

# Imatinib (IM) versus hydroxychloroquine (HCQ) and IM for patients with chronic myeloid leukaemia (CML) in cytogenetic response (CyR) with residual disease detectable by quantitative polymerase chain reaction (Q-PCR)

<b>Submission date</b> 24/08/2009	<b>Recruitment status</b> No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 19/11/2009	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
<b>Last Edited</b> 23/05/2019	<b>Condition category</b> Cancer	<input type="checkbox"/> Individual participant data <input type="checkbox"/> Record updated in last year

## Plain English summary of protocol

<https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-hydroxychloroquine-with-imatinib-for-cml-choices>

(Updated 21/05/2019, previously: <http://www.cancerhelp.org.uk/trials/a-trial-hydroxychloroquine-with-imatinib-for-cml-choices>)

## Contact information

### Type(s)

Scientific

### Contact name

Prof Tessa Holyoake

### Contact details

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## Additional identifiers

### EudraCT/CTIS number

2009-014375-41

**IRAS number**

**ClinicalTrials.gov number**

NCT01227135

**Secondary identifying numbers**

G0900882

## **Study information**

### **Scientific Title**

A randomised Phase II trial of Imatinib (IM) versus Hydroxychloroquine (HCQ) and IM for patients with Chronic Myeloid Leukaemia (CML) in Cytogenetic Response (CyR) with residual disease detectable by quantitative polymer chain reaction (Q-PCR)

### **Acronym**

CHOICES - Chloroquine and imatinib combination to eliminate stem cells

### **Study objectives**

1. To provide preliminary evidence that hydroxychloroquine (HCQ) given in combination with imatinib is more effective than imatinib alone in terms of BCR/ABL levels in chronic myeloid leukaemia (CML) patients who are in moderate cytogenetic response (MCyR) with residual BCR/ABL+ cells after at least one year of imatinib treatment.
2. To determine the safety and tolerability of HCQ given in combination with imatinib in these patients.

### **Ethics approval required**

Old ethics approval format

### **Ethics approval(s)**

West of Scotland REC 1, 01/12/2009, REC ref: 09/S0703/112

### **Study design**

Randomised phase II 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 use the contact details below to request a patient information sheet

### **Health condition(s) or problem(s) studied**

Chronic myeloid leukaemia

### **Interventions**

Imatinib alone arm: Patients will continue to receive the once-daily dose of imatinib (oral) that they were receiving prior to entry in the trial. This is the control arm of the study.

Imatinib + HCQ arm: Patients will continue to receive the once-daily dose of imatinib (oral) that they were receiving prior to entry in the trial. In addition they will receive HCQ (oral), 400 mg twice-daily. This is the interventional treatment under study.

Total duration of interventions: 12 months

Total duration of follow-up: to be confirmed as of 24/08/2009

### **Intervention Type**

Drug

### **Phase**

Phase II

### **Drug/device/biological/vaccine name(s)**

Chloroquine, imatinib

### **Primary outcome measure**

Proportion of treatment "successes" defined as patients who have  $\geq 0.5$  log reductions in their 12 month PCR level from baseline. Patients who withdraw before the 12 month assessment or who have an increase in their IM dose prior to the assessment will be classified as treatment "failures".

All analyses will be conducted on an intention to treat basis.

### **Secondary outcome measures**

1. The proportion of treatment "successes" at 24 months. Again patients who withdraw or increase their IM dose prior to 24 months will be classified as treatment "failures".
2. Molecular response at 12 and 24 months (classified as Complete, Major and No response). Patients who withdraw or increase their IM dose prior to the assessment will be classified as non-responders.
3. The proportion of patients with progression at 12 and 24 months. Patients who withdraw or increase their IM dose prior to the assessment will be classified as progressing.

All analyses will be conducted on an intention to treat basis. The comparisons between the study arms of "success", molecular response rates and progression rates will use Fisher's exact test.

Adverse events will also be recorded throughout the trial.

### **Overall study start date**

01/04/2010

**Completion date**

31/10/2013

## **Eligibility**

### **Key inclusion criteria**

1. Male or female patients aged  $\geq 18$  years old
2. Ability to provide written informed consent prior to participation in the study and any related procedures being performed
3. CML Chronic phase (CP) patients who have been treated with and tolerated imatinib for 1-3 years, have achieved at least MCyR and continue to be BCR/ABL+ by quantitative polymerase chain reaction (Q-PCR). Patients should be receiving a stable dose of imatinib for 6 months prior to study entry.
4. Patients must meet the following laboratory criteria:
  - 4.1. Absolute neutrophil count (ANC) and platelet (PLT) need to be stable and in the normal range for  $\geq 2$  months
  - 4.2. Serum albumin  $> 3$  g/dl
  - 4.3. Aspartate aminotransferase (AST) or alanine aminotransferase (ALT)  $\leq 2.5$  x upper limit of normal (ULN)
  - 4.4. Serum bilirubin  $\leq 1.5$  x ULN
  - 4.5. Serum creatinine  $\leq 1.5$  x ULN or 24-hour creatinine clearance  $\geq 50$  ml/min
  - 4.6. Serum potassium  $\geq$  Lower limit of normal (LLN)
5. Eastern Cooperative Oncology Group (ECOG) Performance Status of  $\leq 2$

### **Participant type(s)**

Patient

### **Age group**

Adult

### **Lower age limit**

18 Years

### **Sex**

Both

### **Target number of participants**

66

### **Key exclusion criteria**

1. Patient who have been treated with imatinib  $< 1$  or  $> 3$  years or patients who have changed dose in previous 6 months
2. Impaired cardiac function including any one of the following:
  - 2.1. Screening electrocardiogram with a QTc  $> 450$  msec
  - 2.2. Patients with congenital long QT syndrome
  - 2.3. History or presence of sustained ventricular tachycardia
  - 2.4. Any history of ventricular fibrillation or torsades de pointes
  - 2.5. Congestive heart failure (New York Heart Association class III or IV)
  - 2.6. Uncontrolled hypertension
3. Patients with severe gastrointestinal (GI) disorder, uncontrolled epilepsy, known G6PD

deficiency, known porphyria, moderate or severe psoriasis, known myaesthesia gravis or other concurrent severe and/or uncontrolled medical conditions

4. Patients who have received chemotherapy, any investigational drug or undergone major surgery <4 weeks prior to starting study drug or who have not recovered from side effects of such therapy

5. Concomitant use of any other anti-cancer therapy or radiation therapy

6. Female patients who are pregnant or breast feeding or patients of reproductive potential not willing to use a double method of contraception including a barrier method (i.e. condom) during the study and 3 months after the end of treatment

7. Women of childbearing potential (WOCBP) must have a negative serum pregnancy test within 7 days of the first administration of oral HCQ

8. Male patients whose sexual partners are WOCBP not willing to use a double method of contraception including condom during the study and 3 months after the end of treatment

9. Patients with any significant history of non-compliance to medical regimens or with inability to grant a reliable informed consent

**Date of first enrolment**

01/04/2010

**Date of final enrolment**

31/10/2013

## **Locations**

**Countries of recruitment**

Scotland

United Kingdom

**Study participating centre**

**Gartnavel General Hospital**

Glasgow

United Kingdom

G12 0XB

## **Sponsor information**

**Organisation**

NHS Greater Glasgow and Clyde (UK)

**Sponsor details**

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**Sponsor type**  
Government

**Website**  
<http://www.nhsggc.org.uk>

**ROR**  
<https://ror.org/05kdz4d87>

## **Funder(s)**

**Funder type**  
Research council

**Funder Name**  
Medical Research Council (MRC) (UK)

**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**  
01/08/2019

**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?
<a href="#">HRA research summary</a>			28/06/2023	No	No