ISRCTN98986889 https://doi.org/10.1186/ISRCTN98986889

Management of Transformed Chronic myeloid leukaemia: Ponatinib and Intensive chemotherapy

Submission date 05/03/2014	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 05/03/2014	**Overall study status** Completed	
Last Edited 16/12/2021	**Condition category** Cancer	

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

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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 ≥30% in peripheral blood or bone marrow Extramedullary blast proliferation or large foci or clusters of blasts in the bone marrow biopsy
2. Age: ≥18
3. Suitable for intensive chemotherapy (FLAGIDA)
4. Adequate renal function defined as serum creatinine ≤1.5 X upper limit of normal (ULN)
5. Adequate liver function defined as: Total bilirubin < 1.5 X ULN Alanine aminotransferase (ALT) or aspartate aminotransferase (AST) < 2.5 X ULN (< 5 X ULN if liver involvement with leukaemia)
6. Normal pancreatic status Lipase ≤ 1.5 X ULN and Amylase ≤ 1.5 X ULN
7. Normal QTcF interval on screening ECG evaluation, defined as QTcF of ≤ 450 ms in males or ≤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 leukaemiastyle 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
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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?
Results article		10/12/2021	16/12/2021	Yes	No
HRA research summary			28/06/2023	No	No