

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	☒ Prospectively registered ☐ Protocol
Registration date 11/12/2013	Overall study status Completed	☐ Statistical analysis plan ☒ Results
Last Edited 04/12/2024	Condition category Cancer	☐ 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

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Additional identifiers

ClinicalTrials.gov (NCT)

NCT03141203

Clinical Trials Information System (CTIS)

2013-001879-20

Protocol serial number

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

Primary study design

Interventional

Study design

Non-randomized interventional treatment trial

Study type(s)

Treatment

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(s)

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

Key secondary outcome(s)

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

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 $\geq 1.0 \times 10^9$ /l and platelets $\geq 100 \times 10^9$ /l or $\geq 75 \times 10^9$ /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 ≤ 2 x ULN)
8. Adequate renal function (creatinine clearance ≥ 20 ml/min as assessed by Cockcroft and Gault calculation)
9. Serum potassium ≥ 3.8 mmol/l, calcium ≥ 2.2 mmol/l and magnesium $\geq$ 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 Tcell lymphoma 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 $\geq 1.0 \times 10^9$ /l and platelets $\geq 100 \times 10^9$ /l or $\geq 75 \times 10^9$ /l if marrow involvement documented)
 7. Adequate liver function (bilirubin $\leq 1.5 \times$ ULN, AST / ALT $\leq 2 \times$ ULN)
 8. Adequate renal function (creatinine clearance ≥ 20 ml/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 > 1.5 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.

Participant type(s)

Patient

Healthy volunteers allowed

No

Age group

Adult

Lower age limit

16 Years

Sex

All

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 deacetylase inhibitor or proteasome inhibitor
3. Need for any other concurrent anticancer drug (apart from corticosteroids at a dose equivalent to prednisolone ≤ 7.5 mg 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 investigational agents 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 $\geq$ 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 $\geq$ 2
2. Previous treatment with histone deacetylase inhibitor or proteasome inhibitor
3. Need for any other concurrent anticancer drug (apart from corticosteroids at a dose equivalent to prednisolone $\leq$ 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 investigational agents 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 $\geq$ 480ms or patients taking medications that significantly prolong the QT interval (Appendix 7)
12. Clinically significant cardiac disease $\geq$ 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

United Kingdom

England

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)

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

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