
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

79 healthy adults were recruited into the single-site study, between 14 September 2015 and 16 June 2016. Following screening, subjects were randomised in 1 of 2 groups using a ratio of 2:1 (FF-3:placebo). All subjects received training in the appropriate use of the Early Phase I Clinical (EPIC) dry powder inhaler prior to dosing.

Pre-assignment

Screening details:

Potential subjects were screened to determine their susceptibility to infection with the challenge strain as indicated by a serum antibody titre less than 1:10. Only subjects susceptible to the challenge strain qualified for study specific screening.

Period 1

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

Blinding implementation details:

All subjects and staff members responsible for administering the treatment to the subjects and all other aspects of study management remained blinded, unless unblinding was necessary for safety reasons.

Arms

Are arms mutually exclusive?	Yes
Arm title	FF-3

Arm description:

FF-3 dry powder was administered as a nasal inhalation aerosol with the EPIC dry powder inhaler. Subjects were dosed twice daily (approximately 12 hours apart) for 5 days and a single dose on the morning of Day 6 at a dose of 9 milligrams (mg). The total daily dose of FF-3 was 18 mg and subjects received a total of 11 doses. The first dose of FF-3 was administered approximately 4 hours before the challenge virus. A single dose of challenge virus (influenza A/California/H1N1/2009) was administered by intranasal administration in a total volume of 0.5 millilitres (mL) (0.25 mL per nostril). A second dose of FF-3 was administered approximately 4 hours after nasal inoculation with the challenge virus.

Arm type	Experimental
Investigational medicinal product name	FF-3
Investigational medicinal product code	
Other name	Flufirvitide-3
Pharmaceutical forms	Inhalation powder, pre-dispensed
Routes of administration	Nasal use

Dosage and administration details:

FF-3 was provided in unit dose blisters containing 4.5 mg of FF-3 in a powder formulation for administration as nasal inhalation aerosol with the EPIC dry powder inhaler. The EPIC dry powder inhaler is a single-dose, breath-activated device that delivers a powder formulation. In addition to 4.5 mg FF-3, each contained dibasic potassium phosphate, trehalose, and monobasic potassium phosphate.

Arm title	Placebo

Arm description:

A matching placebo was administered as a nasal inhalation aerosol with the EPIC dry powder inhaler twice daily (approximately 12 hours apart) for five days and a single dose on morning of Day 6. Subjects received a total of 11 doses.
The first dose of placebo was administered approximately 4 hours before the challenge virus. A single dose of challenge virus (influenza A/California/H1N1/2009) was administered by intranasal administration in a total volume of 0.5 mL (0.25 mL per nostril). A second dose of placebo was administered approximately 4 hours after nasal inoculation with the challenge virus.

Arm type	Placebo

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder, pre-dispensed
Routes of administration	Nasal use

Dosage and administration details:

Placebo was provided in unit dose blisters, which matched the appearance of the FF-3 blister packs for nasal inhalation as nasal inhalation aerosol with the EPIC dry powder inhaler. Each blister contained monobasic potassium phosphate, dibasic potassium phosphate, and trehalose.

Number of subjects in period 1	FF-3	Placebo
Started	53	26
Completed	53	26

Baseline characteristics

Reporting groups	
Reporting group title	FF-3

Reporting group description:

FF-3 dry powder was administered as a nasal inhalation aerosol with the EPIC dry powder inhaler. Subjects were dosed twice daily (approximately 12 hours apart) for 5 days and a single dose on the morning of Day 6 at a dose of 9 milligrams (mg). The total daily dose of FF-3 was 18 mg and subjects received a total of 11 doses. The first dose of FF-3 was administered approximately 4 hours before the challenge virus. A single dose of challenge virus (influenza A/California/H1N1/2009) was administered by intranasal administration in a total volume of 0.5 millilitres (mL) (0.25 mL per nostril). A second dose of FF-3 was administered approximately 4 hours after nasal inoculation with the challenge virus.

Reporting group title	Placebo

Reporting group description:

A matching placebo was administered as a nasal inhalation aerosol with the EPIC dry powder inhaler twice daily (approximately 12 hours apart) for five days and a single dose on morning of Day 6. Subjects received a total of 11 doses.
The first dose of placebo was administered approximately 4 hours before the challenge virus. A single dose of challenge virus (influenza A/California/H1N1/2009) was administered by intranasal administration in a total volume of 0.5 mL (0.25 mL per nostril). A second dose of placebo was administered approximately 4 hours after nasal inoculation with the challenge virus.

Reporting group values	FF-3	Placebo	Total
Number of subjects	53	26	79
Age categorical Units: Subjects			
Age Continuous Units: years			
arithmetic mean	31.7	32.7	
standard deviation	± 8.5	± 9.3	-
Gender Categorical Units: Subjects			
Male	40	14	54
Female	13	12	25

End points

End points reporting groups

Reporting group title	FF-3

Reporting group description:

FF-3 dry powder was administered as a nasal inhalation aerosol with the EPIC dry powder inhaler. Subjects were dosed twice daily (approximately 12 hours apart) for 5 days and a single dose on the morning of Day 6 at a dose of 9 milligrams (mg). The total daily dose of FF-3 was 18 mg and subjects received a total of 11 doses. The first dose of FF-3 was administered approximately 4 hours before the challenge virus. A single dose of challenge virus (influenza A/California/H1N1/2009) was administered by intranasal administration in a total volume of 0.5 millilitres (mL) (0.25 mL per nostril). A second dose of FF-3 was administered approximately 4 hours after nasal inoculation with the challenge virus.

Reporting group title	Placebo

Reporting group description:

A matching placebo was administered as a nasal inhalation aerosol with the EPIC dry powder inhaler twice daily (approximately 12 hours apart) for five days and a single dose on morning of Day 6. Subjects received a total of 11 doses.
The first dose of placebo was administered approximately 4 hours before the challenge virus. A single dose of challenge virus (influenza A/California/H1N1/2009) was administered by intranasal administration in a total volume of 0.5 mL (0.25 mL per nostril). A second dose of placebo was administered approximately 4 hours after nasal inoculation with the challenge virus.

Primary: Percentage of Subjects Demonstrating Viral Shedding.

End point title	Percentage of Subjects Demonstrating Viral Shedding.

End point description:

Nasal washes were collected from all subjects to assess the magnitude and duration of viral shedding before the virus inoculation and once daily on Day 2 through Day 10. Evidence of viral shedding was defined as a positive real time reverse transcription polymerase chain reaction (RT-PCR) result for the challenge virus obtained on at least one post inoculation day in the time interval beginning on Day 2 and ending on the completion of the inpatient observation period on Day 10. The percentage of subjects demonstrating viral shedding was estimated for each treatment with corresponding asymptotic 95% confidence intervals, based on the normal approximation to the binomial distribution (Wilsons's method).

End point type	Primary

End point timeframe:

Day 2-Day 10

End point values	FF-3	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	53	26		
Units: percentage of Subjects				
number (confidence interval 95%)	96.2 (87.2 to 99)	84.6 (66.5 to 93.8)		

Statistical analyses

Statistical analysis title	Comparison of Relative Risk
Comparison groups	Placebo v FF-3

Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	= 0.1436 [2]
Method	Chi-squared
Parameter estimate	Risk ratio (RR)
Point estimate	1.14
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.98
upper limit	1.31

Notes:

[1] - This study is powered to 80% to detect a 2- to 3-fold reduction in infectivity due to FF-3 treatment.
[2] - P-value is based on the normal approximation for the ratio of binomial distributions on the log scale. Significance level = 10%.

Primary: Percentage of Subjects Demonstrating Viral Infection.

End point title	Percentage of Subjects Demonstrating Viral Infection.

End point description:

Nasal washes were collected from all subjects to assess infection rate, before the virus inoculation and once daily, on Day 2 through Day 10. Evidence of infectivity was defined as a positive tissue culture result (median tissue culture infective dose [TCID50]) for the challenge virus obtained on at least one post inoculation day in the time interval beginning on Day 2 and ending on the completion of the inpatient observation period on Day 10. The percentage of subjects demonstrating viral infection was estimated for each treatment with corresponding asymptotic 95% confidence intervals, based on the normal approximation to the binomial distribution (Wilsons's method).

End point type	Primary

End point timeframe:

Day 2-Day 10

End point values	FF-3	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	53	26		
Units: percentage of subjects				
number (confidence interval 95%)	69.8 (56.5 to 80.5)	73.1 (53.9 to 86.3)		

Statistical analyses

Statistical analysis title	Comparison of Relative Risk
Comparison groups	FF-3 v Placebo

Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	superiority[3]
P-value	= 0.7596 [4]
Method	Chi-squared
Parameter estimate	Risk ratio (RR)
Point estimate	0.96
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.75
upper limit	1.22

Notes:

[3] - This study is powered to 80% to detect a 2- to 3-fold reduction in infectivity due to FF-3 treatment.
[4] - P-value is based on the normal approximation for the ratio of binomial distributions on the log scale. Significance level = 10%

Primary: Percentage of Subjects Demonstrating Sero-Conversion.

End point title	Percentage of Subjects Demonstrating Sero-Conversion.

End point description:

Evidence of sero-conversion against the challenge virus is defined as a 4-fold or greater rise in serum Haemagglutinin inhibition (HAI) antibody titre between subject serum samples obtained at check-in on Study Day -2 and at the post-treatment follow-up on Study Day 30. The percentage of subjects demonstrating sero-conversion at Day 30 was estimated for each treatment with corresponding asymptotic 95% confidence intervals, based on the normal approximation to the binomial distribution (Wilsons's method).

End point type	Primary

End point timeframe:

Day 30

End point values	FF-3	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	53	26		
Units: percentage of subjects				
number (confidence interval 95%)	73.6 (60.4 to 83.6)	65.4 (46.2 to 80.6)		

Statistical analyses

Statistical analysis title	Comparison of Relative Risk
Comparison groups	FF-3 v Placebo
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	superiority[5]
P-value	= 0.4732 [6]
Method	Chi-squared
Parameter estimate	Risk ratio (RR)
Point estimate	1.13

Confidence interval	
level	90 %
sides	2-sided
lower limit	0.86
upper limit	1.48

Notes:

[5] - This study is powered to 80% to detect a 2- to 3-fold reduction in infectivity due to FF-3 treatment.
[6] - P-value is based on the normal approximation for the ratio of binomial distributions on the log scale. Significance level = 10%.

Secondary: Mean Physician and Subject-Reported Influenza Total Sign/Symptom Scores (TSS).

End point title	Mean Physician and Subject-Reported Influenza Total Sign/Symptom Scores (TSS).

End point description:

From Day 1 to Day 10, investigators evaluated 4 signs of illness including fever, nasal discharge, pharyngitis, and new wheezes, rales, or rhonchi on lung auscultation. Subjects also self-evaluated 16 signs and symptoms of illness including nasal stuffiness/congestion, runny nose, sore throat, sneezing, hoarseness, earache, facial or eye pain/tenderness, cough, wheezy chest, breathing difficulty, musculoskeletal ache, nausea/vomiting, feeling hot/feverishness/chills/rigor, headache, fatigue, diarrhoea. All reported symptoms were graded on a 4-point scale: 0-Absent, 1-Mild, 2-Moderate and 3-Severe.
The TSS was calculated for each subject as the mean of 1 or 2 replicate assessments per day of the total symptom count for the 4 physician-reported signs and symptoms and 16 subject-reported symptoms. The overall mean TSS from Day 1 to Day 10 was recorded for both physician and subject-reported influenza symptoms.

End point type	Secondary

End point timeframe:

Day 1-Day 10

End point values	FF-3	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	53	26		
Units: units on a scale				
arithmetic mean (confidence interval 95%)				
Overall Physician-Reported TSS	0.11 (0.07 to 0.15)	0.08 (0.04 to 0.12)		
Overall Subject-Reported TSS	0.8 (0.58 to 1.02)	0.89 (0.51 to 1.27)		

Statistical analyses

Statistical analysis title	Comparison of Physician-Reported TSS
Comparison groups	FF-3 v Placebo

Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.3493 [7]
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	0.03
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.02
upper limit	0.08

Notes:

[7] - Significance level = 10%.

Statistical analysis title	Comparison of Subject-Reported TSS
Comparison groups	FF-3 v Placebo
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.664 [8]
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	-0.09
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.43
upper limit	0.25

Notes:

[8] - Significance level = 10%.

Secondary: Mean Levels of Pro-inflammatory and Antiviral Cytokines.

End point title	Mean Levels of Pro-inflammatory and Antiviral Cytokines.

End point description:

Nasal washes were collected from all subjects once daily, on Day 1 through Day 10 to measure pro-inflammatory and antiviral cytokine concentrations (Interleukin 6, Tumour Necrosis Factor (TNF) alpha, interferon alpha, and interferon gamma). The pro-inflammatory and antiviral cytokine assay results were corrected for sampling dilution inconsistencies by normalising to their corresponding urea nitrogen concentrations. Mean pro-inflammatory and antiviral cytokine concentrations were calculated as the area under the curve (AUC)/time on the log10 scale over Days 1 to 10 for subjects with at least 50% of planned measurements collected. All AUC were calculated using the linear trapezoidal method.

End point type	Secondary

End point timeframe:

Day 1-Day 10

End point values	FF-3	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	53	26		
Units: picograms (pg)/mL				
arithmetic mean (confidence interval 95%)				
Mean Interleukin 6	2.327 (2.161 to 2.493)	2.253 (2.01 to 2.496)		
Mean TNF-Alpha	1.581 (1.484 to 1.677)	1.452 (1.316 to 1.588)		
Mean Interferon-Alpha	2.56 (2.5 to 2.62)	2.53 (2.41 to 2.64)		
Mean Interferon-Gamma	1.122 (0.988 to 1.256)	1.067 (0.857 to 1.276)		

Statistical analyses

Statistical analysis title	Interleukin 6 Comparison
Comparison groups	FF-3 v Placebo
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.6099 [9]
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	0.074
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.166
upper limit	0.314

Notes:

[9] - Significance level = 10%.

Statistical analysis title	TNF-Alpha Comparison
Comparison groups	FF-3 v Placebo
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1242 [10]
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	0.129
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.009
upper limit	0.267

Notes:
[10] - Significance level = 10%.

Statistical analysis title	Interferon-Alpha Comparison
Comparison groups	FF-3 v Placebo
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.6056 [11]
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	0.03
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.07
upper limit	0.12

Notes:
[11] - Significance level = 10%.

Statistical analysis title	Interferon-Gamma Comparison
Comparison groups	FF-3 v Placebo
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.6423 [12]
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	0.056
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.143
upper limit	0.254

Notes:
[12] - Significance level = 10%.

Secondary: Mean Viral Load.

End point title	Mean Viral Load.

End point description:

Nasal washes were collected from all subjects to assess viral load once daily on Day 1 through Day 10. Mean viral load was calculated as AUC/time on the log10 scale for both the RT-PCR and TCID50 methods over Days 1 to 10 for subjects with at least 50% of planned measurements collected. All AUC were calculated using the linear trapezoidal method.

End point type	Secondary

End point timeframe:

Day 1-Day 10

End point values	FF-3	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	53	26		
Units: copies/mL				
arithmetic mean (confidence interval 95%)				
Mean RT-PCR	2.918 (2.376 to 3.46)	2.877 (2.086 to 3.668)		
Mean TCID50	1.528 (1.338 to 1.719)	1.441 (1.177 to 1.706)		

Statistical analyses

Statistical analysis title	TCID50 Viral Load Comparison
Comparison groups	FF-3 v Placebo
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.5928 [13]
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	0.087
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.183
upper limit	0.358

Notes:

[13] - Significance level = 10%.

Statistical analysis title	RT-PCR Viral Load Comparsion
Comparison groups	FF-3 v Placebo
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.9311 [14]
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	0.041
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.742
upper limit	0.824

Notes:

[14] - Significance level = 10%.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to Day 30 (+/- 3 days).

Adverse event reporting additional description:

A treatment-emergent adverse event (TEAE) was defined as an adverse event which occurred after the start of dosing or which was present pre-dose and became more severe after the start of dosing. The Safety analysis set included all subjects who received at least one dose of treatment (FF-3 or placebo).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.1

Reporting groups

Reporting group title	FF-3

Reporting group description:

FF-3 dry powder was administered as a nasal inhalation aerosol with the EPIC dry powder inhaler twice daily (approximately 12 hours apart) for 5 days and a single dose on the morning of Day 6 at a dose of 9 milligrams (mg). The total daily dose of FF-3 was 18 mg and subjects received a total of 11 doses. The first dose of FF-3 was administered approximately 4 hours before the challenge virus. A single dose of challenge virus (influenza A/California/H1N1/2009) was administered by intranasal administration in a total volume of 0.5 millilitres (mL) (0.25 mL per nostril). A second dose of FF-3 was administered approximately 4 hours after the nasal inoculation with challenge virus.

Reporting group title	Placebo

Reporting group description:

A matching placebo was administered as a nasal inhalation aerosol with the EPIC dry powder inhaler twice daily (approximately 12 hours apart) for five days and a single dose on morning of Day 6. Subjects received a total of 11 doses.
The first dose of placebo was administered approximately 4 hours before the challenge virus. A single dose of challenge virus (influenza A/California/H1N1/2009) was administered by intranasal administration in a total volume of 0.5 mL (0.25 mL per nostril). A second dose of placebo was administered approximately 4 hours after the nasal inoculation with challenge virus.

Serious adverse events	FF-3	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 53 (0.00%)	0 / 26 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	FF-3	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	46 / 53 (86.79%)	23 / 26 (88.46%)	
Injury, poisoning and procedural complications			

Limb Injury			
subjects affected / exposed	1 / 53 (1.89%)	0 / 26 (0.00%)	
occurrences (all)	2	0	
Accidental Exposure To Product			
subjects affected / exposed	0 / 53 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Musculoskeletal Injury			
subjects affected / exposed	0 / 53 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Nervous system disorders			
Headache			
subjects affected / exposed	5 / 53 (9.43%)	1 / 26 (3.85%)	
occurrences (all)	5	1	
Lethargy			
subjects affected / exposed	2 / 53 (3.77%)	0 / 26 (0.00%)	
occurrences (all)	2	0	
Dysgeusia			
subjects affected / exposed	1 / 53 (1.89%)	2 / 26 (7.69%)	
occurrences (all)	1	2	
Restless Legs Syndrome			
subjects affected / exposed	0 / 53 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Influenza Like Illness			
subjects affected / exposed	34 / 53 (64.15%)	14 / 26 (53.85%)	
occurrences (all)	36	14	
Fatigue			
subjects affected / exposed	1 / 53 (1.89%)	1 / 26 (3.85%)	
occurrences (all)	1	1	
Vessel Puncture Site Haematoma			
subjects affected / exposed	1 / 53 (1.89%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Feeling Hot			
subjects affected / exposed	0 / 53 (0.00%)	3 / 26 (11.54%)	
occurrences (all)	0	3	
Medical Device Site Rash			

subjects affected / exposed	0 / 53 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Eye disorders			
Eye Pain			
subjects affected / exposed	1 / 53 (1.89%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	2 / 53 (3.77%)	3 / 26 (11.54%)	
occurrences (all)	2	3	
Diarrhoea			
subjects affected / exposed	1 / 53 (1.89%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Nasal Congestion			
subjects affected / exposed	5 / 53 (9.43%)	6 / 26 (23.08%)	
occurrences (all)	5	6	
Oropharyngeal Pain			
subjects affected / exposed	5 / 53 (9.43%)	7 / 26 (26.92%)	
occurrences (all)	6	8	
Rhinorrhoea			
subjects affected / exposed	5 / 53 (9.43%)	0 / 26 (0.00%)	
occurrences (all)	5	0	
Cough			
subjects affected / exposed	2 / 53 (3.77%)	1 / 26 (3.85%)	
occurrences (all)	2	2	
Nasal Discomfort			
subjects affected / exposed	2 / 53 (3.77%)	0 / 26 (0.00%)	
occurrences (all)	2	0	
Dyspnoea			
subjects affected / exposed	1 / 53 (1.89%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Epistaxis			
subjects affected / exposed	1 / 53 (1.89%)	1 / 26 (3.85%)	
occurrences (all)	1	1	
Wheezing			

subjects affected / exposed	1 / 53 (1.89%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Sneezing			
subjects affected / exposed	0 / 53 (0.00%)	2 / 26 (7.69%)	
occurrences (all)	0	2	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	2 / 53 (3.77%)	0 / 26 (0.00%)	
occurrences (all)	2	0	
Pruritus			
subjects affected / exposed	1 / 53 (1.89%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Back Pain			
subjects affected / exposed	1 / 53 (1.89%)	1 / 26 (3.85%)	
occurrences (all)	1	1	
Pain In Extremity			
subjects affected / exposed	1 / 53 (1.89%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Myalgia			
subjects affected / exposed	0 / 53 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Paraesthesia			
subjects affected / exposed	0 / 53 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Infections and infestations			
Otitis Media			
subjects affected / exposed	1 / 53 (1.89%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Conjunctivitis			
subjects affected / exposed	0 / 53 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported