Clinical trial results:
A Phase 2b, Randomized, Double-Blind, Placebo Controlled, Parallel-Group, Multicenter Study of 2 Dose Levels of VX 787 Administered as Monotherapy and One Dose Level of VX-787 Administered in Combination With Oseltamivir for the Treatment of Acute Uncomplicated Seasonal Influenza A in Adult Subjects

Summary

EudraCT number	2014-004068-39
Trial protocol	EE LV BE DE
Global end of trial date	25 May 2016

Results information

Result version number	v1 (current)
This version publication date	21 July 2017
First version publication date	21 July 2017

Trial information

Trial identification

Sponsor protocol code	63623872FLZ2001 (VX14-787-103)

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02342249
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Janssen Research & Development, LLC
Sponsor organisation address	920 Route 202, Raritan, NJ, United States, 08869
Public contact	Clinical Registry Group, Janssen Research & Development, LLC, ClinicalTrialsEU@its.jnj.com
Scientific contact	Clinical Registry Group, Janssen Research & Development, LLC, ClinicalTrialsEU@its.jnj.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?	
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	25 May 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	25 May 2016
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The main objective of the study was to evaluate the antiviral effect, as measured by viral load as measured by quantitative reverse transcriptase polymerase chain reaction (qRT-PCR), in nasal secretions in adults with acute uncomplicated seasonal influenza A following administration of JNJ-63623872.

Protection of trial subjects:

This study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with Good Clinical Practices and applicable regulatory requirements. Safety evaluations included monitoring of adverse events (AEs), clinical laboratory assessments (biochemistry, coagulation, hematology, and urinalysis), 12-lead electrocardiogram (ECGs), vital signs measurements (blood pressure, pulse rate, respiratory rate, and oral temperature), and physical examination (height and body weight).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	19 December 2014
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	Belgium: 19
Country: Number of subjects enrolled	Bulgaria: 3
Country: Number of subjects enrolled	Canada: 7
Country: Number of subjects enrolled	Estonia: 21
Country: Number of subjects enrolled	Latvia: 4
Country: Number of subjects enrolled	United States: 230
Country: Number of subjects enrolled	South Africa: 8
Worldwide total number of subjects	292
EEA total number of subjects	47

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)	291
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 967 subjects were screened out of which 292 subjects were randomized and treated, 223 were confirmed influenza A positive.

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, Carer

Arms

Are arms mutually exclusive?	Yes
Arm title	JNJ-63623872 Placebo BID + Oseltamivir Placebo BID

Arm description:

Subjects received JNJ-63623872 matching placebo tablets and oseltamivir matching placebo capsule orally, twice daily (BID) with approximately 12 hour intervals, over 5 days.

Arm type	Placebo
Investigational medicinal product name	JNJ-63623872 placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received matching placebo tablets of JNJ-63623872 orally BID over 5 days.

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

Dosage and administration details:

Subjects received matching placebo capsule of oseltamivir orally BID over 5 days.

Arm title	JNJ-63623872 300 mg BID + Oseltamivir Placebo BID

Arm description:

Subjects received JNJ-63623872 300 milligram (mg) tablets along with matching placebo capsule of oseltamivir orally BID with approximately 12 hour intervals, over 5 days.

Arm type	Experimental
Investigational medicinal product name	JNJ-63623872
Investigational medicinal product code	
Other name	VX-787
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received 300 mg JNJ-63623872 tablets orally BID over 5 days.

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

Dosage and administration details:

Subjects received matching placebo capsule of oseltamivir orally BID over 5 days.

Arm title	JNJ-63623872 600 mg BID + Oseltamivir Placebo BID

Arm description:

Subjects received JNJ-63623872 600 mg tablets (2 * 300-mg tablets) along with matching placebo capsule of oseltamivir orally BID with approximately 12 hour intervals, over 5 days.

Arm type	Experimental
Investigational medicinal product name	JNJ-63623872
Investigational medicinal product code	
Other name	VX-787
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received 600 mg (2 * 300-mg tablets) JNJ-63623872 tablets orally BID over 5 days.

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

Dosage and administration details:

Subjects received matching placebo capsule of oseltamivir orally BID over 5 days.

Arm title	JNJ-63623872 600 mg BID + Oseltamivir 75 mg BID

Arm description:

Subjects received JNJ-63623872 600 mg tablets (2 * 300-mg tablets) along with 75 mg oseltamir capsule orally BID with approximately 12 hour intervals, over 5 days.

Arm type	Experimental
Investigational medicinal product name	JNJ-63623872
Investigational medicinal product code	
Other name	VX-787
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received 600 mg (2 * 300-mg tablets) JNJ-63623872 tablets orally BID over 5 days.

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

Dosage and administration details:

Subjects received 75 mg oseltamivir capsule orally BID over 5 days.

Number of subjects in period 1	JNJ-63623872 Placebo BID + Oseltamivir Placebo BID	JNJ-63623872 300 mg BID + Oseltamivir Placebo BID	JNJ-63623872 600 mg BID + Oseltamivir Placebo BID
Started	71	74	74
Completed	69	69	67
Not completed	2	5	7
Consent withdrawn by subject	1	3	6
Other	1	1	1
Protocol deviation	-	1	-

Number of subjects in period 1	JNJ-63623872 600 mg BID + Oseltamivir 75 mg BID
Started	73
Completed	70
Not completed	3
Consent withdrawn by subject	1
Other	1
Protocol deviation	1

Baseline characteristics

Reporting groups	
Reporting group title	JNJ-63623872 Placebo BID + Oseltamivir Placebo BID
Reporting group description:	
Subjects received JNJ-63623872 matching placebo tablets and oseltamivir matching placebo capsule orally, twice daily (BID) with approximately 12 hour intervals, over 5 days.	
Reporting group title	JNJ-63623872 300 mg BID + Oseltamivir Placebo BID
Reporting group description:	
Subjects received JNJ-63623872 300 milligram (mg) tablets along with matching placebo capsule of oseltamivir orally BID with approximately 12 hour intervals, over 5 days.	
Reporting group title	JNJ-63623872 600 mg BID + Oseltamivir Placebo BID
Reporting group description:	
Subjects received JNJ-63623872 600 mg tablets (2 * 300-mg tablets) along with matching placebo capsule of oseltamivir orally BID with approximately 12 hour intervals, over 5 days.	
Reporting group title	JNJ-63623872 600 mg BID + Oseltamivir 75 mg BID
Reporting group description:	
Subjects received JNJ-63623872 600 mg tablets (2 * 300-mg tablets) along with 75 mg oseltamir capsule orally BID with approximately 12 hour intervals, over 5 days.	

Reporting group values	JNJ-63623872 Placebo BID + Oseltamivir Placebo BID	JNJ-63623872 300 mg BID + Oseltamivir Placebo BID	JNJ-63623872 600 mg BID + Oseltamivir Placebo BID
Number of subjects	71	74	74
Title for AgeCategorical			
Units: subjects			
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	71	74	73
From 65 to 84 years	0	0	1
85 years and over	0	0	0
Title for AgeContinuous			
Units: years			
arithmetic mean	41.6	41.6	37.6
standard deviation	± 12.51	± 12.79	± 13.49
Title for Gender			
Units: subjects			
Female	31	35	41
Male	40	39	33

Reporting group values	JNJ-63623872 600 mg BID + Oseltamivir 75 mg BID	Total	
Number of subjects	73	292	
Title for AgeCategorical			
Units: subjects			
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	73	291	
From 65 to 84 years	0	1	

85 years and over	0	0	

Title for AgeContinuous Units: years			
arithmetic mean	40.9		
standard deviation	± 12.92	-	
Title for Gender Units: subjects			
Female	43	150	
Male	30	142	

End points

End points reporting groups

Reporting group title	JNJ-63623872 Placebo BID + Oseltamivir Placebo BID
Reporting group description:	
Subjects received JNJ-63623872 matching placebo tablets and oseltamivir matching placebo capsule orally, twice daily (BID) with approximately 12 hour intervals, over 5 days.	
Reporting group title	JNJ-63623872 300 mg BID + Oseltamivir Placebo BID
Reporting group description:	
Subjects received JNJ-63623872 300 milligram (mg) tablets along with matching placebo capsule of oseltamivir orally BID with approximately 12 hour intervals, over 5 days.	
Reporting group title	JNJ-63623872 600 mg BID + Oseltamivir Placebo BID
Reporting group description:	
Subjects received JNJ-63623872 600 mg tablets (2 * 300-mg tablets) along with matching placebo capsule of oseltamivir orally BID with approximately 12 hour intervals, over 5 days.	
Reporting group title	JNJ-63623872 600 mg BID + Oseltamivir 75 mg BID
Reporting group description:	
Subjects received JNJ-63623872 600 mg tablets (2 * 300-mg tablets) along with 75 mg oseltamir capsule orally BID with approximately 12 hour intervals, over 5 days.	

Primary: Area Under the Curve (AUC) of the log10 Nasal Viral Load From Day 1 to Day 8

End point title	Area Under the Curve (AUC) of the log10 Nasal Viral Load From Day 1 to Day 8
End point description:	
Area under the curve (AUC) of the log10 nasal viral load was measured by quantitative reverse transcriptase polymerase chain reaction (qRT-PCR). Full analysis set (FAS) included all randomized participants who received at least 1 dose of study drug and who had a confirmed infection with influenza A. The estimated least square (LS) Means and 95 percent (%) confidence intervals (CIs) for viral load measured by qRT-PCR at each visit are reported here. In the below table, "99999" signifies that no LS mean was estimable at Day 1.	
End point type	Primary
End point timeframe:	
Day 1 to 8, with measurements on Days 1, 3, 4, 6 and 8	

End point values	JNJ-63623872 Placebo BID + Oseltamivir Placebo BID	JNJ-63623872 300 mg BID + Oseltamivir Placebo BID	JNJ-63623872 600 mg BID + Oseltamivir Placebo BID	JNJ-63623872 600 mg BID + Oseltamivir 75 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	51	58	57	57
Units: log10 copies/milliliter (mL)				
least squares mean (confidence interval 95%)				
Day 1	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)
Day 3	5.4 (4.9 to 5.9)	5.2 (4.7 to 5.6)	4.9 (4.5 to 5.4)	4.2 (3.8 to 4.6)
Day 4	4.6 (4 to 5.2)	3.9 (3.4 to 4.5)	3.8 (3.2 to 4.4)	3 (2.4 to 3.5)
Day 6	3.5 (2.9 to 4.1)	2.5 (1.9 to 3.1)	2.5 (1.9 to 3.1)	1.7 (1.1 to 2.3)
Day 8	1.5 (1 to 2.1)	1.4 (0.8 to 1.9)	1 (0.4 to 1.5)	0.8 (0.3 to 1.3)

Statistical analyses

Statistical analysis title	Statistical analysis from Day 1 to Day 8
Comparison groups	JNJ-63623872 300 mg BID + Oseltamivir Placebo BID v JNJ-63623872 Placebo BID + Oseltamivir Placebo BID
Number of subjects included in analysis	109
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.044
Method	Mixed Model Repeated Measures
Parameter estimate	LS Mean Difference (Difference in AUC)
Point estimate	-3.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.1
upper limit	-0.1

Statistical analysis title	Statistical analysis from Day 1 to Day 8
Comparison groups	JNJ-63623872 600 mg BID + Oseltamivir Placebo BID v JNJ-63623872 Placebo BID + Oseltamivir Placebo BID
Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.012
Method	Mixed Model Repeated Measures
Parameter estimate	LS Mean Difference (Difference in AUC)
Point estimate	-4.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8
upper limit	-1

Statistical analysis title	Statistical analysis from Day 1 to Day 8
Comparison groups	JNJ-63623872 600 mg BID + Oseltamivir 75 mg BID v JNJ-63623872 Placebo BID + Oseltamivir Placebo BID

Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed Model Repeated Measures
Parameter estimate	LS Mean Difference (Difference in AUC)
Point estimate	-8.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12
upper limit	-5.1

Statistical analysis title	Statistical analysis from Day 1 to Day 8
Comparison groups	JNJ-63623872 600 mg BID + Oseltamivir 75 mg BID v JNJ-63623872 600 mg BID + Oseltamivir Placebo BID
Number of subjects included in analysis	114
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.017
Method	Mixed Model Repeated Measures
Parameter estimate	LS Mean Difference (Difference in AUC)
Point estimate	-4.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.4
upper limit	-0.75

Secondary: Time to Resolution of Influenza Symptoms After Initiation of Study Drug

End point title	Time to Resolution of Influenza Symptoms After Initiation of Study Drug

End point description:

Resolution of influenza symptoms was time of first of 3 evaluations (over 24 hours) in which all symptom scores for each of 3 assessments are 0/1 for all 7 primary influenza symptoms of Flu-iiQ^TM. The Flu-iiQ^TM questionnaire consists of 4 modules- 1 module assessing influenza symptoms, 1 module assessing impact of influenza on normal functioning and 2 modules assessing impact of influenza on subject's emotional state. Influenza Symptom assessment (Module 1) is scored on 4 point scale (0=none, 1=mild, 2=moderate, 3= severe) for each of 10 influenza symptoms (cough, sore throat, headache, nasal stuffiness, feverishness/chills, muscle/joint pain associated with current episode, fatigue, neck pain, interrupted sleep and loss of appetite). FAS included all randomized participants who received at least 1 dose of study drug and who had a confirmed infection with influenza A. In the below table, medians represented were Kaplan-Meier estimates.

End point type	Secondary

End point timeframe:

Baseline up to Day 14

End point values	JNJ-63623872 Placebo BID + Oseltamivir Placebo BID	JNJ-63623872 300 mg BID + Oseltamivir Placebo BID	JNJ-63623872 600 mg BID + Oseltamivir Placebo BID	JNJ-63623872 600 mg BID + Oseltamivir 75 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	51	58	57	57
Units: hours				
median (confidence interval 95%)	86.4 (68.68 to 117.27)	99 (71.48 to 150.6)	85.7 (55.28 to 114.88)	70.4 (61.83 to 82.53)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: approximately 24 months	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups	
Reporting group title	JNJ-63623872 Placebo BID + Oseltamivir Placebo BID
Reporting group description: Subjects received JNJ-63623872 matching placebo tablets and oseltamivir matching placebo capsule orally, twice daily (BID) with approximately 12 hour intervals, over 5 days.	
Reporting group title	JNJ-63623872 300 mg BID + Oseltamivir Placebo BID
Reporting group description: Subjects received JNJ-63623872 300 mg tablets along with matching placebo capsule of oseltamivir orally BID with approximately 12 hour intervals, over 5 days.	
Reporting group title	JNJ-63623872 600 mg BID + Oseltamivir Placebo BID
Reporting group description: Subjects received JNJ-63623872 600 mg tablets (2 * 300-mg tablets) along with matching placebo capsule of oseltamivir orally BID with approximately 12 hour intervals, over 5 days.	
Reporting group title	JNJ-63623872 600 mg BID + Oseltamivir 75 mg BID
Reporting group description: Subjects received JNJ-63623872 600 mg tablets (2 * 300-mg tablets) along with 75 mg oseltamivir capsule orally BID with approximately 12 hour intervals, over 5 days.	

Serious adverse events	JNJ-63623872 Placebo BID + Oseltamivir Placebo BID	JNJ-63623872 300 mg BID + Oseltamivir Placebo BID	JNJ-63623872 600 mg BID + Oseltamivir Placebo BID
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 71 (1.41%)	0 / 74 (0.00%)	1 / 74 (1.35%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	0 / 71 (0.00%)	0 / 74 (0.00%)	1 / 74 (1.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Thrombocytopenia			

subjects affected / exposed	1 / 71 (1.41%)	0 / 74 (0.00%)	0 / 74 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	JNJ-63623872 600 mg BID + Oseltamivir 75 mg BID		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 73 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	0 / 73 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	0 / 73 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	JNJ-63623872 Placebo BID + Oseltamivir Placebo BID	JNJ-63623872 300 mg BID + Oseltamivir Placebo BID	JNJ-63623872 600 mg BID + Oseltamivir Placebo BID
Total subjects affected by non-serious adverse events			
subjects affected / exposed	14 / 71 (19.72%)	22 / 74 (29.73%)	30 / 74 (40.54%)
Investigations			
Blood Creatine Phosphokinase Increased			
alternative assessment type: Systematic			
subjects affected / exposed	4 / 71 (5.63%)	2 / 74 (2.70%)	1 / 74 (1.35%)
occurrences (all)	5	2	1
Blood Glucose Increased			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 71 (0.00%)	0 / 74 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	1	1
Haemoglobin Decreased			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 71 (0.00%)	1 / 74 (1.35%)	0 / 74 (0.00%)
occurrences (all)	0	2	0
Glomerular Filtration Rate Decreased			
subjects affected / exposed	2 / 71 (2.82%)	4 / 74 (5.41%)	1 / 74 (1.35%)
occurrences (all)	2	4	1
Neutrophil Count Decreased			
subjects affected / exposed	0 / 71 (0.00%)	1 / 74 (1.35%)	4 / 74 (5.41%)
occurrences (all)	0	1	4
Nervous system disorders			
Dizziness			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 71 (0.00%)	0 / 74 (0.00%)	2 / 74 (2.70%)
occurrences (all)	0	0	2
Headache			
subjects affected / exposed	0 / 71 (0.00%)	2 / 74 (2.70%)	1 / 74 (1.35%)
occurrences (all)	0	2	1
Gastrointestinal disorders			
Abdominal Pain Upper			
subjects affected / exposed	0 / 71 (0.00%)	0 / 74 (0.00%)	2 / 74 (2.70%)
occurrences (all)	0	0	2
Diarrhoea			
subjects affected / exposed	4 / 71 (5.63%)	5 / 74 (6.76%)	20 / 74 (27.03%)
occurrences (all)	4	5	21
Nausea			
subjects affected / exposed	0 / 71 (0.00%)	3 / 74 (4.05%)	3 / 74 (4.05%)
occurrences (all)	0	5	3
Vomiting			
subjects affected / exposed	0 / 71 (0.00%)	1 / 74 (1.35%)	3 / 74 (4.05%)
occurrences (all)	0	1	4
Psychiatric disorders			
Insomnia			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 71 (0.00%)	2 / 74 (2.70%)	1 / 74 (1.35%)
occurrences (all)	0	2	1
Renal and urinary disorders			
Proteinuria			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 71 (1.41%)	3 / 74 (4.05%)	0 / 74 (0.00%)
occurrences (all)	1	3	0
Infections and infestations			
Bronchitis			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 71 (2.82%)	1 / 74 (1.35%)	0 / 74 (0.00%)
occurrences (all)	4	1	0
Sinusitis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 71 (0.00%)	1 / 74 (1.35%)	0 / 74 (0.00%)
occurrences (all)	0	3	0
Metabolism and nutrition disorders			
Hyperglycaemia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 71 (0.00%)	0 / 74 (0.00%)	2 / 74 (2.70%)
occurrences (all)	0	0	2
Hyperkalaemia			
subjects affected / exposed	1 / 71 (1.41%)	0 / 74 (0.00%)	2 / 74 (2.70%)
occurrences (all)	1	0	2
Hypokalaemia			
subjects affected / exposed	2 / 71 (2.82%)	0 / 74 (0.00%)	0 / 74 (0.00%)
occurrences (all)	2	0	0
Hypophosphataemia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 71 (0.00%)	2 / 74 (2.70%)	0 / 74 (0.00%)
occurrences (all)	0	2	0

Non-serious adverse events	JNJ-63623872 600 mg BID + Oseltamivir 75 mg BID		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	26 / 73 (35.62%)		

Investigations			
Blood Creatine Phosphokinase Increased			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 73 (4.11%)		
occurrences (all)	3		
Blood Glucose Increased			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 73 (2.74%)		
occurrences (all)	2		
Haemoglobin Decreased			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 73 (0.00%)		
occurrences (all)	0		
Glomerular Filtration Rate Decreased			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences (all)	1		
Neutrophil Count Decreased			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences (all)	1		
Nervous system disorders			
Dizziness			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences (all)	1		
Headache			
subjects affected / exposed	2 / 73 (2.74%)		
occurrences (all)	2		
Gastrointestinal disorders			
Abdominal Pain Upper			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences (all)	1		
Diarrhoea			
subjects affected / exposed	13 / 73 (17.81%)		
occurrences (all)	13		
Nausea			

subjects affected / exposed	8 / 73 (10.96%)		
occurrences (all)	9		
Vomiting			
subjects affected / exposed	6 / 73 (8.22%)		
occurrences (all)	6		
Psychiatric disorders			
Insomnia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 73 (0.00%)		
occurrences (all)	0		
Renal and urinary disorders			
Proteinuria			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 73 (0.00%)		
occurrences (all)	1		
Infections and infestations			
Bronchitis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 73 (0.00%)		
occurrences (all)	0		
Sinusitis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 73 (0.00%)		
occurrences (all)	0		
Metabolism and nutrition disorders			
Hyperglycaemia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 73 (0.00%)		
occurrences (all)	1		
Hyperkalaemia			
subjects affected / exposed	0 / 73 (0.00%)		
occurrences (all)	0		
Hypokalaemia			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences (all)	1		
Hypophosphataemia			

alternative assessment type: Systematic subjects affected / exposed occurrences (all)	 0 / 73 (0.00%) 0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 October 2014	This amendment included the following changes: changes made in response to the Food and Drug Administration feedback, including further definition of subject self assessment timing; clarification of reasons for and recording of antipyretic treatment, inclusion of a urinalysis sample on Day 3; modification of the analysis plan to include an analysis of the primary efficacy variable on the intent-to-treat (ITT) population as a secondary endpoint and some minor editorial changes, corrections, and clarifications.
29 January 2015	This amendment included the following changes: clarification of inclusion criteria and exclusion criteria, prior and concomitant medications, and withdrawal of subjects; removal of the following exclusion criteria: immunized (intranasal or injected vaccine) against influenza in the 6 months before the study; incorporation of changes made to initiate the treatment part of this study (Part B) in a clinic; addition of an interim analysis and some minor editorial changes, corrections, and clarifications.
16 June 2015	This amendment included the following changes: Incorporation of changes made to streamline the study by removing surveillance (Part A) and including additional testing for screen failures, to refine inclusion/exclusion criteria and to modify language regarding duration of the study to reflect the extension of the study into another season of influenza in the Northern Hemisphere; addition of assessment for confirmation of influenza A per rapid influenza diagnostic test (RIDT) following informed consent. Sites were instructed to take 2 images of each positive RIDT and to file the images as source documents; clarification that all subjects who signed informed consent had to have a virology assessment on their nasopharyngeal (NP) swab, irrespective of enrollment for treatment; exclusion of nasal steroid medications; clarification that screen failures had to undergo virology testing from NP swabs; clarification of the type and use of antipyretic and anti-inflammatory medications allowed; expansion of study duration from 5 to 18 months to obtain desired enrollment of approximately 500 subjects and some minor editorial changes, corrections, and clarifications.
04 April 2016	This amendment included the following changes: Incorporation of changes made to the primary objective from an evaluation of symptom relief to an effect on viral activity. This led to a change in the primary endpoint to viral area under the curve (AUC), and to clinical symptoms becoming the key secondary endpoint. Analytical details were updated accordingly, specifying the dose-response relation of viral AUC following administration of JNJ 63623872 as primary analysis, as well as updating the analysis of the key secondary endpoint. A formal interim analysis was also added at the end of the 2015 2016 Northern Hemisphere season. The intention was to recruit the full 500 planned subjects, unless at the time of the interim analysis a statistically significant positive dose response relationship was concluded. Addition of a potential extension to a second Southern Hemisphere season and the associated increased study duration and some minor editorial changes, corrections, and clarifications.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Early study stop has reduced the probability to detect statistically significant differences for the secondary endpoints and a separate oseltamivir treatment arm to measure the effect of oseltamivir alone was lacking in the study design.

Notes: