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

Submission date 27/09/2013	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 27/09/2013	**Overall study status** Completed	
Last Edited 18/06/2024	**Condition category** Cancer	

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

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Additional identifiers

Clinical Trials Information System (CTIS)
2011-005023-40

Protocol serial number
15082

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

Study type(s)
Treatment

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/m2): 8 mg/m2 d8, 15; Azacitidine (mg/m2): 55 mg/m2 d1-9 (5,2,2)]
Cohort (-1): Dose [(Romidepsin (mg/m2): 8 mg/m2 d8, 15; Azacitidine (mg/m2): 75 mg/m2 d1-9 (5,2,2)]
Cohort [1 (starting dose)]: Dose [(Romidepsin (mg/m2): 10 mg/m2 d8, 15; Azacitidine (mg/m2): 75 mg/m2 d1-9 (5,2,2)]
Cohort (2): Dose [(Romidepsin (mg/m2): 12 mg/m2 d8, 15; Azacitidine (mg/m2): 75 mg/m2 d1-9 (5,2,2)]
Cohort (3): Dose [(Romidepsin (mg/m2): 12 mg/m2 d8, 15, 22; Azacitidine (mg/m2): 75 mg/m2 d1-9 (5,2,2)]

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
Romidespin, azacitidine

Primary outcome(s)
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)

Key secondary outcome(s))
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

Completion date
31/12/2019

Eligibility

Key inclusion criteria
1. Adults (male & female aged ≥ 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 ≤ 2.5 x upper limit of normal (ULN), aspartate aminotransferase / alanine aminotransferase (AST or ALT) ≤ 2.5 x ULN, estimated glomerular filtration rate (eGFR) ≥40mls /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 ≤ 2

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

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
United Kingdom

England

Study participating centre
Queen Elizabeth Hospital
Birmingham
United Kingdom
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Sponsor information

Organisation
University of Birmingham (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

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 ROMAZA mailbox (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?
Results article		06/09/2021	15/03/2022	Yes	No
HRA research summary			28/06/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes