

# Phase 2 study of tefinostat in chronic myelomonocytic leukaemia (CMML)

<b>Submission date</b> 24/09/2015	<b>Recruitment status</b> No longer recruiting	<input type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol
<b>Registration date</b> 25/09/2015	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 18/10/2022	<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-study-of-tefinostat-for-chronic-myelomonocytic-leukaemia-monocle>

## Contact information

### Type(s)

Scientific

### Contact name

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## Additional identifiers

### Clinical Trials Information System (CTIS)

2015-002281-23

### Protocol serial number

SPON 1345-14

# Study information

## Scientific Title

A phase 2 study of the monocyte-targeted histone deacetylase inhibitor tefinostat (CHR-2845) in chronic myelomonocytic leukaemia (CMML)

## Acronym

MONOCLE

## Study objectives

The dual primary objectives of the study are:

1. To evaluate the safety and tolerability of tefinostat (CHR-2845) in chronic myelomonocytic leukaemia
2. To evaluate the overall clinical response rate to tefinostat in patients with chronic myelomonocytic leukaemia (according to Wattel and modified IWG criteria)

## Ethics approval required

Old ethics approval format

## Ethics approval(s)

Wales REC 3, 15/01/2016, REC ref: 15/WA/0391

## Primary study design

Interventional

## Study design

Single-arm phase 2 trial

## Study type(s)

Treatment

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

Chronic myelomonocytic leukaemia is a myelodysplastic / myeloproliferative neoplasm with a high median age of presentation (>70yrs) and poor prognosis; the median survival from diagnosis remains only 11-17 months and very few clinical studies have addressed the disease in isolation.

## Interventions

All patients will receive tefinostat (CHR-2845) which is a novel monocyte/macrophage-targeted HDAC inhibitor that is cleaved to an active acid (CHR-2847) by an intracellular esterase (hCE-1) that is found only in cells of monocytoid lineage. CHR-2847 selectively accumulates within hCE-1 expressing cells resulting in a 20 to 100-fold increase in potency of tefinostat for monocytic tumour cells, which make up the majority of the disease cells in CMML. In a previous first-in-man study of tefinostat in patients with refractory haematological malignancies treated with continuous doses of 20 to 640mg, tefinostat was well-tolerated with no 'maximum tolerated dose' being defined. Selective targeted increases in protein acetylation in monocytoid cells were demonstrated between 40 and 320mg. Of 2 CMML patients treated in that study, one achieved a bone marrow complete response at relatively small doses (20-80mg).

## Intervention Type

Drug

## Phase

Phase II

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

Tefinostat

## Primary outcome(s)

1. Safety and tolerability of tefinostat defined as the proportion of patients experiencing CTC grade 3-4 non-haematological toxicity or death thought to be at least possibly related to tefinostat
2. Overall clinical response rate (according to Wattel and modified IWG criteria)

Patients will receive tefinostat continuously for 6 continuous 4-week cycles (24 weeks). Primary outcome measures will be assessed continuously over this period, including fortnightly peripheral blood assessment (full blood count, blood film/differential) and bone marrow assessments performed after 12 and 24 weeks of therapy.

## Key secondary outcome(s)

1. Incidence and duration of CR/PR/haematological improvement
2. Achievement of red blood cell and platelet transfusion independence
3. Overall survival
4. Progression-free survival
5. Incidence of transformation of CMML to acute myeloid leukaemia (AML), and the time to AML transformation
6. Duration of tefinostat therapy
7. Biological correlates including hCE-1 expression, changes in protein acetylation

Patients will receive tefinostat continuously for 6 continuous 4-week cycles (24 weeks). Secondary outcome measures will be assessed continuously over this period, including fortnightly peripheral blood assessment (full blood count, blood film/differential) and bone marrow assessments performed after 12 and 24 weeks of therapy.

## Completion date

26/07/2019

## Eligibility

### Key inclusion criteria

1. All CMML-2 patients are eligible
2. For patients classified as CMML-1, the following must be present:
  - 2.1. Symptomatic bone marrow failure / myeloproliferation defined as one or more of: red cell transfusion dependence with pre-transfusion Hb <90g/l symptomatic anaemia (Hb <115g/l) thrombocytopenia (platelets <50 x 10<sup>9</sup>/l) symptomatic bleeding due to platelet function defect or DIC/fibrinolysis white blood cell count >50 x 10<sup>9</sup>/l and/or
  - 2.2. CMML-specific Prognostic Score (CPSS) of intermediate-2 or high risk (16) (details of derivation of CPSS score given below) and/or
  - 2.3. Systemic symptoms including weight loss with no alternative explanation (10% of baseline

weight

within previous 6 months)

2.4. Symptomatic splenomegaly

2.5. Symptomatic extramedullary involvement, eg. skin infiltration, serous effusions

3. Subject is able and willing to sign the informed consent form

4. Age greater than or equal to 18 years at the time of signing the informed consent form

5. Willingness to undergo scheduled assessments as per the study protocol including bone marrow assessments

6. ECOG performance status of 0-2 at study entry

7. Women of childbearing potential must have a negative urine pregnancy test within 7 days prior to starting study drug

8. Women of childbearing potential must use at least two effective contraceptive methods throughout the study and for three months following the date of the last dose of study drug

9. Men whose partner is a woman of childbearing potential must use at least two effective contraceptive

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

Patient

### **Healthy volunteers allowed**

No

### **Age group**

Adult

### **Lower age limit**

18 Years

### **Sex**

All

### **Total final enrolment**

21

### **Key exclusion criteria**

1. CMML with eosinophilia and 5q33 abnormality

2. Previous chemotherapy for CMML except Hydroxycarbamide and 5-azacitidine

3. Creatinine concentration > 2x the institutional upper limit of normal range

4. Liver transaminases (AST / ALT) > 3x the institutional upper limit of normal range or serum bilirubin > 4x the institutional upper limit of normal range

5. Pregnant or lactating females

6. Use of experimental drug or therapy within 28 days of registration

7. Other malignancy within the last 3 years other than curatively-treated basal cell or squamous cell skin cancer, carcinoma in situ of the cervix, organ-confined or treated non-metastatic prostate cancer with negative prostate-specific antigen, in situ breast carcinoma after complete surgical resection, or superficial transitional cell bladder carcinoma

8. Known seropositivity for HIV infection or infectious hepatitis (type B or C)

9. Uncontrolled inter-current illness including, but not limited to, ongoing infection, psychiatric illness or social situation that the treating physician judges would limit compliance with study requirements

**Date of first enrolment**

01/09/2015

**Date of final enrolment**

21/09/2017

**Locations****Countries of recruitment**

United Kingdom

England

Scotland

Wales

**Study participating centre****Cardiff University**

Department of Haematology

Cardiff University

Heath Park

Cardiff

United Kingdom

CF14 4XN

**Study participating centre****University Hospital of Wales**

Heath Park Way

Cardiff

United Kingdom

CF14 4XW

**Study participating centre****St James's University Hospital**

Beckett Street

Leeds

United Kingdom

LS9 7TF

**Study participating centre****The Christie Hospital**

Wilmslow Road

Manchester  
United Kingdom  
M20 4BX

**Study participating centre**  
**Aberdeen Royal Infirmary**  
Foresterhill Health Campus  
Foresterhill Road  
Aberdeen  
United Kingdom  
AB25 2ZN

**Study participating centre**  
**Churchill Hospital**  
Old Road  
Oxford  
United Kingdom  
OX3 7LE

**Study participating centre**  
**Guy's Hospital**  
Great Maze Pond  
London  
United Kingdom  
SE1 9RT

**Study participating centre**  
**Beatson West of Scotland Cancer Centre**  
1053 Great Western Road  
Glasgow  
United Kingdom  
G12 0YN

**Study participating centre**  
**Ysbyty Gwynedd**  
Bangor  
United Kingdom  
LL57 2PW

**Study participating centre**  
**Bristol Haematology and Oncology Centre**  
Horfield Road  
Avon  
Bristol  
United Kingdom  
BS2 8ED

**Study participating centre**  
**Nottingham City Hospital**  
Hucknall Road  
Nottingham  
United Kingdom  
NG5 1PB

**Study participating centre**  
**Castle Hill Hospital**  
Castle Road  
Cottingham  
United Kingdom  
HU16 5JQ

**Study participating centre**  
**Kent and Canterbury Hospital**  
Ethelbert Road  
Canterbury  
United Kingdom  
CT1 3NG

**Study participating centre**  
**Freeman Hospital**  
Freeman Road  
High Heaton  
Newcastle upon Tyne  
United Kingdom  
NE7 7DN

**Sponsor information**

## Organisation

Cardiff University (UK)

## ROR

<https://ror.org/03kk7td41>

## Funder(s)

### Funder type

Charity

### Funder Name

Leukaemia and Lymphoma Research

### Alternative Name(s)

### Funding Body Type

Private sector organisation

### Funding Body Subtype

Other non-profit organizations

### Location

United Kingdom

## Results and Publications

### Individual participant data (IPD) sharing plan

Not provided at time of registration

### IPD sharing plan summary

Not expected to be made available

### Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Abstract results</a>	results presented at ASH	29/11/2018	21/07/2020	No	No
<a href="#">HRA research summary</a>			28/06/2023	No	No
<a href="#">Participant information sheet</a>		23/10/2018	23/10/2018	No	Yes
<a href="#">Plain English results</a>			23/06/2020	No	Yes
<a href="#">Protocol file</a>	version 3.0	28/03/2017	18/10/2022	No	No