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Antivirals for influenza-like illness? Are they effective?

Submission date
21/10/2015

Recruitment status
No longer recruiting

Registration date
22/10/2015

Overall study status
Completed

Last Edited
18/11/2024

Condition category
Infections and Infestations

[X] Prospectively registered

[X] Protocol

[_] Statistical analysis plan

[X] Results

[_] Individual participant data

Plain English summary of protocol

Background and study aims
Influenza, also known as the flu, is caused by a common virus which attacks the nose, throat, sinuses and lungs (respiratory system). Sufferers usually also experience a high temperature (fever), aching muscles and tiredness, as their bodies work to fight the infection. Most people are able to recover from the flu within one or two weeks, as their immune systems are able to destroy the virus. However, in the very young, the elderly and those with pre-existing serious medical conditions, the flu can lead to serious complications and even death. These “at risk” people are routinely offered vaccinations (flu jab) to help prevent the flu, and anti-viral medicines such as oseltamivir (Tamiflu), to help their bodies to fight the flu virus. There are many other viruses which cause symptoms similar to the flu, and are known as influenza-like illnesses (ILI). Currently, there is no way of quickly testing whether someone with influenza-like illness actually has real flu. Current treatment options such as Tamiflu seem to work best when real flu is present, and so more effective ways of targeting flu treatment are needed. This study aims to find out whether adding antiviral treatment to best usual primary care is effective in reducing the time it takes for a person to return to usual daily activity. The study also aims to look at the link between the virus that a person is suffering from and the effectiveness of the antiviral treatment.

Who can participate?
All patients over one year old, who are experiencing a flu-like illness.

What does the study involve?
Participants are randomly allocated to one of two groups. Those in the first group receive standard care from their doctor (best primary care), such as advice about looking after themselves by drinking plenty of fluids and resting. Those in the second group receive the standard care from their doctor but are also given a dose of oseltamivir (Tamiflu) for a period of five days. Participants in both groups are asked to fill in a diary for two weeks so that their symptoms can be recorded. At day 14 and day 28, participants receive a follow-up phone call to find out whether their symptoms are gone and they are back to normal. Additionally, a group of participants will have a swab taken at the start of the study so that the virus they are suffering from can be identified in the lab to find out whether the anti-viral treatment works better for real flu or ILI.

What are the possible benefits and risks of participating?
There are no direct benefits for participants taking part in this study. There are some risks involved with taking Tamiflu, such as headache and nausea (feeling sick), however these will be closely monitored.

Where is the study run from?
25 health centres in England and Wales (UK) and 15 other European countries.

When is the study starting and how long is it expected to run for?
December 2015 to March 2018

Who is funding the study?
European Commission's Seventh Framework Programme (Belgium)

Who is the main contact?
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Contact information

Type(s)
Public

Contact name
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Additional identifiers

EudraCT/CTIS number
2014-004471-23

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
19749

Study information

Scientific Title
Antivirals for influenza-Like Illness? An rCt of Clinical and Cost effectiveness in primary CarE (ALIC4E)

Acronym
ALIC4E

Study objectives
The aim of this study is to determine whether adding antiviral treatment to best usual primary care is effective in reducing time to return to usual daily activity.

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. UK: South Central - Oxford B Research Ethics Committee, 31/03/2015, ref: 15/SC/0138
2. Netherlands: METC UMC Utrecht, 23/12/2015, ref: 15-420
3. Greece: Scientific Council, 10/11/2015, ref: 8829
4. Lithuania: Lithuanian Bioethics Committee, Vilnius, 21/09/2015, ref: P-15-73
5. Ireland: Tallaght Hospital / St. James's Hospital Joint Research Ethics Committee (REC), 07/10/2015, ref: 2015-09-LIST35 (2)
6. Switzerland: Ethikkommission Nordwest- und Zentralschweiz (EKNZ), 09/12/2015, ref: EKNZ 2015-232
7. France: Comité de Protection des Personnes Sud-Mediterannee V, 09/09/2015, ref: 15.068
8. Sweden: Regionala Etikprövningsnämnden i Göteborg, 29/09/2015
9. Belgium: Ethisch comité UZA, 17/08/2015, ref: 15/27/283
10. Spain: Hospitla Clinic Barcelona, 15/12/2015, ref: HCB/2015/0854
11. Denmark: De Videnskabsetiske Komiteer, 05/11/2016, ref: H-15009261
12. Poland: Komisja Bioetyczna przy Uniwersytecie Medycznym w Łodzi, 06/06/2015, ref: RNN/227/15/KE
13. Poland: Komisja Bioetyczna przy Uniwersytecie Medycznym w Bialymstoku, 24/09/2015, ref: R-I-002/316/2015
14. Norway: Regionale komiteer for medisinsk og helsefaglig forskningsetikk Sør-Øst, 24/06/2015, ref: 2015/932/REK
15. Hungry: Medical Research Council, Ethics Committee For Clinical Pharmacology, 06/08/2015, ref: OGYI/23427-8/2015
16. Czech Republic: Ethics Committee of the General Hospital, Prague, 12/12/2015, ref: 2354/15 S-MEK

Study design
Randomised; Interventional; Design type: Treatment

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Other

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details to request a patient information sheet

Health condition(s) or problem(s) studied
Influenza-like illness

Interventions
Participants are randomly allocated to one of two groups.

