NAI114373: A Phase III international, randomized, doubleblind, double-dummy study to evaluate the efficacy and safety of 300 mg or 600 mg of intravenous zanamivir twice daily compared to 75 mg of oral oseltamivir twice daily in the treatment of hospitalized adults and adolescents with influenza (NAI114373)

Published: 17-12-2010
Last updated: 04-05-2024

Primary: To assess the efficacy of treatment with 300 mg or 600 mg of intravenous (IV) zanamivir twice daily compared to 75 mg of oral oseltamivir twice daily on time to clinical response. Secondary: reduction in viral load from nasopharyngeal swabs...

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

Summary

ID

NL-OMON36811

Source
ToetsingOnline

Brief title
NAI114373

Condition

- Viral infectious disorders

Synonym
flu, influenza

Research involving
Human

Sponsors and support

Primary sponsor: GlaxoSmithKline
Source(s) of monetary or material Support: GlaxoSmithKline BV

Intervention

Keyword: influenza, parenteral, treatment, zanamivir

Outcome measures

Primary outcome

Time to clinical response in subjects with confirmed influenza.

Secondary outcome

Include a series of clinical efficacy, virologic, PK and safety endpoints.

Study description

Background summary

Neuraminidase inhibitors have been shown to be effective and well tolerated in the treatment and prophylaxis of acute uncomplicated seasonal influenza and are available as inhaled zanamivir and oral oseltamivir. An unmet medical need exists for a parenteral formulation.
Emergence of virus isolates resistant to influenza antiviral agents continues to be a potential issue. As of September 2010, 304 cases of oseltamivir-resistant isolates of the pandemic H1N1 2009 virus have been reported. All but one of these isolates have been identified to carry the H275Y mutation and thus remain sensitive to zanamivir. Virtually 100% of seasonal influenza A (H1N1) isolates tested during the 2008-2009 influenza season were resistant to oseltamivir. In addition, sporadic cases of resistance to oseltamivir have also been reported in H5N1 infection. Thus far, these isolates have been reported to remain susceptible to zanamivir.
The purpose of this Phase III study is to obtain comprehensive data on the clinical efficacy, antiviral activity, and safety of 2 dosages of IV zanamivir

relative to oral oseltamivir in adults and adolescents hospitalized with influenza infection.
In the Netherlands no minors will be included.

Study objective

Primary: To assess the efficacy of treatment with 300 mg or 600 mg of intravenous (IV) zanamivir twice daily compared to 75 mg of oral oseltamivir twice daily on time to clinical response. Secondary: reduction in viral load from nasopharyngeal swabs, clinical improvement, safety and tolerability, development of resistance, PK.

Study design

Multicenter randomized double blind double dummy phase III parallel group study.
Randomization (1:1:1) to treatment with:
• Zanamivir 300 mg i.v. infusion (30 minutes) twice daily.
• Zanamivir 600 mg i.v. infusion (30 minutes) twice daily.
• Oseltamivir 75 mg orally twice daily.
Treatment duration 5-10 days.
In case of insufficient clinical response, patients may be switched to 600 mg IV zanamivir twice daily, leading to a maximum treatment duration of 14 days.
Follow-up until 4 weeks post-treatment.
Interim-analysis after 150 patients have completed the study.
IDMC.
Approx 460 patients.
In the Netherlands no minors will be included.

Intervention

Treatment with zanamivir or oseltamivir.

Study burden and risks

Risk: Adverse effects of study medication.
Burden: At study start all patients are hospitalized for medical reasons. Depending on the moment of discharge, there are max. 3 visits to the outpatient clinic and 7 phone contacts.
Tests/procedures: blood tests (2-20 ml/occasion) daily during study treatment and max. 4x thereafter. Pregnancy test (if indicated) 2x, nose swab during study treatment: 1st 5 days: daily, thereafter every 2nd day. ECG 4x.

Contacts

Public
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Scientific
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

• Male or female aged >=16 years (in the Netherlands: 18 years and above).
• 3 or more of the following criteria at Baseline:
o Temperature >= 38,5oC rectal (alternative methods: see protocol) with 2 exceptions (see protocol for details).
o Arterial oxygen saturation <95%.
o Respiration rate >24 breaths per minute.
o HR >100 bpm.
o SBP <90 mmHg.
• Onset of influenza symptoms within 6 days prior to study enrolment.
• Confirmed influenza as determined by a positive RAT for influenza A or B, or a laboratory test for influenza. Subjects with a negative RAT or other test may be enrolled based on strong clinical suspicion of influenza.

• Safe contraception for women of childbearing potential.

Exclusion criteria

• Breastfeeding, pregnancy.
• Subjects who have taken more than a total of 6 doses of approved anti-influenza therapy.
• Life expectancy less than 48 hours.
• Treatment with investigational parenteral anti-influenza drugs in the 4 weeks prior to Baseline.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	16-01-2013
Enrollment:	8
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Relenza
Generic name:	zanamivir
Registration:	Yes - NL outside intended use
Product type:	Medicine

Brand name:	Tamiflu
Generic name:	oseltamivir
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	17-12-2010
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	24-03-2011
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	28-03-2011
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	10-10-2011
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	18-11-2011
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	12-04-2012
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	09-08-2012
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	23-05-2013

Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	13-03-2014
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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
Other	clinicaltrials.gov, registratienummer n.n.b.
EudraCT	EUCTR2010-021621-12-NL
CCMO	NL34832.091.10