A Phase 2, Randomized, Double-blind, Placebo-controlled Study to Evaluate the Pharmacokinetics, Safety, and Antiviral Activity of JNJ-63623872 in Combination With Oseltamivir in Adult and Elderly Hospitalized Patients With Influenza A Infection

Published: 12-10-2015
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The primary objective is to evaluate the pharmacokinetic (PK) parameters of JNJ-63623872 in combination with oseltamivir in elderly subjects (aged 65 to *85 years) compared to adults (aged 18 to *64 years) with influenza A infection.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Viral infectious disorders
Study type	Interventional

Summary

ID

NL-OMON46300

Source
ToetsingOnline

Brief title
OPAL (glObal hosPital InfluenzA triaL)

Condition

- Viral infectious disorders

Synonym
flu, Influenza A

Research involving
Human

Sponsors and support

Primary sponsor: Janssen-Cilag
Source(s) of monetary or material Support: Janssen-Cilag BV

Intervention

Keyword: JNJ-63623872, Oseltamivir

Outcome measures

Primary outcome

The primary objective is to evaluate the pharmacokinetic (PK) parameters of

JNJ-63623872 in

combination with oseltamivir in elderly subjects (aged 65 to *85 years)

compared to adults (aged 18 to *64 years) with influenza A infection.

Secondary outcome

Secondary objectives include the assessment of the following parameters in the

JNJ-63623872

treatment arm compared to the control arm:

1. Safety and tolerability.

2. The time to influenza viral negativity based on quantitative reverse

transcription polymerase

chain reaction (qRT-PCR) and/or viral culture from nasal mid-turbinate (MT)

swabs and, if

applicable, based on PCR-based rapid molecular testing from nasal MT swabs.

3. Viral load over time and rate of decline in viral load during treatment as measured by qRTPCR and/or by viral culture.

4. Area under the curve (AUC) of viral load as measured by qRT-PCR and/or by viral culture.

5. Disease status and incidence of complications associated with influenza after the start of study treatment, and disease progression:

o bacterial pneumonia (culture confirmed where possible),

o other bacterial superinfections,

o respiratory failure,

o pulmonary disease (eg, asthma, chronic obstructive pulmonary disease [COPD]),

o cardiovascular and cerebrovascular disease (eg, myocardial infarction, congestive heart failure [CHF], arrhythmia, stroke).

6. Change in duration and severity of clinical symptoms as measured by the Flu-PRO.

7. Time to improvement of vital signs.

8. Time to improvement of respiratory status.

9. Emergence of drug resistance as detected by genotype or phenotype.

10. Time to return to premorbid functional status.

11. Time to hospital discharge.

12. Hierarchal ordinal scale for clinical outcome

Study description

Background summary

Both seasonal and pandemic influenza are a significant cause of morbidity and mortality worldwide. For example, the 2009 H1N1 influenza pandemic in the United States was responsible for an estimated 60.8 million cases, 274,000 hospitalizations, and over 12,400 deaths.8 Because the efficacy of the current annual hemagglutinin-based or modified live influenza virus vaccines depends on accurately predicting the viral strains prior to each influenza season or pandemic, there exists an unmet need for new antiviral agents that are broadly effective.

Study objective

The primary objective is to evaluate the pharmacokinetic (PK) parameters of JNJ-63623872 in combination with oseltamivir in elderly subjects (aged 65 to *85 years) compared to adults (aged 18 to *64 years) with influenza A infection.

Study design

This is a randomized, double-blind, placebo-controlled, multicenter Phase 2 study to evaluate the effect of JNJ-63623872 600 mg twice daily (bid) versus (vs.) placebo, both in combination with oseltamivir 75 mg bid in adult and elderly hospitalized subjects with influenza A
infection. Up to 90 subjects in total will be enrolled in this study.
Recruitment will be limited to a single northern hemisphere influenza season.

The study will consist of a screening/baseline visit, a double-blind treatment period of 7 days, and a follow-up period of 21 days. The entire study duration for each subject will be 28 days with study assessments daily during the treatment period, and on Days 10, 14, and 28 of the follow-up period. The study is considered complete with the completion of the last study assessment for the last subject participating in the study.

Intervention

Subjects who meet all eligibility criteria will be randomized in a 2:1 ratio to receive 1 of the following 2 treatments:
* JNJ-63623872 600 mg bid + oseltamivir 75 mg bid; OR
* JNJ-63623872 placebo bid + oseltamivir 75 mg bid
All study drugs will be taken orally.

Study burden and risks

Admission to the hospital is a requirement for participation, but is already part of the proposed standard of care. If participant is able to leave the hospital early, daily follow-up by phone by the investigator in the first week. Every call lasts about 15 minutes.

All drugs can cause side effects. Since JNJ-63623872 has only been given to a small number of people, not all possible side effects and risks related to JNJ-63623872 are known. Problems that are not expected may arise and they may be life-threatening. If you have any side effects or problems during your participation in this study, you should let your study doctor know right away.

All medications might have adverse events, known or unknown. In general, JNJ-63623872 has been well tolerated so far. Known adverse events are headache, diarrhoea, higher blood values of liver enzymes, lower phosphate levels in the blood. It is possible you might experience these effects. Please tell you investigator immediately if this is the case. This is regardless of the fact if you think this is related to the treatment or not.

Advantages
JNJ-63623872 may have a possible positive effect on the treatment of your flu, or making the syproms easier. It is however not sure you will experience a personal benefit. Your flu symptoms can remain the same or worsen.
The information which will be collected by this research can contribute to more knowledge about the use of JNJ-63623872 and to further developemtn for a new treatment against flu.

Disadvantages
You might experience a disadvantage because of the extra time commitment you will make during participation, additional visits and/or assessments. Please respect the guidelines of the trial. You might experience adverse events from JNJ-63623872 or from the planned assessments.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Participant requires hospitalization to treat influenza infection and/or to treat complications of influenza infection
- Participant tested positive for influenza A infection within 1 day of signing of the informed consent form (ICF)/assent form using a polymerase chain reaction (PCR)-based rapid molecular diagnostic assay
- Participants must be capable of swallowing study medication tablets and capsules
- Each participant (or their legally acceptable representative) must sign an ICF indicating that he or she understands the purpose of and procedures required for the study and is willing to participate in the study
- Participant must be willing and able to adhere to the prohibitions and restrictions specified in the protocol

Exclusion criteria

- Participant received more than 3 doses of the influenza antiviral medication oseltamivir, zanamivir, or peramivir since the start of the influenza symptoms, or ribavirin within 6 months prior to Screening
- Participant is unwilling to undergo regular nasal Mid-turbinate (MT) swabs or has any physical abnormality which limits the ability to collect regular nasal specimens
- Participant is immunocompromised, whether due to underlying medical condition (example, malignancy) or medical therapy (example, medications, chemotherapy, radiation, post-transplant)
- Participant is undergoing peritoneal dialysis, hemodialysis, or hemofiltration

- Participant has an estimated glomerular filtration rate (eGFR) less than or equal to (<=)30 milliliter (mL)/minute (min)/1.73 meter^2 (m^2) according to the Modification of Diet in Renal Disease (MDRD) equation, assessed at Screening or based on the most recent clinically relevant creatinine value if available

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	14-01-2017
Enrollment:	5
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	JNJ-63623872
Generic name:	/
Product type:	Medicine
Brand name:	Tamiflu
Generic name:	oseltamivir phosphate
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	12-10-2015
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	20-01-2016
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	09-02-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	07-03-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	14-07-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	26-07-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	16-08-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO	

Date:	15-09-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	13-10-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	16-11-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	16-01-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	13-02-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	22-03-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2015-003002-17-NL
ClinicalTrials.gov	NCT02532283;CR107746
CCMO	NL55154.078.15