Clinical trial results:
A randomized, multicenter trial of oseltamivir doses of 75 mg for 5 or 10 days versus 150 mg for 5 or 10 days in influenza patients with pandemic (H1N1) 2009

Summary

EudraCT number	2016-001008-49
Trial protocol	Outside EU/EEA
Global end of trial date	28 June 2010

Results information

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

Trial information

Trial identification

Sponsor protocol code	NV22155

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01032837
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	F. Hoffmann-La Roche Ltd
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	28 June 2010
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	28 June 2010
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To prospectively evaluate the efficacy of four regimens of oseltamivir on the duration of viral shedding in patients infected with pandemic (H1N1) 2009.

Protection of trial subjects:

The conduct of this clinical study met all local legal and regulatory requirements. The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and the International Conference on Harmonization guideline E6: Good Clinical Practice. A Data Review committee (DRC) supervised the participants' safety and performed the pre-specified interim analyses according to the protocol. Before entering the study, the informed consent form was read by and explained to all participants and/or their legally authorized representative. Participants signed informed consent form and could withdraw from the study at any time without any disadvantage and without having to provide a reason for this decision. Only investigators qualified by training and experience were selected as appropriate experts to investigate the study drug.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 November 2009
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	United States: 101
Worldwide total number of subjects	101
EEA total number of subjects	0

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)	4
Children (2-11 years)	21
Adolescents (12-17 years)	11

Adults (18-64 years)	65
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 27 centers in the United States (US). In all, 102 participants were enrolled in this study and 101 received the study medication

Pre-assignment

Screening details:

Overall, 574 participants were screened during the study; 102 were randomized to receive study treatment and one patient withdrew consent prior to first dose. There were 472 screen failures and the main reason for screen failures were a result of a negative rapid influenza test.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Oseltamivir Standard Dose 5 Days

Arm description:

Adults and children 13 years and older received 75 mg oseltamivir and a placebo capsule twice daily for 5 days. Children aged 1 - 12 years received a weight-based dose (from 30 to 75 mg) oseltamivir suspension and placebo suspension orally twice daily for 5 days. Participants received matching placebo for the second 5 days of treatment.

Arm type	Experimental
Investigational medicinal product name	Oseltamivir
Investigational medicinal product code	Ro 64-0796
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Adults and children 13 years and older received 75mg oral capsule two times a day for five days.

Investigational medicinal product name	Oseltamivir
Investigational medicinal product code	Ro 64-0796
Other name	
Pharmaceutical forms	Powder for oral suspension
Routes of administration	Oral use

Dosage and administration details:

Children aged 1 - 12 years received a weight-based dose (from 30 to 75 mg) oseltamivir suspension orally twice daily for five days.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Adults and children 13 years and older received 75 mg matching oral placebo capsule twice daily for 5 days. Participants received matching placebo for the second 5 days of treatment.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for oral solution
Routes of administration	Oral use

Dosage and administration details:

Children aged 1 - 12 years received a weight-based dose (from 30 to 75 mg) matching placebo suspension orally twice daily for five days. Participants received matching placebo for the second 5 days of treatment.

Arm title	Oseltamivir Standard Dose 10 Days

Arm description:

Adults and children 13 years and older received 75 mg oseltamivir and a placebo capsule twice daily for 10 days. Children aged 1 - 12 years received a weight-based dose (from 30 to 75 mg) oseltamivir suspension and placebo suspension orally twice daily for 10 days.

Arm type	Experimental
Investigational medicinal product name	Oseltamivir
Investigational medicinal product code	Ro 64-0796
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Adults and children 13 years and older received 75mg oral capsule two times a day for ten days.

Investigational medicinal product name	Oseltamivir
Investigational medicinal product code	Ro 64-0796
Other name	
Pharmaceutical forms	Powder for oral suspension
Routes of administration	Oral use

Dosage and administration details:

Children aged 1 - 12 years received a weight-based dose (from 30 to 75 mg) oseltamivir suspension orally twice daily for ten days.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Adults and children 13 years and older received 75 mg matching oral placebo capsule twice daily for 10 days.

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

Dosage and administration details:

Children aged 1 - 12 years received a weight-based dose (from 30 to 75 mg) matching placebo suspension orally twice daily for ten days.

Arm title	Oseltamivir High Dose 5 Days

Arm description:

Adults and children 13 years and older received 150 mg (2 x 75 mg) oseltamivir capsules twice daily for 5 days. Children aged 1 - 12 years received a weight-based dose (from 60 to 150 mg) oseltamivir suspension orally twice daily for 5 days. Participants received matching placebo for the second 5 days of treatment.

Arm type	Experimental

Investigational medicinal product name	Oseltamivir
Investigational medicinal product code	Ro 64-0796
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Adults and children 13 years and older received 150 mg (2 x 75 mg) oseltamivir oral capsule two times a day for five days.

Investigational medicinal product name	Oseltamivir
Investigational medicinal product code	Ro 64-0796
Other name	
Pharmaceutical forms	Powder for oral suspension
Routes of administration	Oral use

Dosage and administration details:

Children aged 1 - 12 years received a weight-based dose (from 60 to 150 mg) oseltamivir suspension orally twice daily for five days.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Participants received matching placebo for the second 5 days of treatment.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for oral solution
Routes of administration	Oral use

Dosage and administration details:

Participants received matching placebo for the second 5 days of treatment.

Arm title	Oseltamivir High Dose 10 Days

Arm description:

Adults and children 13 years and older received 150 mg (2 x 75 mg) oseltamivir capsules twice daily for 10 days. Children aged 1- 12 years received a weight-based dose (from 60 to 150 mg) oseltamivir suspension orally twice daily for 10 days

Arm type	Experimental
Investigational medicinal product name	Oseltamivir
Investigational medicinal product code	Ro 64-0796
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Adults and children 13 years and older received 150 mg (2 x 75 mg) oseltamivir capsules twice daily for 10 days.

Investigational medicinal product name	Oseltamivir
Investigational medicinal product code	Ro 64-0796
Other name	
Pharmaceutical forms	Powder for oral suspension
Routes of administration	Oral use

Dosage and administration details:

Children aged 1- 12 years received a weight-based dose (from 60 to 150 mg) oseltamivir suspension orally twice daily for 10 days.

Number of subjects in period 1	Oseltamivir Standard Dose 5 Days	Oseltamivir Standard Dose 10 Days	Oseltamivir High Dose 5 Days
Started	26	26	25
Completed	26	23	24
Not completed	0	3	1
Adverse event, not serious	-	1	-
Consent withdrawn by subject	-	2	-
Refused treatment	-	-	-
Lost to follow-up	-	-	1

Number of subjects in period 1	Oseltamivir High Dose 10 Days
Started	24
Completed	22
Not completed	2
Adverse event, not serious	1
Consent withdrawn by subject	-
Refused treatment	1
Lost to follow-up	-

Baseline characteristics

Reporting groups	
Reporting group title	Oseltamivir Standard Dose 5 Days
Reporting group description:	
Adults and children 13 years and older received 75 mg oseltamivir and a placebo capsule twice daily for 5 days. Children aged 1 - 12 years received a weight-based dose (from 30 to 75 mg) oseltamivir suspension and placebo suspension orally twice daily for 5 days. Participants received matching placebo for the second 5 days of treatment.	
Reporting group title	Oseltamivir Standard Dose 10 Days
Reporting group description:	
Adults and children 13 years and older received 75 mg oseltamivir and a placebo capsule twice daily for 10 days. Children aged 1 - 12 years received a weight-based dose (from 30 to 75 mg) oseltamivir suspension and placebo suspension orally twice daily for 10 days.	
Reporting group title	Oseltamivir High Dose 5 Days
Reporting group description:	
Adults and children 13 years and older received 150 mg (2 x 75 mg) oseltamivir capsules twice daily for 5 days. Children aged 1 - 12 years received a weight-based dose (from 60 to 150 mg) oseltamivir suspension orally twice daily for 5 days. Participants received matching placebo for the second 5 days of treatment.	
Reporting group title	Oseltamivir High Dose 10 Days
Reporting group description:	
Adults and children 13 years and older received 150 mg (2 x 75 mg) oseltamivir capsules twice daily for 10 days. Children aged 1- 12 years received a weight-based dose (from 60 to 150 mg) oseltamivir suspension orally twice daily for 10 days	

Reporting group values	Oseltamivir Standard Dose 5 Days	Oseltamivir Standard Dose 10 Days	Oseltamivir High Dose 5 Days
Number of subjects	26	26	25
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	2	1
Children (2-11 years)	6	4	6
Adolescents (12-17 years)	2	2	4
Adults (18-64 years)	18	18	14
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	28	27.3	27.2
standard deviation	± 17.84	± 17.42	± 20.7
Gender categorical Units: Subjects			
Female	13	15	14
Male	13	11	11

Reporting group values	Oseltamivir High Dose 10 Days	Total	

Number of subjects	24	101	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	1	4	
Children (2-11 years)	5	21	
Adolescents (12-17 years)	3	11	
Adults (18-64 years)	15	65	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	22.4		
standard deviation	± 14.39	-	
Gender categorical Units: Subjects			
Female	12	54	
Male	12	47	

End points

End points reporting groups

Reporting group title	Oseltamivir Standard Dose 5 Days
Reporting group description:	
Adults and children 13 years and older received 75 mg oseltamivir and a placebo capsule twice daily for 5 days. Children aged 1 - 12 years received a weight-based dose (from 30 to 75 mg) oseltamivir suspension and placebo suspension orally twice daily for 5 days. Participants received matching placebo for the second 5 days of treatment.	
Reporting group title	Oseltamivir Standard Dose 10 Days
Reporting group description:	
Adults and children 13 years and older received 75 mg oseltamivir and a placebo capsule twice daily for 10 days. Children aged 1 - 12 years received a weight-based dose (from 30 to 75 mg) oseltamivir suspension and placebo suspension orally twice daily for 10 days.	
Reporting group title	Oseltamivir High Dose 5 Days
Reporting group description:	
Adults and children 13 years and older received 150 mg (2 x 75 mg) oseltamivir capsules twice daily for 5 days. Children aged 1 - 12 years received a weight-based dose (from 60 to 150 mg) oseltamivir suspension orally twice daily for 5 days. Participants received matching placebo for the second 5 days of treatment.	
Reporting group title	Oseltamivir High Dose 10 Days
Reporting group description:	
Adults and children 13 years and older received 150 mg (2 x 75 mg) oseltamivir capsules twice daily for 10 days. Children aged 1- 12 years received a weight-based dose (from 60 to 150 mg) oseltamivir suspension orally twice daily for 10 days	

Primary: Time to Cessation of Viral Shedding

End point title	Time to Cessation of Viral Shedding[1]
End point description:	
The time to cessation of viral shedding was measured by viral culture and defined as the time from treatment initiation to the time of the first negative culture with no subsequent positive cultures. Any patient with a positive culture at the last sample time was censored at that time point. Median time to cessation was estimated from the Kaplan-Meier curve.	
End point type	Primary
End point timeframe:	
Day 1 to Day 40	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Study data were analyzed by descriptive summaries. No formal hypothesis testing was planned.

End point values	Oseltamivir Standard Dose 5 Days	Oseltamivir Standard Dose 10 Days	Oseltamivir High Dose 5 Days	Oseltamivir High Dose 10 Days
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	19	18	16	17
Units: hours				
median (confidence interval 95%)				
Time to Cessation of Viral Shedding	65.6 (47.5 to 79.9)	70.8 (62.1 to 101.7)	58.1 (27.3 to 93.3)	74.1 (48.6 to 117.5)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Viral Shedding by Clinic Visit as Measured by Viral Culture

End point title	Number of Participants With Viral Shedding by Clinic Visit as Measured by Viral Culture

End point description:

Viral shedding was measured by viral culture from samples obtained from nasal and throat swabs and performed by the central laboratory. Only the numbers of participants available at the particular time point were included in the analysis.

