ISRCTN24967173 https://doi.org/10.1186/ISRCTN24967173

Enhancing immunity to influenza in elderly individuals through reversal of immune senescence mediated by herpes virus infection

Submission date 17/08/2011	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol
Registration date 17/08/2011	**Overall study status** Completed	[_] Statistical analysis plan [_] Results
Last Edited 10/05/2018	**Condition category** Respiratory	[_] Individual participant data [_] Record updated in last year

Plain English summary of protocol

Background and study aims
Flu is a major health concern and although flu vaccination is given every year to people over the age of 65, a lot of people have a poor immune response to the vaccine. It is now clear that one reason why older people can develop problems with their immune system (the body's protection mechanism to defend against microbes, bacteria and viruses) is that they carry chronic viral infections such as cytomegalovirus (CMV). The immune system has to work very hard to control these infections and this diverts them away from new infections such as flu. We propose to use drugs that fight viruses, known as antiviral drugs (often used to treat diseases such as cold sores), to lessen the strength of CMV and therefore allow the immune system to recover from fighting the virus. We anticipate that the immune system will then have a stronger response to flu vaccination. In the first part of the study we will find the dose that works best and see how long it needs to be taken for. In the second part we will use this dose in a larger group of patients receiving their flu vaccine. We will therefore test if this treatment works well. If proven, this treatment could be valuable in a wide range of clinical conditions.

Who can participate?
Healthy volunteers aged over 65

What does the study involve?
Part One:
Participants provide blood and urine samples and are randomly allocated to a particular dose of the treatment drug. The medication needs to be taken every day for the prescribed length of time (three or six months). Over the course of the next six months, participants visit their GP or practice nurse at monthly intervals to complete a questionnaire, provide blood and urine samples, and collect the following month's medication. In addition to this, participants attend two follow-up clinics at 9 months and 12 months after starting the study .

Part Two:
Participants provide a blood sample and are randomly allocated to one of two groups. Half of the participants are prescribed the medication and the other half are prescribed a placebo (a

tablet that looks exactly the same as the active medication but contains no active drug). The medication needs to be taken every day for the prescribed length of time (three months). After two months participants attend the surgery to have a seasonal flu vaccination. At this point a further blood sample is taken and a questionnaire is completed. Over the course of the next four months, participants visit their GP or practice nurse for follow-up clinics at regular intervals (14, 21, 28 days and 4 months) to complete a questionnaire and provide a blood sample.

What are the possible benefits and risks of participating?
It is possible that the immune system will have improved by taking the treatment and therefore the flu vaccine may be more effective. However, it is possible that participants will not benefit directly from taking part in this study if they are in the placebo group. The results of the study may help us to improve and develop new treatments for patients suffering from different diseases. All drugs have side effects, and no drug is without risk. However, the drugs used in this study are all standard and the GP will be able to adjust them should you suffer any side effects.

Where is the study run from?
This study is being coordinated by the Primary Care Clinical Research and Trials Unit (PCCRTU, fully accredited by the National Institute for Health Research as a trials unit) at the University of Birmingham. We will initially be working with General Practices within the Midland Research Practices Consortium (MidReC).

When is the study starting and how long is it expected to run for?
November 2011 to January 2014

Who is funding the study?
Medical Research Council (UK)

Who is the main contact?
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Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

EudraCT/CTIS number
2011-000092-13

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
10177

Study information

Scientific Title
A randomised controlled trial aimed at enhancing immunity to influenza in elderly individuals through reversal of immune senescence mediated by herpes virus infection

Acronym
ASPIRE

Study objectives
ASPIRE - A Study Promoting the Influenza Response in the Elderly. We intend to treat immunocompetent elderly individuals with the anti-viral drug valaciclovir in order to reduce the level of endogenous cytomegalovirus (CMV) replication. This is expected to subsequently reduce the magnitude of the CMV-specific immune response and therefore enhance immunity to other infections. This will be investigated by monitoring the immune response to influenza vaccination.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Leicestershire, Northamptonshire & Rutland Research Ethics Committee 1, First MREC approval date 14/02/2011, ref:11/H0406/10

Study design
ASPIRE is a two-part study:
Part One: Dose-finding study.
Part Two: Phase II randomised controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
GP practice

Study type(s)
Treatment

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

Health condition(s) or problem(s) studied
Topic: Primary Care Research Network for England, Inflammatory and Immune System; Subtopic: Not Assigned, Inflammatory and Immune System (all Subtopics); Disease: Immunology and inflammation, All Diseases

Interventions
Valaciclovir Hydrocloride, Part One:
50 eligible patients will be randomised into five treatment arms and the optimal treatment dose and duration of valaciclovir to suppress CMV levels by 85% determined over six months of treatment and six months follow-up.

Placebo, Part Two:
Half of the eligible patients (110) will be randomly allocated to placebo treatment. The duration and timing of treatment will be designed to match the active treatment arm. Both arms will receive a seasonal influenza vaccine after treatment and the immune response they mount quantified.

Part Two:
Half of the eligible patients (110) will be randomly allocated to valaciclovir treatment. The dose, duration and timing of treatment will be determined from Part One. Both arms will receive a seasonal influenza vaccine after treatment and the immune r; Follow Up Length: 12 month(s); Study Entry : Registration and One or More Randomisations

Intervention Type
Drug

Phase
Phase II

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

Primary outcome measure
The magnitude of the CMV-specific CD8+ T cell immune response.; Timepoint(s): Part One: Screening, Baseline, Months 1,2,3,4,5,6,9,12

Secondary outcome measures
1. Quality of Life; Timepoint(s): Part One: Baseline, Months 1,2,3,4,5,6,9,12
2. The CMV viral load in urine.; Timepoint(s): Part One: Baseline, Months 1,2,3,4,5,6,9,12
3. The improvement in proportion of individuals making an adequate response to seasonal flu; Timepoint(s): Part Two: 14, 21, 28, 120 days post-vaccination
4. The magnitude of the CMV-specific CD4+ T cell immune response.; Timepoint(s): Part One: Screening, Baseline, Months 1,2,3,4,5,6,9,12
5. The magnitude of the influenza-specific CD4+ T cell immune response.; Timepoint(s): Part Two: Baseline, Months 1 & 2, Vaccination - 14, 21, 28, 120 days post-vaccination
6. The magnitude of the influenza-specific CD8+ T cell immune response.; Timepoint(s): Part Two: Baseline, Months 1 & 2, Vaccination - 14, 21, 28, 120 days post-vaccination

7. The titre of the CMV-specific antibody response.; Timepoint(s): Part One: Screening, Baseline, Months 1,2,3,4,5,6,9,12
8. The titre of the H1, H3 and influenza B antibodies.; Timepoint(s): Part Two: Baseline, Months 1 & 2, Vaccination - 14, 21, 28, 120 days post-vaccination
9. Tolerability of the treatment.; Timepoint(s): Part One: Baseline, Months 1,2,3,4,5,6,9,12

Overall study start date
01/11/2011

Completion date
01/01/2014

Eligibility

Key inclusion criteria
1. Aged 65 years or above (30% 65-74 yrs old, 70% aged over 75 yrs)
2. Cytomegalovirus (CMV) seropositive
3. CMV-specific CD8+ and CD4+ T cell response over 0.5% of T cell pool at randomisation
4. Human leuckocyte antigen (HLA) type of HLA-A1, A2, B7 or B8
5. Predicted epidermal growth factor receptor (eGFR) > 50ml/min
6. Liver function tests (LFT) in normal range
Target Gender: Male & Female ; Lower Age Limit 65 years

Participant type(s)
Patient

Age group
Senior

Sex
Both

Target number of participants
Planned Sample Size: 700; UK Sample Size: 700. Part One: 50 (200 screened); Part Two: 220 (500 screened)

Key exclusion criteria
1. On the following medication : Steroids, ciclosporin, mycophenolate, probenecid, tacrolimus, theophylline
2. Significant chronic illness as assessed by clinical team
3. History of cardiovascular event in the last 6 months
4. General practitoner (GP) considers inappropriate to take part
5. Unable to provide written consent

Date of first enrolment
01/11/2011

Date of final enrolment
01/01/2014

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
University of Birmingham
Birmingham
United Kingdom
B15 2TT

Sponsor information

Organisation
University of Birmingham (UK)

Sponsor details
Edgbaston
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Sponsor type
University/education

ROR
https://ror.org/03angcq70

Funder(s)

Funder type
Research council

Funder Name
Medical Research Council (MRC) (UK) (Grant Codes: 94820)

Alternative Name(s)
Medical Research Council (United Kingdom), UK Medical Research Council, MRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No