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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)

Submission date 24/08/2009	**Recruitment status** No longer recruiting	[X] Prospectively registered [ ] Protocol [ ] Statistical analysis plan [ ] Results [ ] Individual participant data [ ] Record updated in last year
Registration date 19/11/2009	**Overall study status** Completed	
Last Edited 23/05/2019	**Condition category** Cancer	

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

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Additional identifiers

Clinical Trials Information System (CTIS)
2009-014375-41

ClinicalTrials.gov (NCT)
NCT01227135

Protocol serial number
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

Study type(s)
Treatment

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(s)
Proportion of treatment "successes" defined as patients who have ≥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.

Key secondary outcome(s))
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.

Completion date
31/10/2013

Eligibility

Key inclusion criteria
1. Male or female patients aged ≥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 ≥2 months
4.2. Serum albumin >3 g/dl

4.3. Aspartate aminotransferase (AST) or alanine aminotransferase (ALT) ≤2.5 x upper limit of normal (ULN)
4.4. Serum bilirubin ≤1.5 x ULN
4.5. Serum creatinine ≤1.5 x ULN or 24-hour creatinine clearance >=50 ml/min
4.6. Serum potassium ≥ Lower limit of normal (LLN)
5. Eastern Cooperative Oncology Group (ECOG) Performance Status of ≤2

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

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 myaesthenia 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
United Kingdom

Scotland

Study participating centre
Gartnavel General Hospital
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Sponsor information

Organisation
NHS Greater Glasgow and Clyde (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, 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?
HRA research summary			28/06/2023	No	No