ISRCTN89747147 https://doi.org/10.1186/ISRCTN89747147

C34-PEG-4-Chol - a new fusion inhibitor for the treatment of HIV

Submission date
28/01/2015

Recruitment status
No longer recruiting

Registration date
29/01/2015

Overall study status
Completed

Last Edited
09/07/2018

Condition category
Infections and Infestations

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
HIV (human immunodeficiency virus) is a virus that damages a persons immune system, making them less able to fight infections and disease. There is no cure for the infection , but there are now some very effective treatments, called antiretrovirals, that stop the virus from replicating and therefore help infected people have long and healthy lives. The success of these treatments means that HIV-positive people are now aging. This poses new problems such as heart, kidney, bone and liver diseases which, although associated with ageing, may be more widespread due to the long-term side-effects of anti-HIV drugs. Additionally, drug-drug interactions become increasingly frequent and more complex when treating people who are on treatment for other problems. Therefore, developing new anti-HIV drugs, with less toxicity and likelihood for interactions, is critical. C34-PEG-4-Chol belongs to a family of anti-HIV medications called "fusion inhibitors". C34-PEG-4-Chol is similar to another drug in this family called enfuvirtide. Due to how it is broken down by the body enfurvitide shows little general toxicity and few drug interactions. However it requires injection under the skin twice daily and injection site reactions are common. C34-PEG-4-Chol is expected to need injecting less frequently resulting in fewer reactions. This study will investigate whether giving this drug to humans is safe.

Who can participate?
HIV-positive men aged 18-60

What does the study involve?
Participants are randomly allocated into one of two groups. Those in group 1 are given C34-PEG-4-Chol. Those in group 2 are given a placebo. Samples from each participant are then collected at various time points. Stage 1 involves giving a single dose, allowing researchers to work out the best dose and how often to give it. Stage 2 involves giving 4 doses then checking how much drug gets into the bloodstream and how much the HIV level drops. Each stage should take about 6 months to complete.

What are the possible benefits and risks of participating?
There are no specific advantages of taking part in this study. Risks include side effects to C34-PEG4-Chol which may include injection site reactions (redness, swelling, feeling itchy, bruises, hardened skin or bumps, pain, feeling sore or tender), diarrhoea, nausea / vomiting, raised white

blood cell count, pneumonia, feeling weak or tired, headache, feeling dizzy, not being able to sleep, feeling anxious or low in mood, fever, weight loss, poor appetite, pain and feeling numb in hands, feet or legs, swollen glands (lymph nodes). However C34-PEG4-Chol has never been given to humans before so it is possible other unpredictable side effects could occur. As the study involves giving C34-PEG4-Chol without any other anti-HIV drugs, it is possible that HIV resistance to C34-PEG4-Chol could develop. This could also mean that resistance develops to enfuvirtide and any other fusion inhibitor drugs developed in the future. It is possible that if C34-PEG4-Chol were given to a person who was planning to become pregnant with their partner that it might harm an unborn child. Blood tests can sometimes cause bruising and soreness of the arms or, very rarely, a blockage of a vein or a small nerve injury which can cause numbness and pain. Normally these problems disappear with time. Some people may faint while the blood is being drawn.

Where is the study run from?
Imperial College Healthcare NHS Trust (UK)

When is the study starting and how long is it expected to run for?
February 2015 to November 2015

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

Who is the main contact?
Mrs Nicki Doyle

Contact information

Type(s)
Scientific

Contact name
Mrs Nicki Doyle

Contact details
St Mary's Hospital
Imperial College Healthcare NHS Trust
10th Floor QEQM Building Imperial College
St Mary's Campus
South Wharf Road
London
United Kingdom
W2 1NY

Additional identifiers

Clinical Trials Information System (CTIS)
2014-002671-28

Protocol serial number
17974

Study information

Scientific Title
A phase 1, first in man, study to assess the safety, pharmacokinetic profile and antiretroviral efficacy of C34-PEG-4-Chol, a novel peptide fusion inhibitor for the treatment of HIV infection

Study objectives
The aims of the study are:
1. To assess the safety, pharmacokinetics and pharmacodynamics of C34-PEG4-Chol in HIV-positive individuals.
2. To determine the optimal dose and dosing schedule for C34-PEG4-Chol.

Ethics approval required
Old ethics approval format

Ethics approval(s)
NRES Committee London - Central, 24/12/2014, ref: 14/LO/2078

Primary study design
Interventional

Study design
Randomised; Interventional; Design type: Treatment

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Topic: Infectious diseases and microbiology; Subtopic: Infection (all Subtopics); Disease: Infectious diseases and microbiology

Interventions
1. C34-PEG4-Chol (Peptivir-H), HIV fusion inhibitor
2. Placebo, sodium chloride 0.9% solution

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
C34-PEG-4-Chol

Primary outcome(s)
1. Safety, pharmacokinetic & pharmacodynamic (viral decay - stage 2 only) parameters; Timepoint (s): Stage 1 - up to day 84 post-single dose
2. Stage 2 - follow up duration to be determined from stage 1

Key secondary outcome(s)

1. Changes in plasma HIV RNA; Timepoint(s): Stage 1 - measured up to day 28 post-single dose
2. Detailed pharmacokinetic profile of C34-PEG4-Chol when administered at different single doses. Timepoint(s): Stage 1 - profile at day 84 post-single dose
3. Detailed pharmacokinetic profile of C34-PEG4-Chol when administered following multiple dosing; Timepoint(s): Stage 2 - profile at final follow up (duration to be determined from stage 1)
4. Emergence of mutations within heptad repeat-1 (HR-1) region of gp41; Timepoint(s): Stage 2 - measured up to 4th follow up visit (duration of follow up to be determined from stage 1)
5. Listing of all adverse events (grade 1 and above); Timepoint(s): Stage 1-up to day 84 post-single dose
Stage 2-up to final follow up (fu determined from stage 1)

Completion date
01/04/2016

Eligibility

Key inclusion criteria
1. The ability to understand and sign a written informed consent form, prior to participation in any screening procedures, and be willing to comply with all study requirements
2. Male
3. Between 18 to 60 years, inclusive
4. Documented HIV-1 infected for ≥6 months from screening
5. Comorbidities, if present, optimally managed and stable
6. Normal physical examination
7. No clinically significant abnormalities on laboratory screening test
8. BMI 19-28, inclusive
9. Patients who are heterosexually active must agree to use two effective forms of contraception (e.g., condom with spermicide and established hormonal contraception) during heterosexual intercourse, from screening through to completion of the study
10. CD4 count ≥400 cells/μL at screening
11. Plasma HIV RNA ≥10000 copies/mL at screening
12. In the opinion of the investigator not likely to require ART in the next 4 months
13. No clinically significant abnormalities on 12-lead ECG

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
Male

Key exclusion criteria

1. Any serious or active medical or psychiatric illness which, in the opinion of the investigator, would interfere with patient treatment, assessment, or compliance with the protocol. This would include any active clinically significant renal, cardiac, hepatic, pulmonary, vascular, metabolic (thyroid disorders, adrenal disease) disease immunodeficiency disorders, active infection, or malignancy
2. Participation in an investigational trial involving administration of any investigational compound within 90 days of screening
3. History of alcohol use considered by the investigator to be sufficient to hinder compliance with treatment, follow-up procedures or evaluation of adverse events. Smoking is permitted, but tobacco intake should be expected to remain consistent throughout the study
4. History of recreational drug use within 14 days of screening or a positive drug screen on day of screening
5. Any medication taken listed in Section 8.3 of the protocol (Interaction with other drugs) including over-the-counter medications and herbal products, within 28 days of screening with the exception of vitamins and/or paracetamol. When a concomitant medication is necessary this will be reviewed by the investigator and if not contraindicated may be continued
6. History of drug sensitivity or drug allergy which in the opinion of the investigator may put the patient at increased risk of drug reactions during the study
7. Patients with female partners who are not using 2 effective forms of contraception or with partners who are pregnant
8. Documented resistance of clinical relevance to any other class of HIV antiretroviral drugs
9. Previous exposure to fusion inhibitors (T20/enfuvirtide)
10. Receiving ART within 6 months of screening

Date of first enrolment
01/03/2015

Date of final enrolment
01/12/2015

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
St Mary's Hospital
Imperial College Healthcare NHS Trust
10th Floor QEQM Building Imperial College
St Mary's Campus
South Wharf Road
London
United Kingdom
W2 1NY

Sponsor information

Organisation
Imperial College London

ROR
https://ror.org/041kmwe10

Funder(s)

Funder type
Government

Funder Name
Medical Research Council

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

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

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?
Results article	results	25/08/2017		Yes	No
HRA research summary			28/06/2023	No	No