A randomised controlled trial on the effectiveness of post-exposure prophylaxis (PEP) with oseltamivir in preventing influenza transmission in nursing home units

Published: 01-09-2009
Last updated: 04-05-2024

If proven (cost)effective, without inducing antivral resistance, oseltamivir could have considerable benefits in this setting, although constraints relating to implementation need to be addressed as well. If not (cost)effective if this fragile...

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

Summary

ID

NL-OMON33181

Source
ToetsingOnline

Brief title
RCT oseltamivir PEP nursing homes

Condition

- Viral infectious disorders
- Respiratory tract infections

Synonym
flu, influenza like illness (ILI)

Research involving
Human

Sponsors and support

Primary sponsor: RIVM
Source(s) of monetary or material Support: ZonMw;RIVM

Intervention

Keyword: Influenza transmission, nursing home network, oseltamivir, post-exposure prophylaxis

Outcome measures

Primary outcome

Transmission, the primary trial outcome measurement, is defined as a newly laboratory confirmed influenza in the same unit 12 hours or more after the start of PEP.

Assuming 30 homes participate, that annually 30% of nursinghomes experience a confirmed influenza outbreak in on average two units, than we can recruit 20 units per season. Assuming that without effective prophylaxis ongoing transmission occurs in 40% of the units, we will have at least 80% power after 3 seasons with a two-sided alpha=0.05 to demonstrate a reduction in transmission of 70%.

Secondary outcome

This trial offers an excellent opportunity to evaluate the possible emergence of resistance against oseltamivir if used under such circumstances, by analysing the occurrence of viral mutations under oseltamivir therapy (for index- and for any secondary cases). In addition, we will assess the relative cost-effectiveness of PEP with oseltamivir per nursing home unit, compared to not using PEP by prospectively collecting information on the number of influenza infections and related complications, duration of symptoms, use of

medical services by secondary cases, as well as sickness leave of staff.

Finally, potential ethical and logistical restrictions for the large scale use

of oseltamivir will be documented prospectively

Study description

Background summary

The incidence of severe morbidity and mortality following an influenza infection during the annual influenza epidemics is highest among the elderly population and 90% of influenza-associated mortality occurs in this group. Vaccination is considered the best preventive intervention available but offers only partial protection. The protective effect decreases with advancing age and existing co-morbidity. Therefore, in spite of high compliance with vaccination, the risk of influenza-related complications among nursing-home residents, is particularly high, and consequently also the associated disease and economic burden. There is debate on the potential health benefit of the antiviral activity of oseltamivir as an effective supplementary intervention to prevent or contain influenza outbreaks in nursing homes. Although effectiveness of post-exposure prophylaxis (PEP) with oseltamivir on preventing transmission has been demonstrated in trials among healthy (mainly unvaccinated) adults and children, effectiveness has not yet been assessed among vulnerable vaccinated high-risk groups, such as the elderly population in nursing homes. If proven (cost)effective, oseltamivir could have considerable benefits in this setting, although constraints relating to implementation need to be addressed as well.

Study objective

If proven (cost)effective, without inducing antivral resistance, oseltamivir could have considerable benefits in this setting, although constraints relating to implementation need to be addressed as well.
If not (cost)effective if this fragile population, resources can be better spent on other activities to support nursing home residents.

Study design

A randomised controlled trial on the effect of PEP with oseltamivir on transmission of influenza in nursing homes, linked to virological monitoring of possible development of resistance and impact on transmission and outcome, a cost effectiveness analysis, and an exploration of logistical and ethical issues which could interfere with successful implementation.

Intervention

Post-exposition prophylaxis with oseltamivir or placebo.
Once laboratory confirmation has been obtained in an index case, all residents and staff of that implicated unit only will be randomly assigned to PEP with either oseltamivir or placebo for 10 days. Data on co-morbidity, medication and other potential confounders for susceptibility to a clinical influenza infection will be collected prior to the start of PEP. The index patient (and any secondary patients) will be treated therapeutically with oseltamivir.

Study burden and risks

Burden and risks of this trial will be minimal, as we will not deviate from current standing practices, in which some nursing homes offer PEP and others don't, following the diagnosis of influenza on a unit.

Contacts

Public
RIVM

Postbus 1
3720 BA Bilthoven
NL
Scientific
RIVM

Postbus 1
3720 BA Bilthoven
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age

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

Inclusion criteria

The unit of randomisation will be nursing home units in nursing homes willing to participate, and where virologically confirmed influenza is diagnosed in an index case. In these units, all residents (apart from the index case(s)) and staff are eligible for randomisation to PEP with oseltamivir or PEP with placebo.

Exclusion criteria

No consent, medical contra-indication to oseltamivir.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Health services research

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-07-2010
Enrollment:	4000
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Tamiflu

Generic name:	oseltamivir
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	01-09-2009
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	20-10-2009
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	04-11-2009
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	20-05-2011
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	15-10-2012
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

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	2006-000749-21
EudraCT	EUCTR2006-000749-21-NL
CCMO	NL27938.041.09