ISRCTN42054893 https://doi.org/10.1186/ISRCTN42054893

A study to determine the maximum tolerated dose and activity of the combination of romidepsin and carfilzomib in relapsed or refractory peripheral T-cell lymphoma

Submission date
11/12/2013

Recruitment status
No longer recruiting

Registration date
11/12/2013

Overall study status
Completed

Last Edited
04/12/2024

Condition category
Cancer

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol
http://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-looking-at-romidepsin-and-carfilzomib-for-people-with-peripheral-t-cell-lymphoma-that-has

Contact information

Type(s)
Scientific

Contact name
Ms Eszter Nagy

Contact details
Cancer Research UK Clinical Trials Unit
The University of Birmingham
Edgbaston
Birmingham
United Kingdom
B15 2TT
+44 (0)121 371 7862
romicar@trials.bham.ac.uk

Additional identifiers

EudraCT/CTIS number
2013-001879-20

IRAS number

ClinicalTrials.gov number
NCT03141203

Secondary identifying numbers
15553

Study information

Scientific Title
Phase I/II study to determine the maximum tolerated dose and activity of the combination of romidepsin and carfilzomib in relapsed or refractory peripheral T-cell lymphoma

Acronym
RomiCar

Study objectives
RomiCar is a prospective, single arm, multicentre phase I/II clinical trial for patients with relapsed or refractory peripheral T-cell lymphoma.

The following designs will be used in each phase:
Phase I: Continual Reassessment Method (CRM) to determine the Maximum Tolerated Dose (MTD) of the combination of romidepsin and carfilzomib.
Phase II: A'Hern's single stage design to assess the activity (best overall response rate (PR + CR)) of the combination of romidepsin and carfilzomib over 8 cycles of treatment.

Ethics approval required
Old ethics approval format

Ethics approval(s)
NRES Committee East Midlands - Northampton, 30/12/2013, ref:13/EM/0462

Study design
Non-randomized interventional treatment trial

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 contact details to request a participant information sheet

Health condition(s) or problem(s) studied
Peripheral T-cell lymphoma

Interventions
Carfilzomib, Proteasome inhibitor
Romidepsin, Histone deacetylase (HDAC) inhibitor

Romidepsin dose (days 1, 8, 15)
Dose level 1: 8 mg/m2
Dose level 2 (starting dose):10 mg/m2
Dose level 3: 10 mg/m2
Dose level 4: 12 mg/m2
Dose level 5: 12 mg/m2
Dose level 6: 14 mg/m2

Carfilzomib dose* (days 1, 2, 8, 9, 15, 16)
Dose level 1: 20/36 mg/m2
Dose level 2 (starting dose): 20/36 mg/m2
Dose level 3: 20/45 mg/m2
Dose level 4: 20/45 mg/m2
Dose level 5: 20/56 mg/m2
Dose level 6: 20/56 mg/m2

* For all dose levels, the carfilzomib dose will be 20 mg/m2 for the first 2 doses (i.e. day 1 and 2 of cycle 1), rising to the target dose for subsequent doses and cycles.

Patients in the phase II will receive the Maximum Tolerated Dose determined by phase I results. Treatment is intravenous and given in cycles (each lasting 28 days). Treatment is given on the days stated in the table above. Patients will receive treatment for 8 cycles and further cycles may be given at the investigator's discretion if the patient has not progressed. Follow-up is a minimum of 1 year.

Follow Up Length: 12 month(s)
Study Entry: Registration only

Intervention Type
Drug

Phase
Phase I/II

Drug/device/biological/vaccine name(s)
Romidepsin, carfilzomib

Primary outcome measure
Current primary outcome measures as of 11/06/2018:
1. Maximum Tolerated Dose (MTD) of the combination of romidepsin and carfilzomib (Phase I); Timepoint(s): Within 4 weeks of treatment with the combination
2. Best Overall Response Rate (Phase II); Timepoint(s): During 8 cycles of treatment with the combination

Previous primary outcome measures:
Maximum Tolerated Dose (MTD) of the combination of romidepsin and carfilzomib (Phase I); Timepoint(s): Within 4 weeks of treatment with the combination

Secondary outcome measures
Current secondary outcome measures as of 11/06/2018:
1. Best Overall Response Rate (Phase II); Timepoint(s): During treatment and until the end of the trial
2. Duration of response from time of first documented response until relapse or progression; Timepoint(s): From first response through to end of follow-up
3. Maximum % change in the radiological sum of the products of the diameters from baseline; Timepoint(s): During 8 cycles of combination treatment
4. Overall Survival; Timepoint(s): From baseline until the end of the trial
5. Progression Free Survival (Phase II); Timepoint(s): From baseline until the end of the trial
6. Toxicity of the combination of romidepsin and carfilzomib; Timepoint(s): During combination treatment

Previous secondary outcome measures:
1. Best Overall Response Rate (Phase II); Timepoint(s): During 8 cycles of treatment with the combination
2. Duration of response from time of first documented response until relapse or progression; Timepoint(s): From first response through to end of follow-up
3. Maximum % change in the radiological sum of the products of the diameters from baseline; Timepoint(s): During 8 cycles of combination treatment
4. Overall Survival; Timepoint(s): From baseline to 6, 12, 24 and 36 months
5. Progression Free Survival (Phase II); Timepoint(s): From baseline to 6, 12, 24 and 36 months
6. Toxicity of the combination of romidepsin and carfilzomib; Timepoint(s): During combination treatment

Overall study start date
13/07/2015

Completion date
23/09/2021

Eligibility

Key inclusion criteria
Current inclusion criteria as of 11/06/2018:
1. Aged ≥16 years
2. Life expectancy > 12 weeks
3. ECOG performance status ≤2
4. Relapsed or refractory* peripheral Tcell lymphoma including the following histologies: peripheral Tcelllymphoma not otherwise specified, angioimmunoblastic Tcell lymphoma, anaplastic large cell lymphoma, enteropathy associated Tcell lymphoma, extranodal NK/Tcell lymphoma, transformed mycosis fungoides, hepatosplenic Tcell lymphoma
5. Failed at least 1 prior therapy (but no upper limit of prior regimens)
6. Adequate haematopoietic reserve (Hb ≥ 9 g/dl, neutrophils ≥1.0x10(9)/l and platelets ≥100x10(9)/l or ≥75x10(9)/l if marrow involvement documented)
7. Adequate liver function (bilirubin ≤1.5 x upper limit of normal (ULN) (unless due to Gilbert's syndrome), AST / ALT ≤2x ULN)

8. Adequate renal function (creatinine clearance ≥ 20ml/min as assessed by Cockcroft and Gault calculation)
9. Serum potassium ≥ 3.8 mmol/l, calcium ≥ 2.2 mmol/l and magnesium ≥ LLN prior to trial entry (supplements permitted)
10. CT measurable disease with at least 1 lesion having short axis >1.5 cm or splenomegaly >14 cm in craniocaudal
length attributable to relapsed lymphoma
11. Ability to give informed consent
*For all relapsed patients, relapse must be confirmed by tissue biopsy (or bone marrow trephine if no other tissue available). For refractory patients, a biopsy must have been obtained within the last 6 months and preferably to confirm refractory disease. In rare cases (such as when re-biopsy is not possible), the initial diagnostic biopsy may be accepted, provided that the patient has been reviewed at the local MDT who agreed that the presentation is consistent with relapsed /refractory T cell lymphoma, and this has been documented.

Previous inclusion criteria:
1. Age ≥ 16 years of age
2. Life expectancy > 12 weeks
3. ECOG performance status ≤ 2
4. Relapsed or refractory* peripheral Tcell lymphoma including the following histologies: peripheral Tcelllymphoma not otherwise specified, angioimmunoblastic Tcell lymphoma, anaplastic large cell lymphoma, enteropathy associated Tcell lymphoma, extranodal NK/Tcell lymphoma, transformed mycosis fungoides, hepatosplenic Tcell lymphoma
5. Failed at least 1 prior therapy (but no upper limit of prior regimens)
6. Adequate haematopoietic reserve (Hb ≥ 9g/dl, neutrophils ≥ 1.0x109/l and platelets ≥ 100x109 /l or ≥ 75x109/l if marrow involvement documented)
7. Adequate liver function (bilirubin ≤ 1.5 x ULN, AST / ALT ≤ 2x ULN)
8. Adequate renal function (creatinine clearance ≥ 20ml/min as assessed by Cockcroft and Gault calculation)
9. Serum potassium ≥ 4.0 mmol/l, calcium ≥ 2.2 mmol/l and magnesium ≥ 0.85 mmol/l prior to trial entry
10. CT measurable disease with at least 1 lesion having short axis > 1.5cm or splenomegaly > 14cm in craniocaudal
length attributable to relapsed lymphoma
11. Ability to give informed consent
* For all relapsed patients, relapse must be confirmed by tissue biopsy (or bone marrow trephine if no other tissue available). For refractory patients, a biopsy must have been obtained within the last 6 months and preferably to confirm refractory disease.

Participant type(s)
Patient

Age group
Adult

Lower age limit
16 Years

Sex
Both

Target number of participants
Planned Sample Size: 58; UK Sample Size: 58

Total final enrolment
50

Key exclusion criteria
Current exclusion criteria as of 11/06/2018:
1. Persistent treatment related toxicities of CTCAE v4.0 grade ≥ 2
2. Previous treatment with histone deactylase inhibitor or proteasome inhibitor
3. Need for any other concurrent anticancer drug (apart from corticosteroids at a dose equivalent to prednisolone ≤7.5mg daily). A steroid prephase may be used but should be stopped by the first day of cycle 1.
4. Concurrent medical illness deemed by the investigator as uncontrolled and/or clinically significant
5. Coexisting active infection requiring parenteral antibiotics
6. Patients unable to swallow oral medication
7. Active infection with HIV, hepatitis B or hepatitis C
8. Radiotherapy* (except for palliative reasons), endocrine therapy, immunotherapy or use of other investigationalagents within 28 days prior to trial entry (or a longer period depending on the defined characteristics of the agents used, please contact the trials office for confirmation). *Limited field radiotherapy to an isolated lesion in bone or soft tissue must be completed 2 weeks prior to trial entry
9. Major surgery within 4 weeks of trial entry
10. Patients with proven CNS involvement
11. QTc interval of >450ms or patients taking medications that significantly prolong the QT interval
12. Clinically significant cardiac disease ≥ NYHA Class III, symptomatic ischaemia, conduction abnormalities uncontrolled by conventional intervention or myocardial infarction within 6 months of trial entry
13. Pregnant and lactating patients (patients of childbearing potential must have a negative pregnancy test prior to study entry and within 7 days prior to the start of treatment. Postmenopausal females (> 45 years old and without menstruation for > 1 year) and surgically sterilised females are exempt from a pregnancy test)
14. Patients and partners of childbearing potential not willing to use effective contraception during and for 3 months after therapy
15. Concurrent Pulmonary Hypertension
16. Left Ventricular Ejection Fraction (LVEF) of<40%
17. Patients taking any inhibitors or strong inducers of CYP3A4, with the exception of dexamethasone.
18. Previous systemic malignancy within the last 3 years unless treated with curative intent with no sign of recurrence. Other exceptions include non-melanotic skin cancer or carcinoma in-situ of the uterine cervix

Previous exclusion criteria:
1. Persistent treatment related toxicities of CTCAE v4.0 grade ≥ 2
2. Previous treatment with histone deactylase inhibitor or proteasome inhibitor
3. Need for any other concurrent anticancer drug (apart from corticosteroids at a dose equivalent to prednisolone ≤7.5mg daily). A steroid prephase may be used but should be stopped by the first day of cycle 1.
4. Concurrent medical illness deemed by the investigator as uncontrolled and/or clinically

significant
5. Coexisting active infection requiring parenteral antibiotics
6. Patients unable to swallow oral medication
7. Active infection with HIV, hepatitis B or hepatitis C
8. Radiotherapy* (except for palliative reasons), endocrine therapy, immunotherapy or use of other investigationalagents within 28 days prior to trial entry (or a longer period depending on the defined characteristics of the agents used, please contact the trials office for confirmation).
*Limited field radiotherapy to an isolated lesion in bone or soft tissue must be completed 2 weeks prior to trial entry
9. Major surgery within 4 weeks of trial entry
10. Patients with proven CNS involvement
11. QTc interval of ≥ 480ms or patients taking medications that significantly prolong the QT interval (Appendix 7)
12. Clinically significant cardiac disease ≥ NYHA Class III, symptomatic ischaemia, conduction abnormalities uncontrolled by conventional intervention or myocardial infarction within 6 months of trial entry
13. Pregnant and lactating patients (patients of childbearing potential must have a negative pregnancy test prior to study entry and within 7 days prior to the start of treatment. Postmenopausal females (> 45 years old and without menstruation for > 1 year) and surgically sterilised females are exempt from a pregnancy test)
14. Patients and partners of childbearing potential not willing to use effective contraception during and for 3 months after therapy

Date of first enrolment
13/07/2015

Date of final enrolment
31/08/2019

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Christie Hospital
Manchester
United Kingdom
M20 4BX

Study participating centre
Churchill Hospital
Oxford
United Kingdom
OX3 7LE

Study participating centre
Derriford Hospital
Plymouth
United Kingdom
PL6 8DH

Study participating centre
Clatterbridge Cancer Centre
Liverpool
United Kingdom
L7 8XP

Study participating centre
Leicester Royal Infirmary
Leicester
United Kingdom
LE1 5WW

Study participating centre
Nottingham City Hospital
Nottingham
United Kingdom
NG5 1PB

Study participating centre
The Royal Marsden Hospital
Sutton
United Kingdom
SM2 5PT

Study participating centre
Southampton General Hospital
Southampton
United Kingdom
SO16 6YD

Study participating centre
St Bartholomew's Hospital
London
United Kingdom
EC1A 7BE

Study participating centre
St James's University Hospital
Leeds
United Kingdom
LS9 7TF

Study participating centre
The Queen Elizabeth Hospital
Birmingham
United Kingdom
B15 2TH

Study participating centre
University College London Hospital
London
United Kingdom
NW1 2BU

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
-
RomiCar@trials.bham.ac.uk

Sponsor type

University/education

ROR
https://ror.org/03angcq70

Funder(s)

Funder type
Industry

Funder Name
Celgene Europe Ltd

Funder Name
Bloodwise

Alternative Name(s)

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
United Kingdom

Funder Name
Amgen

Alternative Name(s)
Amgen Inc., Applied Molecular Genetics Inc.

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
United States of America

Results and Publications

Publication and dissemination plan
To be confirmed at a later date

Intention to publish date
31/07/2023

Individual participant data (IPD) sharing plan
The datasets generated during the current study will be available upon request from the CRCTU' s Director's Committee (CRCTU-General@adf.bham.ac.uk) within 6 months after the publication of the outcome measures, unless the trial results are to be used as part of a regulatory submission where release of the data may be delayed or be subject to the approval of a third party. In addition, for trials with long-term follow-up primary outcome data (e.g. response) may be available before secondary outcome data (e.g. survival). Only scientifically sound proposals from appropriately qualified research groups will be considered for data and/or sample sharing. A data sharing agreement will cover the terms and conditions of the release of trial data and will include publication requirements, authorship and acknowledgements and obligations for the responsible use of data. An anonymised encrypted dataset will be transferred directly using a secure method and in accordance with the University of Birmingham's IT guidance on encryption of datasets.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Basic results		15/02/2023	16/02/2023	No	No
HRA research summary			28/06/2023	No	No
Plain English results			04/12/2024	No	Yes