End point type	Secondary

End point timeframe:

Baseline and Days 3, 6, 8, 11, 15 and 40

End point values	Oseltamivir Standard Dose 5 Days	Oseltamivir Standard Dose 10 Days	Oseltamivir High Dose 5 Days	Oseltamivir High Dose 10 Days
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	19	18	16	17
Units: Percentage of Participants				
Baseline (n=19, 18, 16, 17)	19	18	16	17
Day 3 (n=19, 17, 15, 15)	7	11	7	9
Day 6 (n=19, 17, 15, 15)	0	0	1	2
Day 8 (n=18, 17, 15, 15)	1	0	0	1
Day 11 (n=18, 18, 15, 14)	1	2	0	0
Day 15 (n=18, 14, 15, 12)	0	0	0	0
Day 40 (n=16, 15, 16, 14)	1	2	0	2

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Viral Shedding by Clinic Visit as Measured by Reverse Transcriptase Polymerase Chain Reaction

End point title	Number of Participants With Viral Shedding by Clinic Visit as Measured by Reverse Transcriptase Polymerase Chain Reaction

End point description:

Viral shedding was measured by reverse transcriptase polymerase chain reaction (RT-PCR) from samples obtained from nasal and throat swabs and performed by the central laboratory. Only the numbers of participants available at the particular time point were included in the analysis.

End point type	Secondary

End point timeframe:

Baseline and Days 3, 6, 8, 11, 15 and 40

End point values	Oseltamivir Standard Dose 5 Days	Oseltamivir Standard Dose 10 Days	Oseltamivir High Dose 5 Days	Oseltamivir High Dose 10 Days
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	19	18	16	17
Units: Percentage of Participants				
Baseline (n=19, 18, 16, 17)	17	18	16	17
Day 3 (n=19, 17, 15, 15)	15	15	11	13
Day 6 (n=19, 17, 15, 15)	5	5	8	8
Day 8 (n=18, 17, 15, 15)	2	2	2	2
Day 11 (n=18, 18, 15, 14)	1	1	4	3
Day 15 (n=18, 14, 15, 12)	0	1	0	1
Day 40 (n=16, 15, 16, 14)	1	1	1	0

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Influenza Titer Measured by Viral Culture

End point title	Change From Baseline in Influenza Titer Measured by Viral Culture

End point description:

Influenza virus titer measured by viral culture and expressed on a Log10 scale of the 50% Tissue Culture Infective Dose (TCID50; amount of virus required to kill 50% of inoculated tissue culture cells).

End point type	Secondary

End point timeframe:

Baseline, Days 2 through 15

End point values	Oseltamivir Standard Dose 5 Days	Oseltamivir Standard Dose 10 Days	Oseltamivir High Dose 5 Days	Oseltamivir High Dose 10 Days
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	19	18	16	17
Units: Log10 TCID50				
arithmetic mean (standard deviation)				
Baseline (n=19, 18, 16, 17)	3.74 (± 1.478)	4.06 (± 1.235)	4.14 (± 1.338)	4.54 (± 0.746)
Day 2 (n=19, 18, 15, 17)	-1.82 (± 1.457)	-1.17 (± 1.138)	-1.97 (± 1.584)	-1.15 (± 1.425)
Day 3 (n=19, 18, 15, 17)	-2.38 (± 1.67)	-2.18 (± 1.221)	-2.95 (± 1.286)	-2.88 (± 1.296)
Day 4 (n=19, 18, 15, 17)	-3.18 (± 1.511)	-3.29 (± 1.129)	-3.33 (± 1.368)	-3.76 (± 0.859)

