Clinical trial results:
A Double-blind, Randomized, Placebo Controlled, Multi-center Trial of Oseltamivir for the Seasonal Prophylaxis of Influenza in Immunocompromised Patients

Summary

EudraCT number	2006-002473-47
Trial protocol	HU DE LT FR CZ BE EE IT PL GB ES
Global end of trial date	26 May 2008

Results information

Result version number	v1 (current)
This version publication date	20 May 2016
First version publication date	20 May 2016

Trial information

Trial identification

Sponsor protocol code	NV20235

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00412737
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	F. Hoffmann-La Roche AG
Sponsor organisation address	Grenzacherstrasse 124, Basel, Switzerland, CH-4070
Public contact	Roche Trial Information Hotline, F. Hoffmann-La Roche AG, +41 616878333, global.trial_information@roche.com
Scientific contact	Roche Trial Information Hotline, F. Hoffmann-La Roche AG, +41 616878333, global.trial_information@roche.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	03 June 2008
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	26 May 2008
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was to evaluate prospectively the efficacy of oseltamivir in the seasonal prophylaxis of influenza as measured by the relative incidence of laboratory confirmed clinical influenza in the two treatment groups.

Protection of trial subjects:

This study was conducted in full conformance with the International Conference on Harmonization (ICH) E6 guideline for Good Clinical Practice and the principles of the Declaration of Helsinki, or the laws and regulations of the country in which the research is conducted, whichever afforded the greater protection to the individual. The study complied with the requirements of the ICH E2A guideline (Clinical Safety Data Management: Definitions and Standards for Expedited Reporting). Study also complied with the EU Clinical Trial Directive (2001/20/EC).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 January 2007
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 21
Country: Number of subjects enrolled	United Kingdom: 3
Country: Number of subjects enrolled	Belgium: 43
Country: Number of subjects enrolled	Estonia: 17
Country: Number of subjects enrolled	France: 40
Country: Number of subjects enrolled	Germany: 23
Country: Number of subjects enrolled	Hungary: 99
Country: Number of subjects enrolled	Italy: 5
Country: Number of subjects enrolled	Lithuania: 36
Country: Number of subjects enrolled	Israel: 49
Country: Number of subjects enrolled	United States: 139
Worldwide total number of subjects	475
EEA total number of subjects	287

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)	3
Children (2-11 years)	14
Adolescents (12-17 years)	9
Adults (18-64 years)	377
From 65 to 84 years	72
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Out of total 477 participants who were randomized to receive study treatments, 2 participants were not included in the study population due to lack of efficacy data. Thus, results are reported only for 475 participants.

Pre-assignment

Screening details:

One participant was randomized to placebo group but received oseltamivir for the first 9 weeks of the study. This participant was included in the placebo group in the Intention-to-treat (ITT) analysis population, but in the oseltamivir group in the safety analysis population.

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, Monitor, Data analyst, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Placebo matched to oseltamivir capsule or suspension orally once daily for 12 weeks.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for oral suspension, Capsule
Routes of administration	Oral use

Dosage and administration details:

Placebo matched to oseltamivir capsule or suspension orally once daily for 12 weeks.

Arm title	Oseltamivir

Arm description:

Oseltamivir 30 milligram (mg) to 75 mg capsule or suspension orally once daily for 12 weeks.

Arm type	Experimental
Investigational medicinal product name	Oseltamivir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, Powder for oral suspension
Routes of administration	Oral use

Dosage and administration details:

Oseltamivir 30 mg to 75 mg capsule or suspension orally once daily for 12 weeks.

Number of subjects in period 1	Placebo	Oseltamivir
Started	237	238
Completed	221	232
Not completed	16	6
Adverse event, non-fatal	3	2
Refused Treatment	6	2
Death	1	-
Failure to Return	6	2

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Placebo matched to oseltamivir capsule or suspension orally once daily for 12 weeks.	
Reporting group title	Oseltamivir
Reporting group description:	
Oseltamivir 30 milligram (mg) to 75 mg capsule or suspension orally once daily for 12 weeks.	

Reporting group values	Placebo	Oseltamivir	Total
Number of subjects	237	238	475
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	 48.9 ± 15.67	 49.4 ± 15.47	 -
Gender categorical Units: Subjects			
Female	86	74	160
Male	151	164	315

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Placebo matched to oseltamivir capsule or suspension orally once daily for 12 weeks.	
Reporting group title	Oseltamivir
Reporting group description:	
Oseltamivir 30 milligram (mg) to 75 mg capsule or suspension orally once daily for 12 weeks.	
Subject analysis set title	Placebo
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
ITT population included all randomized participants who received at least 1 dose of study drug and had at least 1 post baseline efficacy assessment.	
Subject analysis set title	Oseltamivir
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
ITT population included all randomized participants who received at least 1 dose of study drug and had at least 1 post baseline efficacy assessment.	

Primary: Number of Participants With Laboratory Confirmed Clinical Influenza, ITT Population

End point title	Number of Participants With Laboratory Confirmed Clinical Influenza, ITT Population
End point description:	
Laboratory-confirmed clinical influenza was defined as a fever (oral or otic temperature greater than [>] 37.2 degrees Celsius [°C]) and a symptom score for cough and/or coryza (nasal congestion on the diary cards, where 0=absent, 1=mild, 2=moderate, and 3=severe) of 1, 2 or 3 on the same day as fever, and laboratory confirmation of influenza either by detection of viral shedding by viral culture from nasopharyngeal swabs within two days of fever and symptoms, and/or by 4-fold or greater increase in serum hemagglutination inhibition (HAI) titers measured from baseline to any point during the study. ITT population included all randomized participants who received at least 1 dose of study drug and had at least 1 post baseline efficacy assessment. Participants were analyzed as per initial randomization.	
End point type	Primary
End point timeframe:	
From baseline up to 28 days after the last dose of study drug (maximum up to 112 days)	

End point values	Placebo	Oseltamivir		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	238[1]	237[2]		
Units: participants	7	5		

Notes:

[1] - Please see information in Pre-Assignment Details.

[2] - Please see information in Pre-Assignment Details.

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

The null hypothesis tested was that there was no difference between the proportions of participants who met the primary endpoint in the two treatment groups. Relative Risk Reduction = (1.0 - Relative Risk).

Comparison groups	Placebo v Oseltamivir
Number of subjects included in analysis	475
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.772
Method	Fisher exact
Parameter estimate	Relative Risk Reduction
Point estimate	0.283
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.3
upper limit	4.1

Secondary: Number of Participants With Laboratory Confirmed Clinical Influenza, Per Protocol (PP) Population

End point title	Number of Participants With Laboratory Confirmed Clinical Influenza, Per Protocol (PP) Population

End point description:

Laboratory-confirmed clinical influenza was defined as a fever (oral or otic temperature greater than 37.2 °C) and a symptom score for cough and/or coryza (nasal congestion on the diary cards, where 0=absent, 1=mild, 2=moderate, and 3=severe) of 1, 2 or 3 on the same day as fever, and laboratory confirmation of influenza either by detection of viral shedding by viral culture from nasopharyngeal swabs within two days of fever and symptoms, and/or by 4-fold or greater increase in serum HAI titers measured from baseline to any point during the study. Per-Protocol (PP) population was defined as the subset of the ITT population who did not have any major protocol violations which would impact the assessment of efficacy.

End point type	Secondary

End point timeframe:

From baseline up to 28 days after the last dose of study drug (maximum up to 112 days)

End point values	Placebo	Oseltamivir		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	208	220		
Units: participants	6	4		

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Relative Risk Reduction = (1.0 - Relative Risk).

Comparison groups	Oseltamivir v Placebo

Number of subjects included in analysis	428
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.534
Method	Fisher exact
Parameter estimate	Relative Risk Reduction
Point estimate	0.37
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.1
upper limit	4.5

Secondary: Number of Participants With Laboratory Confirmed Clinical Influenza, Intent-to-treat Virus Negative at Baseline (ITTNAB) Population

End point title	Number of Participants With Laboratory Confirmed Clinical Influenza, Intent-to-treat Virus Negative at Baseline (ITTNAB) Population

End point description:

Laboratory-confirmed clinical influenza was defined as a fever (oral or otic temperature greater than 37.2 °C) and a symptom score for cough and/or coryza (nasal congestion on the diary cards, where 0=absent, 1=mild, 2=moderate, and 3=severe) of 1, 2 or 3 on the same day as fever, and laboratory confirmation of influenza either by detection of viral shedding by viral culture from nasopharyngeal swabs within two days of fever and symptoms, and/or by 4-fold or greater increase in serum HAI titers measured from baseline to any point during the study. ITTNAB population was defined as the subset of the ITT population who were culture negative at baseline.

End point type	Secondary

End point timeframe:

From baseline up to 28 days after the last dose of study drug (maximum up to 112 days)

End point values	Placebo	Oseltamivir		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	231	232		
Units: participants	7	4		

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Relative Risk Reduction = (1.0 - Relative Risk).

Comparison groups	Placebo v Oseltamivir

Number of subjects included in analysis	463
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.381
Method	Fisher exact
Parameter estimate	Relative Risk Reduction
Point estimate	0.431
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.7
upper limit	4.6

Secondary: Number of Participants With Reverse Transcriptase Polymerase Chain Reaction (RT-PCR) Confirmed Clinical Influenza, ITT Population

End point title	Number of Participants With Reverse Transcriptase Polymerase Chain Reaction (RT-PCR) Confirmed Clinical Influenza, ITT Population

End point description:

RT-PCR confirmed clinical influenza was defined as a confirmation of influenza by positive RT-PCR result within 2 days of symptoms/last dose from baseline to any point during the study. ITT population.

End point type	Secondary

End point timeframe:

From baseline up to 28 days after the last dose of study drug (maximum up to 112 days)

End point values	Placebo	Oseltamivir		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	238[3]	237[4]		
Units: participants	7	2		

Notes:

[3] - Please see information in Pre-Assignment Details.

[4] - Please see information in Pre-Assignment Details.

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Relative Risk Reduction = (1.0 - Relative Risk).

Comparison groups	Placebo v Oseltamivir
Number of subjects included in analysis	475
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Relative Risk Reduction
Point estimate	0.713

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6
upper limit	5.2

Secondary: Number of Participants With RT-PCR Confirmed Clinical Influenza, ITTNAB Population

End point title	Number of Participants With RT-PCR Confirmed Clinical Influenza, ITTNAB Population

End point description:

RT-PCR confirmed clinical influenza was defined as a confirmation of influenza by positive RT-PCR result within 2 days of symptoms/last dose from baseline to any point during the study. ITTNAB population.

End point type	Secondary

End point timeframe:

From baseline up to 28 days after the last dose of study drug (maximum up to 112 days)

End point values	Placebo	Oseltamivir		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	231	232		
Units: participants	7	1		

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Relative Risk Reduction = (1.0 - Relative Risk).

Comparison groups	Placebo v Oseltamivir
Number of subjects included in analysis	463
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Relative Risk Reduction
Point estimate	0.858
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.1
upper limit	5.7

Secondary: Number of Participants With RT-PCR, or Serology/Viral Culture Confirmed Clinical Influenza, ITT Population

End point title	Number of Participants With RT-PCR, or Serology/Viral Culture

	Confirmed Clinical Influenza, ITT Population

End point description:

RT-PCR, or serology/viral culture confirmed clinical influenza was defined as a confirmation of influenza by positive RT-PCR or culture within 2 days of symptoms/ last dose and/or positive serology result from baseline to any point during the study. ITT population.

End point type	Secondary

End point timeframe:

From baseline up to 28 days after the last dose of study drug (maximum up to 112 days)

End point values	Placebo	Oseltamivir		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	238[5]	237[6]		
Units: participants	8	5		

Notes:

[5] - Please see information in Pre-Assignment Details.

[6] - Please see information in Pre-Assignment Details.

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Relative Risk Reduction = (1.0 - Relative Risk).

Comparison groups	Placebo v Oseltamivir
Number of subjects included in analysis	475
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Relative Risk Reduction
Point estimate	0.372
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.9
upper limit	4.6

Secondary: Number of Participants With RT-PCR, or Serology/Viral Culture Confirmed Clinical Influenza, ITTNAB Population

End point title	Number of Participants With RT-PCR, or Serology/Viral Culture Confirmed Clinical Influenza, ITTNAB Population

End point description:

RT-PCR, or serology/viral culture confirmed clinical influenza was defined as a confirmation of influenza by positive RT-PCR or culture within 2 days of symptoms/ last dose and/or positive serology result from baseline to any point during the study. ITTNAB population.

End point type	Secondary

End point timeframe:

From baseline up to 28 days after the last dose of study drug (maximum up to 112 days)

End point values	Placebo	Oseltamivir		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	231	232		
Units: participants	8	4		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description: Relative Risk Reduction = (1.0 - Relative Risk).	
Comparison groups	Placebo v Oseltamivir
Number of subjects included in analysis	463
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Relative Risk Reduction
Point estimate	0.502
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.4
upper limit	5.1

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From baseline up to 2 days after the last dose of study drug (maximum up to 86 days)	
Adverse event reporting additional description:	
The safety population included all participants who received at least 1 dose of study drug and had at least 1 post baseline safety assessment. Participants were analyzed as per actual treatment received.	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	12.0

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Placebo matched to oseltamivir capsule or suspension orally once daily for 12 weeks.	
Reporting group title	Oseltamivir
Reporting group description:	
Oseltamivir 30 milligram (mg) to 75 mg capsule or suspension orally once daily for 12 weeks.	

Serious adverse events	Placebo	Oseltamivir	
Total subjects affected by serious adverse events			
subjects affected / exposed	23 / 237 (9.70%)	18 / 238 (7.56%)	
number of deaths (all causes)	2	0	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute myeloid leukaemia recurrent			
subjects affected / exposed	1 / 237 (0.42%)	0 / 238 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Metastatic neoplasm			
subjects affected / exposed	1 / 237 (0.42%)	0 / 238 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal adenocarcinoma			
subjects affected / exposed	0 / 237 (0.00%)	1 / 238 (0.42%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			

Deep vein thrombosis			
subjects affected / exposed	0 / 237 (0.00%)	1 / 238 (0.42%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Drug interaction			
subjects affected / exposed	0 / 237 (0.00%)	1 / 238 (0.42%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	1 / 237 (0.42%)	0 / 238 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Acute graft versus host disease			
subjects affected / exposed	1 / 237 (0.42%)	0 / 238 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transplant rejection			
subjects affected / exposed	1 / 237 (0.42%)	0 / 238 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Bronchitis chronic			
subjects affected / exposed	1 / 237 (0.42%)	0 / 238 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	1 / 237 (0.42%)	0 / 238 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			

subjects affected / exposed	1 / 237 (0.42%)	0 / 238 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Depression			
subjects affected / exposed	1 / 237 (0.42%)	0 / 238 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Weight decreased			
subjects affected / exposed	0 / 237 (0.00%)	1 / 238 (0.42%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Pelvic fracture			
subjects affected / exposed	1 / 237 (0.42%)	0 / 238 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal compression fracture			
subjects affected / exposed	1 / 237 (0.42%)	0 / 238 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	1 / 237 (0.42%)	0 / 238 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial flutter			
subjects affected / exposed	0 / 237 (0.00%)	1 / 238 (0.42%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericardial effusion			

subjects affected / exposed	1 / 237 (0.42%)	0 / 238 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Amnesia			
subjects affected / exposed	0 / 237 (0.00%)	1 / 238 (0.42%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	0 / 237 (0.00%)	1 / 238 (0.42%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thalamus haemorrhage			
subjects affected / exposed	0 / 237 (0.00%)	1 / 238 (0.42%)	
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			
Febrile neutropenia			
subjects affected / exposed	1 / 237 (0.42%)	0 / 238 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Abnormal sensation in eye			
subjects affected / exposed	0 / 237 (0.00%)	1 / 238 (0.42%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 237 (0.42%)	0 / 238 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper gastrointestinal haemorrhage			

subjects affected / exposed	1 / 237 (0.42%)	1 / 238 (0.42%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholangitis			
subjects affected / exposed	1 / 237 (0.42%)	0 / 238 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis			
subjects affected / exposed	0 / 237 (0.00%)	1 / 238 (0.42%)	
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			
Angioedema			
subjects affected / exposed	1 / 237 (0.42%)	0 / 238 (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			
Nephropathy			
subjects affected / exposed	1 / 237 (0.42%)	0 / 238 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal impairment			
subjects affected / exposed	0 / 237 (0.00%)	2 / 238 (0.84%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 237 (0.42%)	0 / 238 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gouty arthritis			

subjects affected / exposed	1 / 237 (0.42%)	0 / 238 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Polyarthritis			
subjects affected / exposed	1 / 237 (0.42%)	0 / 238 (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			
Abdominal wall abscess			
subjects affected / exposed	0 / 237 (0.00%)	1 / 238 (0.42%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	1 / 237 (0.42%)	0 / 238 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	1 / 237 (0.42%)	4 / 238 (1.68%)	
occurrences causally related to treatment / all	0 / 1	1 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis viral			
subjects affected / exposed	1 / 237 (0.42%)	0 / 238 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	1 / 237 (0.42%)	0 / 238 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	3 / 237 (1.27%)	1 / 238 (0.42%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis acute			

subjects affected / exposed	1 / 237 (0.42%)	1 / 238 (0.42%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	1 / 237 (0.42%)	0 / 238 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 237 (0.42%)	0 / 238 (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	Placebo	Oseltamivir	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	40 / 237 (16.88%)	42 / 238 (17.65%)	
Nervous system disorders			
Headache			
subjects affected / exposed	12 / 237 (5.06%)	11 / 238 (4.62%)	
occurrences (all)	15	14	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	7 / 237 (2.95%)	12 / 238 (5.04%)	
occurrences (all)	7	12	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	18 / 237 (7.59%)	15 / 238 (6.30%)	
occurrences (all)	21	18	
Nausea			
subjects affected / exposed	9 / 237 (3.80%)	13 / 238 (5.46%)	
occurrences (all)	9	14	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 November 2006	Modified the exclusion criterion for the time period from influenza vaccination to randomization from 6 weeks to 4 weeks; modified the exclusion criteria to allow participation by a wider range of transplant recipients; specified that antiviral treatments with activity against influenza (for example, amantadine, rimantidine, zanamivir, ribavirin, and additional oseltamivir) and probenecid were not allowed during the study; specified a window to allow prior administration of lymphocytedepleting monoclonal antibodies; specified the exclusion of intravenous immunoglobulins during the conduct of the study.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported