Clinical trial results:
A Multi Center, Phase IV, Randomized, Controlled, Observer Blind Study to Evaluate the Immunogenicity, Safety, and Tolerability of a Trivalent Subunit Inactivated Influenza Vaccine in Healthy Subjects Aged 50 Years and Above

Summary

EudraCT number	2012-003740-74
Trial protocol	CZ
Global end of trial date	16 December 2013

Results information

Result version number	v2 (current)
This version publication date	29 July 2016
First version publication date	29 November 2014
Version creation reason	• Correction of full data set Required for the re-QC project because of the EudraCT system glitch and possible updates to results may be required. Moreover, a change in system user for this study is necessary.

Trial information

Trial identification

Sponsor protocol code	V71_22

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01867021
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Vaccines and Diagnostics S.r.l.
Sponsor organisation address	Via Fiorentina, 1, Siena, Italy, 53100
Public contact	Lucie Černá Hlavatá, Novartis s.r.l., 420 226293041, lucie.cerna_hlavata@novartis.com
Scientific contact	Lucie Černá Hlavatá, Novartis s.r.l., 420 226293041, lucie.cerna_hlavata@novartis.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	16 December 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	16 December 2013
Global end of trial reached?	Yes
Global end of trial date	16 December 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate the non-inferiority of the post-vaccination (Day 22) hemagglutination inhibition (HI) geometric mean titers (GMTs) of AGRIFLU over the corresponding GMTs of the comparator vaccine for all three influenza strains, in healthy adults aged 50 years and above.
To demonstrate non-inferiority of the percentages of subjects achieving seroconversion in antibody titers at Day 22 in the AGRIFLU group over the corresponding percentages of subjects in the comparator group for all three strains, in healthy adults aged 50 years and above.
Safety Objectives
To evaluate the safety and tolerability of of AGRIFLU or comparator vaccines in healthy adults aged 50 years and above.

Protection of trial subjects:

Novartis Vaccines or the investigator provided the ethics committee (EC) with all appropriate material,including the Informed Consent Form (ICF), according to local regulations. The EC also was asked for a written statement regarding the composition of the committee and to comply with GCP (Good Clinical Practices) and with the applicable regulatory requirement(s). The trial was not initiated until appropriate EC approval of the protocol and the ICF was obtained. In addition, all documents were submitted to other authorities in compliance with local jurisdictions. Prior to enrollment, the sponsor and the investigator exchanged written confirmation that their ethical and legal responsibilities had been observed. The EC and, if applicable, other authorities were informed of protocol amendments in accordance with local legal requirements. Appropriate reports on the progress of the study were made to the EC and the sponsor by the investigator in accordance with applicable governmental regulations and in agreement with policy established by the sponsor

Background therapy: -	
Evidence for comparator: -	
Actual start date of recruitment	31 May 2013
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	36 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Czech Republic: 785
Country: Number of subjects enrolled	Philippines: 500
Country: Number of subjects enrolled	South Africa: 1207
Country: Number of subjects enrolled	Thailand: 410

Worldwide total number of subjects	2902
EEA total number of subjects	785

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)	1441
From 65 to 84 years	1436
85 years and over	25

Subject disposition

Recruitment

Recruitment details:

A total of 24 sites with 3 sites in Thailand, 4 sites in Philippines, 15 sites in South Africa and 2 sites in Czech Republic.

Pre-assignment

Screening details:

All enrolled subjects were included in the trial

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Agriflu

Arm description:

Subjects ≥50 years of age who received one vaccination of an investigational vaccine TIV

Arm type	Experimental
Investigational medicinal product name	Trivalent Subunit Inactivated Influenza Vaccine
Investigational medicinal product code	V71
Other name	
Pharmaceutical forms	Emulsion and suspension for emulsion for injection
Routes of administration	Intramuscular use

Dosage and administration details:

A single 0.5 mL dose of the study vaccine was supplied in prefilled syringes and was administered intramuscular (IM) in the deltoid muscle of (preferably) the nondominant arm.

Arm title	Fluvirin

Arm description:

Subjects ≥50 years of age who received one vaccination of a control vaccine TIVf

Arm type	Active comparator
Investigational medicinal product name	Fluvirin
Investigational medicinal product code	V71
Other name	
Pharmaceutical forms	Emulsion and suspension for emulsion for injection
Routes of administration	Intramuscular use

Dosage and administration details:

A single 0.5 mL dose of the Fluvirin was administered IM in the deltoid muscle of (preferably) the nondominant arm.

Number of subjects in period 1	Agriflu	Fluvirin
Started	1452	1450
Completed	1450	1440
Not completed	2	10
Consent withdrawn by subject	1	6
Adverse event, non-fatal	-	1
Not eligible	-	1
Death	1	-
Lost to follow-up	-	2

Baseline characteristics

Reporting groups	
Reporting group title	Agriflu
Reporting group description:	
Subjects ≥50 years of age who received one vaccination of an investigational vaccine TIV	
Reporting group title	Fluvirin
Reporting group description:	
Subjects ≥50 years of age who received one vaccination of a control vaccine TIVf	

Reporting group values	Agriflu	Fluvirin	Total
Number of subjects	1452	1450	2902
Age categorical			
Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			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)			0
From 65-84 years			0
85 years and over			0
Age continuous			
Units: years			
arithmetic mean	64.2	64.2	
standard deviation	± 8.9	± 8.9	-
Gender categorical			
Units: Subjects			
Female	943	893	1836
Male	509	557	1066

End points

End points reporting groups

Reporting group title	Agriflu
Reporting group description:	
Subjects ≥50 years of age who received one vaccination of an investigational vaccine TIV	
Reporting group title	Fluvirin
Reporting group description:	
Subjects ≥50 years of age who received one vaccination of a control vaccine TIVf	
Subject analysis set title	≥50 to ≤64 years_Agriflu_PPS1
Subject analysis set type	Per protocol
Subject analysis set description:	
Subjects ≥50 to ≤64 years of age who received an investigational vaccine TIV	
Subject analysis set title	≥50 to ≤64 years_Fluvirin_PPS1
Subject analysis set type	Per protocol
Subject analysis set description:	
Subjects ≥50 to ≤64 years of age who received a control vaccine TIVf	
Subject analysis set title	≥65 years_Agriflu_PPS1
Subject analysis set type	Per protocol
Subject analysis set description:	
Subjects ≥65 years of age who received an investigational vaccine TIV	
Subject analysis set title	≥65 years_Fluvirin_PPS1
Subject analysis set type	Per protocol
Subject analysis set description:	
Subjects ≥65 years of age who received a control vaccine TIVf	
Subject analysis set title	≥50 to ≤64 years_Agriflu_PPS2
Subject analysis set type	Per protocol
Subject analysis set description:	
Subjects ≥50 to ≤64 years of age who received an investigational vaccine TIV	
Subject analysis set title	≥50 to ≤64 years_Fluvirin_PPS2
Subject analysis set type	Per protocol
Subject analysis set description:	
Subjects ≥50 to ≤64 years of age who received a control vaccine TIVf	
Subject analysis set title	≥65 years_Agriflu_PPS2
Subject analysis set type	Per protocol
Subject analysis set description:	
Subjects ≥65 years of age who received an investigational vaccine TIV	
Subject analysis set title	≥65 years_Fluvirin_PPS2
Subject analysis set type	Per protocol
Subject analysis set description:	
Subjects ≥65 years of age who received a control vaccine TIVf	
Subject analysis set title	≥50 years_Agriflu_PPS1
Subject analysis set type	Per protocol
Subject analysis set description:	
Subjects ≥50 years of age who received an investigational vaccine TIV	
Subject analysis set title	≥50 years_Fluvirin_PPS1
Subject analysis set type	Per protocol
Subject analysis set description:	
Subjects ≥50 years of age who received a control vaccine TIVf	

Primary: 1.Non-inferiority of Postvaccination Hemagglutination Inhibition (HI) Geometric Mean Titers (GMTs) of TIV Group

End point title	1.Non-inferiority of Postvaccination Hemagglutination Inhibition (HI) Geometric Mean Titers (GMTs) of TIV Group

End point description:

Immunogenicity was measured as the hemagglutination inhibition (HI) geometric mean titers (GMTs) achieved by subjects, against each of three vaccine strains, three weeks after one vaccination of TIV (Trivalent Subunit Inactivated Influenza Vaccine) and TIVf vaccine (day 22), evaluated using HI antigen assay.
The upper limit of the two-sided 95% confidence interval (CI) on the ratio of GMTs (GMT TIVf/GMT TIV) should not exceed the non-inferiority margin of 1.5.

End point type	Primary

End point timeframe:

Day 22

End point values	Agriflu	Fluvirin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1452	1450		
Units: Titers				
geometric mean (confidence interval 95%)				
A/H1N1(1401, 1397)	315 (281 to 352)	581 (519 to 651)		
A/H3N2(1401, 1397)	697 (635 to 764)	1048 (955 to 1149)		
B(1402, 1397)	36 (33 to 39)	36 (33 to 39)		

Statistical analyses

Statistical analysis title	Non-inferiority of HI GMTs of TIV vaccine over HI

Statistical analysis description:

The HI GMTs of TIV vaccine for strain A/H1N1 considered non-inferior to HI GMTs of TIVf vaccine if the upper limit of the two-sided 95% CI on the ratio of GMTs (GMT TIVf / GMT TIV) was ≤1.5

Comparison groups	Fluvirin v Agriflu
Number of subjects included in analysis	2902
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	ANCOVA
Parameter estimate	Ratios of GMTs
Point estimate	1.85
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.66
upper limit	2.06

Statistical analysis title	Non-inferiority of HI GMTs of TIV vaccine over HI

Statistical analysis description:

The HI GMTs of TIV vaccine for strain A/H3N2 considered non-inferior to HI GMTs of TIVf vaccine if the upper limit of the two-sided 95% CI on the ratio of GMTs (GMT TIVf / GMT TIV) was ≤1.5

Comparison groups	Agriflu v Fluvirin
Number of subjects included in analysis	2902
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	ANCOVA
Parameter estimate	Ratio of GMTs
Point estimate	1.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.38
upper limit	1.64

Statistical analysis title	Non-inferiority of HI GMTs of TIV vaccine over HI

Statistical analysis description:

The HI GMTs of TIV vaccine for strain B considered non-inferior to HI GMTs of TIVf vaccine if the upper limit of the two-sided 95% CI on the ratio of GMTs (GMT TIVf / GMT TIV) was ≤1.5

Comparison groups	Agriflu v Fluvirin
Number of subjects included in analysis	2902
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	ANCOVA
Parameter estimate	Ratio of GMTs
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.93
upper limit	1.08

Primary: 2. Non-inferiority of the Percentages of Subjects Achieving Seroconversion (SC) in Antibody Titers At Day 22 in the TIV Group

End point title	2. Non-inferiority of the Percentages of Subjects Achieving Seroconversion (SC) in Antibody Titers At Day 22 in the TIV Group

End point description:

Immunogenicity was measured as the percentages of subjects who achieved seroconversion in HI titers, against each of three vaccine strains, at three weeks after one vaccination of TIV and TIVf vaccine (day 22).
Seroconversion is defined as a prevaccination titer <10 and postvaccination HI ≥40 or as a prevaccination titer ≥10 and at minimum four-fold rise in
postvaccination antibody titer.
The upper limit of the two-sided 95% CI on the difference between the seroconversion rates (Seroconversion TIVf - SeroconversionTIV) should not exceed 10%.

End point type	Primary

End point timeframe:
Day 22

End point values	Agriflu	Fluvirin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1452	1450		
Units: Percentage of subjects				
number (confidence interval 95%)				
A/H1N1(1397,1391)	75 (73 to 78)	84 (82 to 86)		
A/H3N2(1398,1390)	72 (70 to 74)	85 (83 to 87)		
B(1399,1390)	41 (39 to 44)	40 (37 to 43)		

Statistical analyses

Statistical analysis title	Non-inferiority of percentage of subjects with HI

Statistical analysis description:

Percentage of subjects with HI seroconversion of TIV vaccine for strain A/H1N1 considered non-inferior to percentage of subjects with HI seroconversion of TIVf vaccine if
the upper limit of the two-sided 95% CI on the difference between the seroconversion rates (Seroconversion TIVf - Seroconversion TIV) was ≤10%.

Comparison groups	Agriflu v Fluvirin
Number of subjects included in analysis	2902
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen
Parameter estimate	Difference in seroconversion rates
Point estimate	9
Confidence interval	
level	95 %
sides	2-sided
lower limit	5.6
upper limit	11.5

Statistical analysis title	Non-inferiority of percentage of subjects with HI

Statistical analysis description:

Percentage of subjects with HI seroconversion of TIV vaccine for strain A/H1N1 considered non-inferior to percentage of subjects with HI seroconversion of TIVf vaccine if
the upper limit of the two-sided 95% CI on the difference between the seroconversion rates (Seroconversion TIVf - Seroconversion TIV) was ≤10%.

Comparison groups	Agriflu v Fluvirin

Number of subjects included in analysis	2902
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen
Parameter estimate	Difference in seroconversion rates
Point estimate	13
Confidence interval	
level	95 %
sides	2-sided
lower limit	10.1
upper limit	16.1

Statistical analysis title	Non-inferiority of percentage of subjects with HI

Statistical analysis description:

Percentage of subjects with HI seroconversion of TIV vaccine for strain A/H1N1 considered non-inferior to percentage of subjects with HI seroconversion of TIVf vaccine if
the upper limit of the two-sided 95% CI on the difference between the seroconversion rates (Seroconversion TIVf - Seroconversion TIV) was ≤10%.

Comparison groups	Agriflu v Fluvirin
Number of subjects included in analysis	2902
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen
Parameter estimate	Difference in seroconversion rates
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5
upper limit	2.3

Secondary: 3.Percentages of Subjects Who Achieved HI Seroconversion and HI Titer ≥1:40 Against Each of Three Strains

End point title	3.Percentages of Subjects Who Achieved HI Seroconversion and HI Titer ≥1:40 Against Each of Three Strains

End point description:

Percentage of subjects achieving HI seroconversion against each of three vaccine strains was measured three weeks after vaccination of TIV and TIVf vaccine (day 22).
Percentage of subjects who achieved HI titer ≥1:40 against each of three vaccine strains was measured three weeks after one vaccination of TIV and TIVf vaccine.
According to Center for Biologics Evaluation and Research recommendations (CBER 2007), the criterion for seroconversion is considered met if the lower limit of the two-sided 95% CI for the percentage of subjects with HI seroconversion is ≥40% (<65 years) or ≥30% (≥65 years).
As per the CBER criteria, the lower limit of the two-sided 95% CI for the percentage of subjects who achieved HI titer ≥ 1:40 should be ≥70% (<65 years) or ≥60% (≥65 years).

End point type	Secondary

End point timeframe:

Day 22

End point values	≥50 to ≤64 years_Agriflu_PPS1	≥50 to ≤64 years_Fluvirin_PPS1	≥65 years_Agriflu_PPS1	≥65 years_Fluvirin_PPS1
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	691	691	711	706
Units: Percentage of Subjects				
number (confidence interval 95%)				
A/H1N1 –Seroconversion(687,686, 710, 705)	78 (74 to 81)	87 (84 to 89)	73 (70 to 77)	81 (78 to 84)
A/H3N2 –Seroconversion(688,686, 710, 704)	78 (75 to 81)	88 (85 to 90)	66 (63 to 70)	82 (79 to 85)
B –Seroconversion(688,686, 711, 704)	44 (40 to 48)	45 (41 to 49)	39 (35 to 42)	35 (32 to 39)
A/H1N1 – HI≥1:40 (Day 22)[691,691, 710, 706]	94 (92 to 96)	96 (94 to 97)	91 (89 to 93)	92 (90 to 94)
A/H3N2 – HI≥1:40 (Day 22)[691,691, 710, 706]	99 (99 to 100)	99 (98 to 100)	99 (98 to 99)	98 (97 to 99)
B – HI ≥1:40 (Day22)[691, 691, 711,706]	58 (55 to 62)	59 (55 to 63)	59 (55 to 62)	56 (52 to 60)

Statistical analyses

No statistical analyses for this end point

Secondary: 4. Geometric Mean Ratio of Subjects Against Each of Three Strains

End point title	4. Geometric Mean Ratio of Subjects Against Each of Three Strains

End point description:

Geometric mean ratio (GMR) of subjects was calculated as the ratio of postvaccination to prevaccination HI GMTs against each of three vaccine strains, three weeks after vaccination of TIV and TIVf vaccine (day 22).

End point type	Secondary

End point timeframe:

Day 22

End point values	≥50 to ≤64 years_Agriflu_PPS1	≥50 to ≤64 years_Fluvirin_PPS1	≥65 years_Agriflu_PPS1	≥65 years_Fluvirin_PPS1
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	688	686	711	705
Units: Ratios				
geometric mean (confidence interval 95%)				
A/H1N1(687, 686,710, 705)	18 (15 to 22)	35 (29 to 42)	15 (12 to 19)	27 (21 to 33)
A/H3N2(688, 686,710, 704)	13 (11 to 15)	18 (15 to 20)	9.65 (7.94 to 12)	16 (13 to 20)
B(688, 686, 711,704)	3.85 (3.43 to 4.31)	3.91 (3.49 to 4.39)	3.1 (2.71 to 3.54)	3 (2.62 to 3.44)

Statistical analyses

No statistical analyses for this end point

Secondary: 5. Number of Subjects Who Reported Solicited Local and Systemic Adverse Events after One Vaccination of TIV and TIVf

End point title	5. Number of Subjects Who Reported Solicited Local and Systemic Adverse Events after One Vaccination of TIV and TIVf

End point description:

Safety was assessed as the number of subjects who reported solicited local and systemic adverse events from day 1 up to and including day 7 after vaccination of TIV and control.

End point type	Secondary

End point timeframe:

Day 1 to 7 postvaccination

End point values	Agriflu	Fluvirin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1428	1433		
Units: Participants				
Pain(1412, 1424)	264	254		
Ecchymosis Type I(1419, 1425)	26	33		
Ecchymosis Type II(1419, 1425)	7	11		
Erythema Type I(1410, 1427)	91	93		
Erythema Type II(1410, 1427)	16	10		
Induration Type I(1423, 1429)	78	65		
Induration Type II(1423, 1429)	25	19		
Swelling Type I(1419, 1427)	50	44		
Swelling Type II(1419, 1427)	21	15		
Chills(1403,1407)	64	68		
Malaise(1402,1405)	88	95		
Nausea(1401,1405)	48	44		
Myalgia(1400,1403)	128	140		
Arthralgia(1396,1403)	83	87		
Headache(1397,1403)	153	161		
Sweating(1403,1405)	99	102		
Fatigue(1404,1407)	143	145		
Loss of Appetite(1404,1403)	43	59		
Fever(>=38°C)[1422,1428]	20	21		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 22 days

Adverse event reporting additional description:

Serious adverse events (SAEs) were collected from day 1 through day 22. Safety Set (Overall)-All subjects in the Exposed Set who had either postvaccination AE or solicited AE data

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.1

Reporting groups

Reporting group title	Agriflu

Reporting group description:

Subjects ≥50 years of age who received one vaccination of an investigational vaccine TIV

Reporting group title	Fluvirin

Reporting group description:

Subjects ≥50 years of age who received one vaccination of a control vaccine TIVf

Serious adverse events	Agriflu	Fluvirin	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 1452 (0.21%)	5 / 1445 (0.35%)	
number of deaths (all causes)	1	0	
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
FEMUR FRACTURE			
subjects affected / exposed	0 / 1452 (0.00%)	1 / 1445 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
HYPERTENSION			
subjects affected / exposed	0 / 1452 (0.00%)	1 / 1445 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
MYOCARDIAL INFARCTION			

subjects affected / exposed	1 / 1452 (0.07%)	1 / 1445 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Nervous system disorders			
BASAL GANGLIA HAEMORRHAGE			
subjects affected / exposed	0 / 1452 (0.00%)	1 / 1445 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
CEREBROVASCULAR ACCIDENT			
subjects affected / exposed	0 / 1452 (0.00%)	1 / 1445 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
DYSPEPSIA			
subjects affected / exposed	1 / 1452 (0.07%)	0 / 1445 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PEPTIC ULCER			
subjects affected / exposed	1 / 1452 (0.07%)	0 / 1445 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
CHOLELITHIASIS			
subjects affected / exposed	1 / 1452 (0.07%)	0 / 1445 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
JAUNDICE CHOLESTATIC			
subjects affected / exposed	0 / 1452 (0.00%)	1 / 1445 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
URINARY TRACT INFECTION			

subjects affected / exposed	1 / 1452 (0.07%)	0 / 1445 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Agriflu	Fluvirin	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	471 / 1452 (32.44%)	467 / 1445 (32.32%)	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	144 / 1452 (9.92%)	146 / 1445 (10.10%)	
occurrences (all)	162	169	
Injection Site Pain			
subjects affected / exposed	281 / 1452 (19.35%)	276 / 1445 (19.10%)	
occurrences (all)	299	287	
Malaise			
subjects affected / exposed	89 / 1452 (6.13%)	95 / 1445 (6.57%)	
occurrences (all)	97	110	
Skin and subcutaneous tissue disorders			
Hyperhidrosis			
subjects affected / exposed	99 / 1452 (6.82%)	103 / 1445 (7.13%)	
occurrences (all)	116	122	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	85 / 1452 (5.85%)	88 / 1445 (6.09%)	
occurrences (all)	96	105	
Headache			
subjects affected / exposed	159 / 1452 (10.95%)	164 / 1445 (11.35%)	
occurrences (all)	192	192	
Myalgia			
subjects affected / exposed	133 / 1452 (9.16%)	141 / 1445 (9.76%)	
occurrences (all)	145	160	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
22 November 2011	Administrative changes updated

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported