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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 not yet added ? SAP not yet added ✓ Results added ? Raw data not yet added ✓ Study completed
Registration date 22/10/2007	**Overall study status** Completed	
Last Edited 25/07/2012	**Condition category** Infections and Infestations	

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

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

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 hypothesis
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.

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

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet

Not available in web format, please email hcq01@ctu.mrc.ac.uk to request a patient information sheet

Condition
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 measure
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+).

Secondary outcome measures
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 log^10 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

Overall study start date
01/05/2008

Overall study end date
31/12/2010

Eligibility

Participant 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. Naive 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/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

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. Naive to antiretroviral therapy
4. CD4 T-cell count greater than 400 cells/µL 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

Age group
Adult

Lower age limit
18 Years

Upper age limit
65 Years

Sex
Both

Target number of participants
90 (100 as of 29/04/2008)

Participant 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 x 10^9/L
17.3. Platelet count less than 100 x 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 (Cockroft-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 x 10^9/L
15.3. Platelet count less than 120 x 10^9/L
15.4. Alanine aminotransferase (ALT) or aspartate aminotransferase (AST), or alkaline phosphatase above 2.0 x upper limit of normal (ULN)
15.5. Serum creatinine greater than 1.5 x ULN
15.6. Estimated creatinine clearance (Cockroft-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 defected 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 x 10^9/L or thrombocytopenia (platelet count less than 120 x 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 (Cockroft-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

Recruitment start date
01/05/2008

Recruitment end date
31/12/2010

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
MRC Clinical Trials Unit
London
United Kingdom
NW1 2DA

Sponsor information

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

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Sponsor type
Research council

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ROR
https://ror.org/001mm6w73

Funder(s)

Funder type
Charity

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

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?
Results article	results	25/07/2012		Yes	No