

# Management of Transformed Chronic myeloid leukaemia: Ponatinib and Intensive chemotherapy

<b>Submission date</b> 05/03/2014	<b>Recruitment status</b> No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 05/03/2014	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 16/12/2021	<b>Condition category</b> Cancer	<input type="checkbox"/> Individual participant data

## Plain English summary of protocol

<http://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-looking-at-intensive-treatment-and-ponatinib-for-chronic-myeloid-leukaemia-matchpoint>

## Contact information

### Type(s)

Scientific

### Contact name

Prof Mhairi Copland

### Contact details

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## Additional identifiers

### EudraCT/CTIS number

2012-005629-65

### IRAS number

**ClinicalTrials.gov number**

**Secondary identifying numbers**

15879

## **Study information**

### **Scientific Title**

Management of Transformed Chronic myeloid leukaemia: Ponatinib and Intensive chemotherapy: a dose finding trial

### **Acronym**

MATCHPOINT

### **Study objectives**

The aim of this trial is to find a safe and effective dose of a drug called Ponatinib when used in combination with chemotherapy in patients with Chronic Myeloid Leukaemia (CML) whose disease has moved in to blast phase. Ponatinib is a Tyrosine Kinase Inhibitor (TKI). TKIs stop enzymes called Tyrosine Kinases from working. By stopping these enzymes from working the normal signals within the cells are disrupted. TKIs are often used in the treatment of cancers including leukaemias such as CML. 30 patients from the United Kingdom will be invited to take part in this trial.

### **Ethics approval required**

Old ethics approval format

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

NRES Committee South Central - Berkshire B, 11/12/2013, ref.13/SC/0583

### **Study design**

Non-randomised; Interventional; Design type: Treatment

### **Primary study design**

Interventional

### **Secondary study design**

Non randomised study

### **Study setting(s)**

Hospital

### **Study type(s)**

Treatment

### **Participant information sheet**

Not available in web format, please contact your consultant or research nurse for a patient information sheet

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

Topic: National Cancer Research Network; Subtopic: Haematological Oncology; Disease: Leukaemia (chronic)

### **Interventions**

12 lead ECG, 60 minutes, performed by Investigator or delegated qualified person at hospital /clinic; Additional sub-study bloods, Additional OPTIONAL blood samples for sub study - 20 minutes, performed by Investigator or delegated qualified person at hospital/clinic; Biochemistry, Biochemistry including renal and liver profile - 20 minutes, performed by Investigator or delegated qualified person at hospital/clinic; Blood samples, Full blood count with differentials - 20 minutes, performed by Investigator or delegated qualified person at hospital/clinic; Bone marrow evaluation, 60 minutes, performed by Investigator or delegated qualified person at hospital/clinic; Buccal swab, And hair follicle for DNA if buccal swab insufficient to analyse (OPTIONAL); Chemotherapy (FLAGIDA), Chemotherapy (FLAGIDA) cycle administration as per local practice; Physical examination, 30 minutes, performed by Investigator or delegated qualified person at hospital/clinic; Ponatinib administration, Patient prescribed a bottle of tablets to last for each of the 48week cycles of trial treatment, followed by 3 monthly supplies of ponatinib on maintenance as long as the patient requires it.; Pregnancy test, 5 minutes, performed by Investigator or delegated qualified person at hospital/clinic

Follow Up Length: 36 month(s)

Study Entry: Registration only

### **Intervention Type**

Drug

### **Phase**

Phase I/II

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

Ponatinib

### **Primary outcome measure**

Efficacy; Timepoint(s): Efficacy: Complete cytogenetic response (CCyR)

### **Secondary outcome measures**

1. Incidence of Cytomegalovirus (CMV) reactivation rate and Graft Versus Host Disease (GVHD); Timepoint(s): post-transplant
2. Complete Cytogenetic Response (CCyR); Timepoint(s): within 2 cycles of treatment
3. Disease free survival (DFS); Timepoint(s): 3 year
4. Haematological response; Timepoint(s): within 2 cycles of treatment
5. Major Molecular Response (MMR); Timepoint(s): within 2 cycles of treatment
6. Overall survival (OS); Timepoint(s): 3 years
7. Relapse rate post allogeneic transplant or maintenance therapy; Timepoint(s): 1 and 3 year
8. Tolerability
9. Identification of the dose of ponatinib that can be safely delivered in combination
10. Toxicity profile of ponatinib + chemotherapy (FLAG-IDA); Timepoint(s): within 6 months or up to transplant (whichever time point arrives first). Toxicities will be measure; treatment related mortality; Timepoint(s): 1 and 3 year

### **Overall study start date**

15/03/2014

**Completion date**

26/04/2021

## Eligibility

**Key inclusion criteria**

All of the following:

1. Ph positive or BCRABL positive CML in blastic transformation. Defined as one or more of the following being present: Blasts  $\geq 30\%$  in peripheral blood or bone marrow Extramedullary blast proliferation or large foci or clusters of blasts in the bone marrow biopsy
2. Age:  $\geq 18$
3. Suitable for intensive chemotherapy (FLAGIDA)
4. Adequate renal function defined as serum creatinine  $\leq 1.5 \times$  upper limit of normal (ULN)
5. Adequate liver function defined as: Total bilirubin  $< 1.5 \times$  ULN Alanine aminotransferase (ALT) or aspartate aminotransferase (AST)  $< 2.5 \times$  ULN ( $< 5 \times$  ULN if liver involvement with leukaemia)
6. Normal pancreatic status Lipase  $\leq 1.5 \times$  ULN and Amylase  $\leq 1.5 \times$  ULN
7. Normal QTcF interval on screening ECG evaluation, defined as QTcF of  $\leq 450$  ms in males or  $\leq 470$  ms in females.
8. Female and male patients who are of childbearing potential must agree to use an effective form of contraception with their sexual partners throughout participation in this study until 30 days after the last dose of ponatinib.
9. Ability to comply with study procedures, in the Investigator's opinion.
10. Valid Informed Consent

**Participant type(s)**

Patient

**Age group**

Adult

**Lower age limit**

18 Years

**Sex**

Both

**Target number of participants**

Planned Sample Size: 30; UK Sample Size: 30

**Total final enrolment**

17

**Key exclusion criteria**

1. Received chemotherapy other than hydroxycarbamide or anagrelide within 4 weeks of registration
2. Received therapy with a new TKI (i.e. changed TKI) following confirmation of blastic transformation up to two weeks of TKI therapy is allowed for those patients whose CML is in blastic phase at original diagnosis.
3. Previous treatment with intensive acute leukaemia style chemotherapy (FLAGIDA)
4. Prior allogeneic or autologous Stem Cell Transplant

5. Significant or active cardiovascular disease, specifically including but not restricted to:  
Myocardial infarction within 6 months prior to registration  
History of clinically significant atrial or ventricular arrhythmia  
Unstable angina within 6 months prior to registration  
Congestive heart failure within 6 months prior to registration  
History of pancreatitis  
6. Uncontrolled hypertriglyceridaemia (>450mg/dL)  
7. Are pregnant or lactating  
8. Underwent major surgery (with the exception of minor surgical procedures, such as catheter placement or Bone Marrow biopsy) within 14 days prior to registration  
9. Suffer from any condition or illness that, in the opinion of the investigator, would compromise patient safety or interfere with the evaluation of the safety of the study treatment

**Date of first enrolment**

02/12/2014

**Date of final enrolment**

26/04/2018

## **Locations**

**Countries of recruitment**

England

United Kingdom

**Study participating centre**

**Cancer Research UK Clinical Trials Unit**

Birmingham

United Kingdom

B15 2TT

## **Sponsor information**

**Organisation**

University of Birmingham (UK)

**Sponsor details**

Edgbaston

Birmingham

England

United Kingdom

B15 2TT

**Sponsor type**

University/education

**ROR**

<https://ror.org/03angcq70>

## **Funder(s)**

**Funder type**

Industry

**Funder Name**

Incyte Corporation

**Funder Name**

Bloodwise

**Alternative Name(s)**

**Funding Body Type**

Private sector organisation

**Funding Body Subtype**

Other non-profit organizations

**Location**

United Kingdom

## **Results and Publications**

**Publication and dissemination plan**

Planned publication in a high-impact peer reviewed journal.

**Intention to publish date**

31/12/2022

**Individual participant data (IPD) sharing plan**

The data sharing plans for the current study are unknown and will be made available at a later date.

**IPD sharing plan summary**

Data sharing statement to be made available at a later date

**Study outputs**

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Results article</a>		10/12/2021	16/12/2021	Yes	No
<a href="#">HRA research summary</a>			28/06/2023	No	No