

HCQ-01 Trial: evaluation of the efficacy of hydroxychloroquine in decreasing immune activation in asymptomatic human immunodeficiency virus (HIV) infected patients

Submission date 26/09/2007	Recruitment status No longer recruiting	☒ Prospectively registered ☐ Protocol
Registration date 22/10/2007	Overall study status Completed	☐ Statistical analysis plan ☒ Results
Last Edited 25/07/2012	Condition category Infections and Infestations	☐ Individual participant data

Plain English summary of protocol

http://www.ctu.mrc.ac.uk/research_areas/study_details.aspx?s=54

Contact information

Type(s)

Scientific

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Additional identifiers

Protocol serial number

HCQ-01; 082163/Z/07/Z

Study information

Scientific Title

Evaluation of the efficacy of hydroxychloroquine in decreasing immune activation and viral replication in asymptomatic human immunodeficiency virus (HIV)-infected patients: a phase II, multicentre, randomised, double-blind, placebo-controlled clinical trial

Acronym

HCQ-01 (HydroxyChloroQuine study)

Study objectives

The main objective of the study is to determine whether hydroxychloroquine decreases immune activation in human immunodeficiency virus (HIV), as shown by at least a 25% reduction in CD8 T-cell activation after 48 weeks of treatment. The study also intends to examine the effects of hydroxychloroquine on viral load and CD4 T-cell count at week 48, and to assess safety in this patient population.

Please note that this trial record was updated on 29/04/2008. All changes can be found in the relevant field. Please also note that the anticipated start and end dates of this trial have been updated. The previous dates were:

Anticipated start date: 01/11/2007

Anticipated end date: 31/12/2008

As of 11/02/2009 the anticipated end date was again revised from 31/12/2009 to 31/12/2010.

Ethics approval required

Old ethics approval format

Ethics approval(s)

Oxfordshire REC A on 06/03/2008. Revised 13/10/2008.

Primary study design

Interventional

Study design

Phase II, multi-centre, randomised, double-blind, placebo-controlled clinical trial

Study type(s)

Treatment

Health condition(s) or problem(s) studied

Early Human Immunodeficiency Virus (HIV) infection

Interventions

Patients will receive hydroxychloroquine 400 mg/day or matching placebo to be taken once daily by mouth for 48 weeks with food.

Intervention Type

Drug

Phase

Phase II

Drug/device/biological/vaccine name(s)

Hydroxychloroquine

Primary outcome(s)

Change in CD8 T-cell activation at week 48 compared to baseline in the two study groups (as shown by a percentage of the cells expressing CD38+ and HLA-DR+).

Key secondary outcome(s)

Current secondary outcome measures as of 29/04/2008:

Efficacy outcome measures:

Change from baseline to week 48 in:

1. CD4 T-cell activation (as shown by the percentage of the cells expressing CD38+ and HLA-DR+)
2. Absolute CD4 T-cell count
3. IL-6 concentration
4. HIV viral load (expressed in log¹⁰ copies/ml)

Safety outcome measure:

5. Incidence of Serious Adverse Events
6. Incidence of clinical and laboratory grade III and IV adverse events
7. Incidence of retinal changes

Previous secondary outcome measures:

Efficacy outcome measure:

1. Change in HIV Ribonucleic Acid (RNA) and absolute CD4 T-cell count at week 48 compared to baseline (analysis will compare change in hydroxychloroquine and placebo groups)
2. Change in CD4 T-cell activation at week 48 compared to baseline in the two study groups (as shown by a percentage of the cells expressing CD38+ and HLA-DR+)
3. Proliferation of CD4 and CD8 T-cells (as shown by Ki67 expression), assessed at the end of study
4. Quality of life; the Medical Outcomes Study (MOS)-HIV questionnaire will be used and assessed at the end of the study

Safety outcome measure:

5. Clinical and laboratory toxicity monitoring, monitored at every visit

Completion date

31/12/2010

Eligibility**Key inclusion criteria**

Current information as of 11/02/2009 (amended in protocol and approved by ethics on 13/10/2008):

1. Documented HIV infection on Enzyme-Linked Immuno-Sorbent Assay (ELISA) and confirmatory test
2. Age 18 to 65 years, either sex
3. Naïve to antiretroviral therapy (ART) or off ART for at least 12 months prior to study entry
4. CD4 T-cell count greater than 400 cells/μL on screening blood test and on one other test performed within the 3 months prior to screening
5. Plasma HIV RNA viral load greater than 5000 copies/ml on screening blood test
6. Willing and able to provide written informed consent

Current information as of 29/04/2008:

1. Documented HIV infection on Enzyme-Linked Immuno-Sorbent Assay (ELISA) and confirmatory test
2. Age 18 to 65 years, either sex
3. Naïve to antiretroviral therapy (ART) (patients who have taken less than a total of 3 months ART in the past will be eligible, provided that they have been off ART for 1 year prior to study entry)
4. CD4 T-cell count greater than 400 cells/ μ L on screening blood test and on one other test performed within the 3 months prior to screening
5. Plasma HIV RNA viral load greater than 5000 copies/ml on screening blood test
6. Willing and able to provide written informed consent

Initial information at time of registration:

1. Male or female patients with documented HIV infection on Enzyme-Linked Immuno-Sorbent Assay (ELISA) and confirmatory test
2. Age 18 to 60 years
3. Naïve to antiretroviral therapy
4. CD4 T-cell count greater than 400 cells/ μ L on screening blood test and on one other test performed within three months prior to screening
5. Plasma viral load greater than 5000 copies/ml on screening blood test
6. Willing and able to provide written informed consent
7. Women of childbearing age must be willing to use contraception during the study and for a period of three months afterwards
8. Written informed consent

Participant type(s)

Patient

Healthy volunteers allowed

No

Age group

Adult

Lower age limit

18 Years

Upper age limit

65 Years

Sex

All

Key exclusion criteria

Current information as of 11/02/2009 (amended in protocol and approved by ethics on 13/10/2008):

1. History of psoriasis, porphyria cutanea tarda, epilepsy, myasthenia gravis, myopathy of any cause, cardiac arrhythmias, glucose 6-phosphate dehydrogenase (G6PD) deficiency
2. Insulin-dependent or non-insulin-dependent diabetes mellitus
3. Chronic liver disease of any cause or alcoholism

4. Primary HIV infection within 12 months prior to screening, either confirmed (previous negative HIV antibody test within 12 months), or suspected (symptoms strongly suggestive of HIV seroconversion illness within the previous 12 months and patient not known to be HIV antibody positive prior to the illness)
5. Pneumonia, meningitis, septicaemia or any other serious infection in the 2 months prior to screening
6. Any acute infection with fever and systemic symptoms within the last 24 hours
7. Any vaccinations in the 2 months prior to screening
8. Active malignancy (patients are eligible if treatment for the malignancy was completed more than 2 years prior to screening and there has been no subsequent clinical evidence of active disease) or any active immune-mediated or inflammatory disease
9. Any known suicide attempts (at any time in the past) or current or past history of depression requiring treatment within the 2 years prior to screening. Patients who have not had depression in the previous 2 years but who have had depression in the past may be included if, in the opinion of the physician, the nature of the past episode of depression and the patients current psychological state indicate that the risk of recurrence of depression during the trial is likely to be low. Patients who have received anti-depressant medication for reasons other than symptomatic depression can be included in the trial.
10. A woman who is currently pregnant or breastfeeding
11. A woman of child-bearing potential who is planning to become pregnant during the course of the study, or is unwilling to take adequate contraception (including barrier contraception) throughout the course of the study
12. Use of systemic corticosteroids or other immunomodulatory drugs within the 12 months prior to screening
13. Current use of medication with known serious hepatotoxic effects or known interaction with hydroxychloroquine
14. Evidence of cardiac conduction defects or cardiac arrhythmia on screening electrocardiogram (ECG)
15. Retinopathy or visual field changes detected on screening eye examination
16. Hepatitis B surface antigen (HBsAg) positive or Hepatitis C PCR positive (patients who are Hepatitis C antibody positive are allowed to participate provided that PCR is negative)
17. Any of the following laboratory abnormalities on screening blood test:
 - 17.1. Haemoglobin less than 10.5 g/dl
 - 17.2. Absolute neutrophil count less than $1.0 \times 10^9/L$
 - 17.3. Platelet count less than $100 \times 10^9/L$
 - 17.4. Alanine aminotransferase (ALT) or aspartate aminotransferase (AST), or alkaline phosphatase above 2.5 x upper limit of normal (ULN)
 - 17.5. Serum creatinine greater than 1.5 x upper limit of normal (ULN)
 - 17.6. Estimated creatinine clearance (Cockcroft-Gault equation) below 60 ml/min
18. Inability to attend or comply with treatment or follow-up scheduling
19. Current participation in any other clinical intervention trial

Current information as of 29/04/2008:

1. History of psoriasis, porphyria cutanea tarda, epilepsy, myasthenia gravis, myopathy of any cause, cardiac arrhythmias, glucose 6-phosphate dehydrogenase (G6PD) deficiency
2. Insulin-dependent or non-insulin-dependent diabetes mellitus
3. Chronic liver disease of any cause or alcoholism
4. Primary HIV infection within 12 months prior to screening, either confirmed (previous negative HIV antibody test within 12 months), or suspected (symptoms strongly suggestive of HIV seroconversion illness within the previous 12 months and patient not known to be HIV antibody positive prior to the illness)
5. Any acute infection (opportunistic or non-opportunistic) requiring systemic anti-microbial

treatment during the 6 months prior to enrolment

6. Malignancy or any active immune-mediated or inflammatory disease

7. Past or current history of depression requiring medication or any known previous suicide attempts

8. A woman who is currently pregnant or breastfeeding

9. A woman of child-bearing potential who is planning to become pregnant during the course of the study, or is unwilling to take adequate contraception (including barrier contraception) throughout the course of the study

10. Use of corticosteroids or other immunomodulatory drugs within the 12 months prior to screening

11. Current use of medication with hepatotoxic effects or known interaction with hydroxychloroquine

12. Evidence of cardiac conduction defects or cardiac arrhythmia on screening electrocardiogram (ECG)

13. Retinopathy or visual field changes detected on screening eye examination

14. Hepatitis B surface antigen (HBsAg) positive or Hepatitis C antibody positive (or Hepatitis C polymerase chain reaction [PCR] positive, if known)

15. Any of the following laboratory abnormalities on screening blood test:

15.1. Haemoglobin less than 10.5 g/dl

15.2. Absolute neutrophil count less than $1.0 \times 10^9/L$

15.3. Platelet count less than $120 \times 10^9/L$

15.4. Alanine aminotransferase (ALT) or aspartate aminotransferase (AST), or alkaline phosphatase above $2.0 \times$ upper limit of normal (ULN)

15.5. Serum creatinine greater than $1.5 \times$ ULN

15.6. Estimated creatinine clearance (Cockcroft-Gault equation*) below 60 ml/min

16. Inability to attend or comply with treatment or follow-up scheduling

17. Current participation in any other clinical intervention trial

Initial information at time of registration:

1. Use of corticosteroids or other immunomodulatory drugs within the 12 months prior to enrolment

2. History of psoriasis, porphyria, epilepsy, myasthenia gravis, cardiac arrhythmias, Glucose 6-Phosphate Dehydrogenase (G6PD) deficiency

3. Hepatitis B surface Antigen (HBsAg) positive or Hepatitis C antibody positive

4. Retinopathy or visual field changes detected at eye screening

5. Evidence of cardiac conduction defects on screening Electrocardiogram (ECG)

6. Anaemia (haemoglobin less than 10 g/dl), neutropenia (absolute neutrophil count less than $1.0 \times 10^9/L$ or thrombocytopenia (platelet count less than $120 \times 10^9/L$) at study screening

7. Liver function tests greater than twice upper limit of normal at study screening

8. Serum creatinine greater than 1.5 times upper limit of normal or estimated creatinine clearance (Cockcroft-Gault equation) below 60 ml/min at screening

9. Requirement for use of medication with hepatotoxic effects or known interaction with hydroxychloroquine

10. Depression or previous suicidal attempts

11. Pregnancy or planned pregnancy during the study or lactating women

12. Inability to attend or comply with treatment or follow-up scheduling

Date of first enrolment

01/05/2008

Date of final enrolment

31/12/2010

Locations

Countries of recruitment

United Kingdom

England

Study participating centre

MRC Clinical Trials Unit

London

United Kingdom

NW1 2DA

Sponsor information

Organisation

Medical Research Council Clinical Trials Unit (MRC CTU) (UK)

ROR

<https://ror.org/001mm6w73>

Funder(s)

Funder type

Charity

Funder Name

The Wellcome Trust (UK) (grant ref: 082163)

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	25/07/2012		Yes	No