

# ROMAZA: Phase I study of romidespin and azacitidine in acute myeloid leukaemia patients

<b>Submission date</b> 27/09/2013	<b>Recruitment status</b> No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 27/09/2013	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 18/06/2024	<b>Condition category</b> Cancer	<input type="checkbox"/> Individual participant data

## Plain English summary of protocol

<https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-looking-romidepsin-azacitidine-acute-myeloid-leukaemia-romaza>

## Contact information

### Type(s)

Scientific

### Contact name

Mrs Nadira Jilani

### Contact details

Centre for Clinical Haematology  
Queen Elizabeth Hospital  
Edgbaston  
Birmingham  
United Kingdom  
B15 2TH

-

romaza@trials.bham.ac.uk

## Additional identifiers

### EudraCT/CTIS number

2011-005023-40

### IRAS number

### ClinicalTrials.gov number

### Secondary identifying numbers

## Study information

### Scientific Title

ROMAZA: Phase I trial of combination therapy with romidepsin and azacitidine in patients with newly diagnosed, relapsed or refractory acute myeloid leukaemia ineligible for conventional chemotherapy

### Acronym

ROMAZA

### Study objectives

This is a phase I, multicentre, dose finding trial of the use of Romidepsin in combination with Azacitidine in patients with newly diagnosed, relapsed or refractory Acute Myeloid Leukaemia (AML).

#### Primary objective:

To determine the maximum tolerated dose (MTD) of Romidepsin in combination with Azacitidine.

#### Secondary objectives:

1. To determine the tolerability and safety of Romidepsin in combination with Azacitidine.
2. To determine the clinical activity of combined Romidepsin and Azacitidine treatment in patients with high risk AML.

### Ethics approval required

Old ethics approval format

### Ethics approval(s)

NRES Committee South Central Oxford C, First MREC approval date 08/05/2013, ref: 13/SC/0157

### Study design

Non-randomised interventional and observational; Design type: Treatment, Cohort study

### 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 use the contact details to request a patient information sheet

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

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

## Interventions

Patients with newly diagnosed, relapsed or refractory AML who are ineligible for conventional chemotherapy will be recruited to this trial. Up to 18 patients will be recruited to determine the MTD. Once the MTD has been determined an additional 12 patients will be recruited and treated at the MTD in order to gain further safety and efficacy data.

The MTD of Romidepsin in combination with Azacitidine will be determined using an escalating, de-escalating 3+3 cohort design. The first patients will be recruited to Cohort 1 of the study.

Patients will receive up to six cycles of the combination therapy (each cycle being 28 days). Each cycle of therapy will consist of Romidepsin infusion on days 8, 15 (and 22 if dose level 3) and seven consecutive days excluding the weekend of subcutaneous injections of Azacitidine, starting on day 1 of a 28 day cycle. The decision as to whether to escalate/de-escalate/expand the cohort will depend on the number of dose-limiting toxicities (DLTs) experienced.

There are five cohorts in total which will consist of differing strengths of doses for azacitidine and romidepsin depending on which cohort it is:

Cohort (-2): Dose [(Romidepsin (mg/m<sup>2</sup>): 8 mg/m<sup>2</sup> d8, 15; Azacitidine (mg/m<sup>2</sup>): 55 mg/m<sup>2</sup> d1-9 (5,2,2)]

Cohort (-1): Dose [(Romidepsin (mg/m<sup>2</sup>): 8 mg/m<sup>2</sup> d8, 15; Azacitidine (mg/m<sup>2</sup>): 75 mg/m<sup>2</sup> d1-9 (5,2,2)]

Cohort [1 (starting dose)]: Dose [(Romidepsin (mg/m<sup>2</sup>): 10 mg/m<sup>2</sup> d8, 15; Azacitidine (mg/m<sup>2</sup>): 75 mg/m<sup>2</sup> d1-9 (5,2,2)]

Cohort (2): Dose [(Romidepsin (mg/m<sup>2</sup>): 12 mg/m<sup>2</sup> d8, 15; Azacitidine (mg/m<sup>2</sup>): 75 mg/m<sup>2</sup> d1-9 (5,2,2)]

Cohort (3): Dose [(Romidepsin (mg/m<sup>2</sup>): 12 mg/m<sup>2</sup> d8, 15, 22; Azacitidine (mg/m<sup>2</sup>): 75 mg/m<sup>2</sup> d1-9 (5,2,2)]

## Intervention Type

Drug

## Phase

Phase I

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

Romidespin, azacitidine

## Primary outcome measure

Assessment of MTD of Romidepsin in combination with Azacitidine; Timepoint(s): Once six patients have been treated at the proposed MTD (provided DLT's did not occur in two or more)

## Secondary outcome measures

1. Assessment of tolerability and safety of Romidepsin in combination with Azacitidine (graded according to NCI CTCAE version 4) from the date of commencing treatment until 28 days following treatment discontinuation

2. Major response rate (CR, CRi and PR), as defined by Cheson criteria and assessed at the end of cycles 3 and 6 of treatment

**Overall study start date**

01/10/2013

**Completion date**

31/12/2019

## Eligibility

**Key inclusion criteria**

1. Adults (male & female aged  $\geq 16$  years) with newly diagnosed, relapsed or refractory AML (except Acute Promyelocytic Leukaemia (APML) as defined by the WHO classification scheme)
2. Patients deemed ineligible for conventional chemotherapy on the grounds of age or comorbidities
3. Patients able to receive treatment as an outpatient
4. Patients must have adequate renal and hepatic function as defined below:  
Total bilirubin  $\leq 2.5 \times$  upper limit of normal (ULN), aspartate aminotransferase / alanine aminotransferase (AST or ALT)  $\leq 2.5 \times$  ULN, estimated glomerular filtration rate (eGFR)  $\geq 40$ mls/min
5. Patients have given written informed consent
6. Be willing to comply with the protocol for the duration of the study
7. Eastern Cooperative Oncology Group (ECOG) performance status  $\leq 2$

**Participant type(s)**

Patient

**Age group**

Adult

**Sex**

Both

**Target number of participants**

Planned Sample Size: 30; UK Sample Size: 30

**Total final enrolment**

48

**Key exclusion criteria**

1. Patients with allergies or contraindications to Romidepsin or Azacitidine
2. Patients with greater than class 3 New York Heart Association (NYHA) cardiac impairment
3. Blastic transformation of chronic myeloid leukaemia (CML)
4. Pregnant or lactating women (women of childbearing potential must have a negative urine or serum pregnancy test within 7 days prior to registration)
5. Females of childbearing potential (i.e. not postmenopausal or surgically sterilised) who are not willing to use adequate methods of contraception to prevent pregnancy or abstain from heterosexual activity for the duration of the trial and for at least 3 months following treatment discontinuation. This includes females who are not willing to use additional methods of contraception in addition to oestrogen containing contraceptives
6. Male patients who are not willing to use an adequate method of contraception for the duration of the trial treatment if engaged in sexual activity with a female of childbearing

potential and for at least 3 months following treatment discontinuation

7. Patients with unstable angina, congenital long QT syndrome or a history of myocardial infarction (MI) within the last 6 months

8. Patients with concurrent active malignancy

9. Any co-morbidity that could limit compliance with the trial, including but not limited to the following:

9.1. Uncontrolled hypertension

9.2. Symptomatic congestive heart failure

9.3. Uncontrolled cardiac arrhythmia

9.4. Psychiatric or social conditions that may interfere with patients compliance or any other condition (including laboratory abnormalities) that in the Investigators opinion will affect the patients participation in this trial

10. Patients who have taken any other investigational medicinal product within 4 weeks of study entry

11. Active symptomatic fungal, bacterial, and/or viral infection including known human immunodeficiency virus (HIV) or known viral (A, B or C) Hepatitis

12. Patients who are high medical risks due to non-malignant systemic disease as well as those with active uncontrolled infection

**Date of first enrolment**

01/10/2013

**Date of final enrolment**

06/10/2017

## **Locations**

**Countries of recruitment**

England

United Kingdom

**Study participating centre**

**Queen Elizabeth Hospital**

Birmingham

United Kingdom

B15 2TH

## **Sponsor information**

**Organisation**

University of Birmingham (UK)

**Sponsor details**

Cancer Research UK Clinical Trials Unit

Institute for Cancer Studies

Edgbaston  
Birmingham  
England  
United Kingdom  
B15 2TT

**Sponsor type**

University/education

**Website**

<http://www.birmingham.ac.uk>

**ROR**

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

## **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**

**Publication and dissemination plan**

Not provided at time of registration

**Intention to publish date**

31/12/2020

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

The datasets generated during and/or analysed during the current study are/will be available upon request from the ROMA ZA mailbox ([romaza@trials.bham.ac.uk](mailto:romaza@trials.bham.ac.uk)). Data anonymised in

compliance with the Information Commissioners Office requirements, using a procedure based on guidelines from the Medical Research Council Methodology Hubs, will be available for sharing upon request from the Trial Management Group.

## IPD sharing plan summary

Available on request

## Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Results article</a>		06/09/2021	15/03/2022	Yes	No
<a href="#">HRA research summary</a>			28/06/2023	No	No