Group 1: Participants in the first group are given best primary care (standard practice)
Group 2: Participants in the first group are given oseltamivir in the standard dose for their age for five days, as well as best primary care (standard practice)

Participants in both groups are asked to complete a 2 week symptom diary and will receive follow up phone calls at days 2--4, 14--28 and after day 28.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Oseltamivir

Primary outcome measure
Time to return to usual activity is determined using a symptom diary recorded between day 1-14 and a telephone call on days 14 and 28.

Secondary outcome measures
1. Cost effectiveness measures through health resource use and EQ-5D-5L - completed by the patient on Days 1-14
2. Number of hospital admissions, collected in a patient symptom diary on day 14 and day 28
3. Attendance hospital emergency care, or Out of Hours (OOH) centres with symptoms or complications and the reasons for them and the basis for diagnosis, such as pneumonia collected in the patient diary on days 1-14
4. Attendance at GP Practice, hospital emergency care, or Out of Hours (OOH) centres with ILI symptoms collected in the patient diary on days 1-14
5. Time to alleviation of ILI symptoms, measured using symptom scoring and VAS on days 1-14
6. Incidence of new or worsening symptoms measured using symptom scoring and VAS on days 1-14
7. Report of time to onset of symptom relief measured using symptom scoring and VAS on days 1-14
8. Duration of moderately severe or worse symptoms measured using symptom scoring and VAS

on days 1-14
9. Use of over-the-counter medications and prescription medications, including antibiotics collected in symptom diary through direct questioning on days 1-14
10. Report of new cases if ILI within household collected in symptom diary through direct questioning on days 1-14
11. Patient reported self-management, medication use, rest and activity collected in symptom diary through direct questioning on days 1-14
12. Analysis of benefit according to age, illness duration, severity and co-morbidity measured is recorded using the patient symptom diary on days 1-14 and through a telephone interview on days 14 and 28

Overall study start date
01/02/2014

Completion date
31/01/2019

Eligibility

Key inclusion criteria
1. Aged at least one year old
2. Presenting with influenza-like illness* in primary care during a period of increased influenza activity.
3. Is able and willing to comply with all trial requirements
4. Participant or legal guardian(s) of a child is willing and able to give informed consent
5. Agrees not to take antiviral agents apart from study antiviral agents according to patient randomisation

*Sudden onset of self reported fever, with at least one respiratory symptom (cough, sore throat, running or congested nose) and one systematic symptom (headache, muscle ache, sweats or chills or tiredness), with a symptom duration of 72 hours or less.

Participant type(s)
Patient

Age group
Mixed

Sex
Both

Target number of participants
Planned Sample Size: 675; UK Sample Size: 675. 464 participants were recruited in the UK and 3266 worldwide.

Total final enrolment
464

Key exclusion criteria

1. Chronic renal failure e.g. known (recorded in GP clinical records) or estimated creatinine glomerular filtration rate of less than 60 mg/L
2. Condition or treatment associated with significant impaired immunity (e.g. long-term oral steroids, chemotherapy, or
immune disorder)
3. Those who in the opinion of the responsible clinician should be prescribed immediate antiviral treatment
4. Allergic to oseltamivir, or any other trial medication
5. Scheduled elective surgery or other procedures requiring general anaesthesia during the subsequent two weeks
6. Participant with life expectancy estimate by a clinician to be less than 6 months
7. Patient with severe hepatic impairment
8. Responsible clinician considers urgent hospital admission is required
9. Any other significant disease or disorder which, in the opinion of the responsible clinician, may either put the participants at risk because of participation in the trial, or may influence the result of the trial, or may affect the participant's ability to participate in the trial
10. Involvement, including completion of any follow up procedures, in another clinical trial of an investigational medicinal product in the last 90 days
11. Previous ALIC4E trial participation
12. Patients unable to be randomised within 72 hours after onset of symptoms
13. Requirement for any live viral vaccine in the next 7 days

Date of first enrolment
01/12/2015

Date of final enrolment
13/04/2018

Locations

Countries of recruitment
Belgium

Croatia

Czech Republic

Denmark

England

France

Greece

Hungary

Ireland

Lithuania

Netherlands

Norway

Poland

Spain

Sweden

Switzerland

United Kingdom

Wales

Study participating centre
Windrush Health Centre
Welch Way
Witney
United Kingdom
OX28 6JS

Study participating centre
South Oxford Health Centre
Lake Street
Oxford
United Kingdom
OX1 4RP

Study participating centre
Wokingham Medical Centre
23 Rose Street
Wokingham
United Kingdom
RG40 1XS

Study participating centre
Aston Clinton Surgery
136 London Road
Aston Clinton

Aylesbury
United Kingdom
HP22 5LB

Study participating centre
Eynsham Medical Practice
Conduit Lane
Eynsham
Witney
United Kingdom
OX29 4QB

Study participating centre
Didcot Health Centre
Britwell Road
Didcot
United Kingdom
OX11 7JH

Study participating centre
White Horse Medical Practice
Volunteer Way
Faringdon
United Kingdom
SN7 7YU

Study participating centre
The Boathouse Surgery
Whitchurch Road
Pangbourne
Reading
United Kingdom
RG8 7DP

Study participating centre
Yorkley Health Centre
Bailey Hill
Yorkley
Lydney
United Kingdom
GL15 4RS

Study participating centre
Portland Practice
St Paul's Medical Centre
121 Swindon Road
Cheltenham
United Kingdom
GL50 4DP

Study participating centre
London Medical Practice
Aspen Centre
Horton Road
Gloucester
United Kingdom
GL1 3PX

Study participating centre
Forest End Surgery
Forest End
Waterlooville
United Kingdom
P07 7AH

Study participating centre
Wareham Surgery
Streche Road
Wareham
United Kingdom
BH20 4PG

Study participating centre
Cowplain Practice
30 London Road
Cowplain
Waterlooville
United Kingdom
PO8 8DL

Study participating centre
Chawton Park Surgery
Chawton Park Road
Alton
United Kingdom
GU34 1RJ

Study participating centre
Bridges Medical Centre
26 Commercial Road
Weymouth
United Kingdom
DT3 6SA

Study participating centre
Three Swans Surgery
Rollestone Street
Salisbury
United Kingdom
SP1 1DX

Study participating centre
Friarsgate Surgery
Stockbridge Road
Winchester
United Kingdom
SO22 6EL

Study participating centre
Clifton Surgery
151-153 Newport Road
Cardiff
United Kingdom
CF24 1AG

Study participating centre
Dinas Powys Medical Centre
75 Cardiff Road
Dinas Powys
United Kingdom
CF64 4JT

Study participating centre
Llandaff and Pentyrch Surgery
19A High Street
Cardiff
United Kingdom
CF5 2DY

Study participating centre
Llandaff North Medical Practice
99 Station Road
Cardiff
United Kingdom
CF14 2FD

Study participating centre
Llanedeyrn Health Centre
Maelfa
Llanedeyrn
Cardiff
United Kingdom
CF23 3PN

Study participating centre
The Practice Of Health
31 Barry Road
Barry
United Kingdom
CF63 1BA

Study participating centre
Waterfront Medical Practice
Heol Y Llongau
Barry
United Kingdom
CF63 4AR

Study participating centre

Huisartsenpraktijk Valk & Meijer
Leusderweg 272
Amersfoort
Netherlands
3817 KJ

Study participating centre
Health Center of Agia Varvara
Agia Varvara Monofatsiou
Crete
Greece
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Study participating centre
Turloughmore Medical Centre
Turloughmore
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Ireland
-

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Praxis Hammer
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Switzerland
CH-4057

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Spitalstrasse 33
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H-4031

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Mouille-Blanc Cécile
43 Avenue Henri Matisse
Nice
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06200

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Närhälsan Ängabo vårdcentral
Sundsbergsvägen 7
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SE-441 50

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Praktijk Sorghvliedt
Lelieplaats 15
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Belgium
2660

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C/ Rosselló 161
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08036

Study participating centre
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Rødovre Centrum
Rødovre
Denmark
2610

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Nygaards alle 4A
Stokke
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38160

Study participating centre
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Kossuth Lajos str. 20
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Hungary
-

Study participating centre
Ordinace PL Karlín, s.r.o.
Šaldova 504/24
Prague
Czech Republic
186 00

Study participating centre
Practice Jelena Stanic
Kauzlaricev prilaz 7
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10 000

Sponsor information

Organisation
University of Oxford

Sponsor details
Research Services
Clinical Trials and Research Governance
Headley Way
Headington
Oxford
England
United Kingdom
OX3 9DU

Sponsor type
Hospital/treatment centre

ROR
https://ror.org/052gg0110

Funder(s)

Funder type
Government

Funder Name
Seventh Framework Programme

Alternative Name(s)
EC Seventh Framework Programme, European Commission Seventh Framework Programme, EU Seventh Framework Programme, European Union Seventh Framework Programme, FP7

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location

Results and Publications

Publication and dissemination plan
Planned publication of a trial protocol in 2018 and a results paper in 2019. Findings of the trial will also be disseminated to all the recruiters and participants involved through flyers at the recruiting GP Practice.

Intention to publish date
30/06/2019

Individual participant data (IPD) sharing plan
The data sharing plans for the current study are unknown and will be made available at a later date.

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Basic results				No	No
Protocol article	protocol	12/07/2018	17/10/2019	Yes	No
Results article	results	04/01/2020	17/12/2019	Yes	No
HRA research summary			28/06/2023	No	No
Other publications	Conditional versus non-conditional incentives to maximise return of participant completed questionnaires in clinical trials: a cluster randomised study within a trial	07/11/2023	18/11/2024	Yes	No