Day 5 (n=19, 18, 16, 17)	-3 (± 1.656)	-3.43 (± 1.14)	-3.45 (± 1.453)	-3.91 (± 0.765)
Day 6 (n=19, 18, 15, 17)	-3.22 (± 1.488)	-3.56 (± 1.235)	-3.45 (± 1.53)	-3.99 (± 0.726)
Day 7 (n=19, 18, 16, 17)	-3.22 (± 1.469)	-3.53 (± 1.218)	-3.58 (± 1.331)	-4.04 (± 0.746)
Day 8 (n=19, 18, 15, 17)	-3.18 (± 1.457)	-3.56 (± 1.235)	-3.65 (± 1.385)	-4.04 (± 0.746)
Day 9 (n=19, 18, 14, 16)	-3.24 (± 1.478)	-3.53 (± 1.218)	-3.57 (± 1.381)	-4.08 (± 0.688)
Day 10 (n=19, 18, 15, 16)	-3.21 (± 1.463)	-3.5 (± 1.26)	-3.55 (± 1.334)	-4.14 (± 0.652)
Day 11 (n=19, 16, 16, 15)	-3.22 (± 1.469)	-3.42 (± 1.524)	-3.64 (± 1.338)	-4.08 (± 0.632)
Day 12 (n=19, 18, 15, 15)	-3.11 (± 1.669)	-3.47 (± 1.289)	-3.63 (± 1.385)	-4.1 (± 0.653)
Day 13 (n=19, 18, 16, 15)	-3.17 (± 1.458)	-3.43 (± 1.248)	-3.64 (± 1.338)	-4.1 (± 0.653)
Day 14 (n=18, 18, 15, 15)	-3.17 (± 1.488)	-3.56 (± 1.235)	-3.55 (± 1.334)	-4.1 (± 0.653)
Day 15 (n=18, 17, 14, 15)	-3.14 (± 1.456)	-3.5 (± 1.25)	-3.55 (± 1.401)	-4.1 (± 0.653)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Development of Oseltamivir-Resistant Influenza Virus

End point title	Number of Participants With Development of Oseltamivir-Resistant Influenza Virus

End point description:

The last positive viral isolate from each patient was tested for reduced sensitivity to oseltamivir. Phenotypic assay was performed to determine the susceptibility of the last positive viral isolate from each patient. If required, a genotypic assay to determine the contribution of both the neuraminidase (NA) and hemagglutinin (HA) genes to decreased susceptibility was also performed.

End point type	Secondary

End point timeframe:

40 Days

End point values	Oseltamivir Standard Dose 5 Days	Oseltamivir Standard Dose 10 Days	Oseltamivir High Dose 5 Days	Oseltamivir High Dose 10 Days
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	19	18	16	17
Units: Number of Participants				
Development of Oseltamivir-Resistant Influenza	0	1	1	0

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Resolution of Fever

End point title	Time to Resolution of Fever

End point description:

Temperature was recorded by the patient in a diary twice daily for 10 days and once daily thereafter. Fever was defined as a body temperature greater than or including 37.8 degrees Celsius (or ≥ 100.04 Fahrenheit). Time to resolution of fever was defined as the total number of hours from the first dose of study medication to the first time at which temperature is ≤ 37.2 degrees Celsius and lasts at least 21.5 hours. Patients who were still febrile at the end of the study period were censored at that time.

End point type	Secondary

End point timeframe:

Day 1 through Day 40

End point values	Oseltamivir Standard Dose 5 Days	Oseltamivir Standard Dose 10 Days	Oseltamivir High Dose 5 Days	Oseltamivir High Dose 10 Days
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	6	8	3
Units: Hours				
median (confidence interval 95%)				
Time to Resolution of Fever	19.3 (10.6 to 58.4)	35.5 (12.7 to 53.1)	24.9 (15.7 to 45.2)	20 (15.9 to 74.3)

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Alleviation of All Clinical Symptoms - Children

End point title	Time to Alleviation of All Clinical Symptoms - Children

End point description:

Daily influenza-like symptoms (such as poor appetite, irritability, low energy, nasal congestion, runny nose etc) were recorded in a diary on a scale from 0 (no problem) to 3 (major problem). A patient is considered free of all clinical influenza symptoms if all symptoms were checked as 'no problem' or 'minor problem' (i.e., symptom score ≤1). Time to alleviation of all clinical symptoms was defined as the number of hours from the first dose to the first time the patient had alleviation of all symptoms. Patients without alleviation of symptoms were censored at the last available assessment.

End point type	Secondary

End point timeframe:

Day 1 to Day 40

End point values	Oseltamivir Standard Dose 5 Days	Oseltamivir Standard Dose 10 Days	Oseltamivir High Dose 5 Days	Oseltamivir High Dose 10 Days
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	4	4	3
Units: hours				
median (confidence interval 95%)				
Time to Alleviation of All Clinical Symptoms	176.8 (67.5 to 302)	127.7 (32.6 to 281.8)	118.8 (46.3 to 228.2)	123.1 (7.1 to 232.3)

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Alleviation of All Clinical Symptoms - Adults

End point title	Time to Alleviation of All Clinical Symptoms - Adults

End point description:

Daily influenza-like symptoms (such as nasal congestion, sore throat, cough, aches and pains, fatigue, headache, chills) were recorded in a diary on a scale from 0 (absent) to 3 (severe). A patient is considered free of all clinical influenza symptoms if all symptoms were checked as 'absent' or 'mild' (i.e., symptom score ≤1). Time to alleviation of all clinical symptoms was defined as the number of hours from the first dose to the first time the patient had alleviation of all symptoms. Patients without alleviation of symptoms were censored at the last available assessment.

End point type	Secondary

End point timeframe:

Day 1 to Day 40

End point values	Oseltamivir Standard Dose 5 Days	Oseltamivir Standard Dose 10 Days	Oseltamivir High Dose 5 Days	Oseltamivir High Dose 10 Days
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	13	14	12	14
Units: hours				
median (confidence interval 95%)				
Time to Alleviation of All Clinical Symptoms	140 (99.8 to 183.1)	181.8 (87 to 354.6)	146.8 (109.1 to 237.8)	94.9 (57.2 to 261.2)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Who Developed Secondary Illnesses During the Study

End point title	Number of Participants Who Developed Secondary Illnesses During the Study

End point description:

The number of participants who developed secondary illnesses due to influenza, including four pre-defined adverse events: otitis media, bronchitis, pneumonia, or sinusitis at any time during the study.

End point type	Secondary

End point timeframe:

Day 1 through Day 40

End point values	Oseltamivir Standard Dose 5 Days	Oseltamivir Standard Dose 10 Days	Oseltamivir High Dose 5 Days	Oseltamivir High Dose 10 Days
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	19	18	16	17
Units: Number of Participants				
Bronchitis	1	0	0	0
Otitis media	0	0	0	0
Pneumonia	0	0	0	0
Sinusitis	0	0	0	2
Any secondary illness	1	0	0	2

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Who Developed Secondary Illnesses That Were Treated With Antibiotics

End point title	Number of Participants Who Developed Secondary Illnesses That Were Treated With Antibiotics

End point description:

The number of participants who developed secondary illnesses due to influenza, including otitis media, bronchitis, pneumonia, or sinusitis at any time during the study which were treated with antibiotics.

End point type	Secondary

End point timeframe:

Day 1 through Day 40

End point values	Oseltamivir Standard Dose 5 Days	Oseltamivir Standard Dose 10 Days	Oseltamivir High Dose 5 Days	Oseltamivir High Dose 10 Days
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	19	18	16	17
Units: Number of Participants	0	0	0	2

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with any Adverse Event (AE) or Serious Adverse

Event (SAE)

End point title	Number of Participants with any Adverse Event (AE) or Serious Adverse Event (SAE)

End point description:

An AE is defined as any untoward medical occurrence in a participant or clinical investigation participant, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. SAEs are defined as those events that were fatal or immediately life-threatening, and those events that resulted in hospitalization; prolonged an existing hospitalization; resulted in disability; or was a congenital anomaly.

End point type	Secondary

End point timeframe:

Up to 1 year

End point values	Oseltamivir Standard Dose 5 Days	Oseltamivir Standard Dose 10 Days	Oseltamivir High Dose 5 Days	Oseltamivir High Dose 10 Days
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	26	26	25	24
Units: Number of Participants				
Total patients with at least one AE	10	11	7	10
Total number of AE’s	17	15	9	19
Total number of SAE’s	0	0	0	0
Total number of Deaths	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to Day 40

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	14.1

Reporting groups

Reporting group title	Oseltamivir Standard Dose 5 Days

Reporting group description:

Adults and children 13 years and older received 75 mg oseltamivir and a placebo capsule twice daily for 5 days. Children aged 1 - 12 years received a weight-based dose (from 30 to 75 mg) oseltamivir suspension and placebo suspension orally twice daily for 5 days. Participants received matching placebo for the second 5 days of treatment.

Reporting group title	Oseltamivir Standard Dose 10 Days

Reporting group description:

Adults and children 13 years and older received 75 mg oseltamivir and a placebo capsule twice daily for 10 days. Children aged 1 - 12 years received a weight-based dose (from 30 to 75 mg) oseltamivir suspension and placebo suspension orally twice daily for 10 days.

Reporting group title	Oseltamivir High Dose 5 Days

Reporting group description:

Adults and children 13 years and older received 150 mg (2 x 75 mg) oseltamivir capsules twice daily for 5 days. Children aged 1 - 12 years received a weight-based dose (from 60 to 150 mg) oseltamivir suspension orally twice daily for 5 days. Participants received matching placebo for the second 5 days of treatment.

Reporting group title	Oseltamivir High Dose 10 Days

Reporting group description:

Adults and children 13 years and older received 150 mg (2 x 75 mg) oseltamivir capsules twice daily for 10 days. Children aged 1- 12 years received a weight-based dose (from 60 to 150 mg) oseltamivir suspension orally twice daily for 10 days

Serious adverse events	Oseltamivir Standard Dose 5 Days	Oseltamivir Standard Dose 10 Days	Oseltamivir High Dose 5 Days
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 25 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Serious adverse events	Oseltamivir High Dose 10 Days		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 24 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	Oseltamivir Standard Dose 5 Days	Oseltamivir Standard Dose 10 Days	Oseltamivir High Dose 5 Days
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 26 (11.54%)	5 / 26 (19.23%)	3 / 25 (12.00%)
Injury, poisoning and procedural complications			
Accidental overdose			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	2
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	0 / 26 (0.00%)	2 / 26 (7.69%)	0 / 25 (0.00%)
occurrences (all)	0	3	0
Nausea			
subjects affected / exposed	1 / 26 (3.85%)	1 / 26 (3.85%)	1 / 25 (4.00%)
occurrences (all)	1	1	2
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	2 / 26 (7.69%)	0 / 26 (0.00%)	0 / 25 (0.00%)
occurrences (all)	2	0	0
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	1 / 26 (3.85%)	2 / 26 (7.69%)	0 / 25 (0.00%)
occurrences (all)	1	2	0

Non-serious adverse events	Oseltamivir High Dose 10 Days		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 24 (25.00%)		
Injury, poisoning and procedural complications			
Accidental overdose			
subjects affected / exposed	2 / 24 (8.33%)		
occurrences (all)	2		

Gastrointestinal disorders Vomiting subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all)	 6 / 24 (25.00%) 7 2 / 24 (8.33%) 2		
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all)	 0 / 24 (0.00%) 0		
Infections and infestations Upper respiratory tract infection subjects affected / exposed occurrences (all)	 0 / 24 (0.00%) 0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 October 2009	This protocol amendment included addition of the exclusion criterion for vaccination with live attenuated influenza vaccine and Inclusion of patients with influenza A without further specification of pandemic influenza A (H1N1) 2009

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported