ISRCTN15028850 https://doi.org/10.1186/ISRCTN15028850

A randomised phase II trial of selinexor with cyclophosphamide and prednisolone in relapsed or refractory multiple myeloma (RRMM) patients

Submission date
05/03/2018

Recruitment status
No longer recruiting

Registration date
21/03/2018

Overall study status
Completed

Last Edited
28/10/2024

Condition category
Cancer

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

Plain English summary of protocol
https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-of-selinexor-cyclophosphamide-and-prednisolone-for-myeloma-muk-twelve#undefined

Contact information

Type(s)
Scientific

Contact name
Mr Saqib Saghir

ORCID ID
https://orcid.org/0000-0002-9209-1290

Contact details
Clinical Trials Research Unit
Leeds Institute of Clinical Trials Research
University of Leeds
Leeds
United Kingdom
LS2 9JT
+44 (0)113 343 1454
S.Saghir@leeds.ac.uk

Additional identifiers

Clinical Trials Information System (CTIS)

2017-001736-19

Protocol serial number
36466

Study information

Scientific Title
A randomised phase II trial of selinexor, cyclophosphamide and prednisone vs cyclophosphamide and prednisone in relapsed or refractory multiple myeloma (RRMM) patients

Acronym
MUK Twelve

Study objectives
This study is designed to compare a new combination of Selinexor, cyclophosphamide and prednisone, with cyclophosphamide and prednisone alone followed by SCP at disease progression.

Ethics approval required
Old ethics approval format

Ethics approval(s)
London – Hampstead Research Ethics Committee, 20/12/2017, ref: 17/LO/1847

Primary study design
Interventional

Study design
Randomised; Interventional; Design type: Treatment, Drug

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Relapsed or refractory multiple myeloma

Interventions
The trial is designed as a randomised, controlled, open, parallel group, multicentre phase II trial to evaluate the clinical efficacy of selinexor in combination with cyclophosphamide and prednisolone. A calibration group will receive cyclophosphamide plus prednisolone alone, and will be used to evaluate the validity of the outcome in the experimental group. Participants will be randomised on a 3:1 basis to receive either selinexor + cyclophosphamide + prednisolone (SCP) or cyclophosphamide + prednisolone (CP).

A maximum of 60 participants will be recruited (45 participants in the SCP arm, and 15 participants in the CP arm). Participants who experience disease progression on the CP arm may receive SCP, once progression has been confirmed by the CTRU and the participant has been

deemed eligible to receive SCP. Patients randomised to SCP have no further trial treatment stipulated following SCP therapy. The analysis of the treatment switch phase of the trial is exploratory.

SCP combination
Selinexor oral 100mg once a week – days 1 , 8 , 15 & 22
Cyclophosphamide oral 50mg once daily, starting on day 1
Prednisolone oral 30mg every other day, starting on day 1

CP combination
Cyclophosphamide oral 50mg once daily, starting on day 1
Prednisolone oral 30mg every other day, starting on day 1
Followed by SCP Combination
Selinexor oral 100mg once a week – days 1, 8, 15 & 22
Cyclophosphamide oral 50mg (or dose given previously) once daily, starting on day 1
Prednisolone oral 30mg (or dose given previously) every other day, starting on day 1

The final analysis will take place after all patients have been followed up for at least 6 months or have progressed on the first phase of treatment (whichever is sooner). Further analyses relating to the treatment switch phase of the trial will take place after all patients have been followed up for at least 6 months or have progressed (whichever is sooner).

Intervention Type
Drug

Phase
Phase II

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

Primary outcome(s)
Progression free survival at 6 months

Key secondary outcome(s)
1. Safety and toxicity, via adverse reactions and adverse events from consent until 28 days post last dose of trial treatment
2. Progression-free survival at 6 months or until disease progression, monitored via blood results
3. Maximum response, monitored via blood results throughout the trial
4. Time to maximum response, monitored via blood results throughout the trial
5. Duration of response, monitored via blood results throughout the trial
6. Compliance to therapy, measured at all stages of the trial

Completion date
14/11/2023

Eligibility

Key inclusion criteria
1. Able to give informed consent and willing to follow all trial protocol assessments
2. Aged 18 years or over

3. Participants with confirmed myeloma based on International Myeloma Working Group (IMWG) criteria
4. Measurable disease with at least one of the following:
4.1. Paraprotein ≥5g/L
4.2. Serum free light chains ≥100mg/L with abnormal ratio for light chain only myeloma
4.3. Bence Jones protein ≥200mg/24h
5. Participants with relapsed or relapsed refractory myeloma who have received ≥ 2 prior anti-myeloma treatments including a proteasome inhibitor and lenalidomide, and now require further treatment
6. Patients for which cyclophosphamide and prednisolone alone would be a suitable treatment
7. Eastern Cooperative Oncology Group (ECOG) performance status of ≤ 2
8. Female participants of childbearing potential must agree to use two methods of contraception (including one highly effective and one effective method of contraception, see section 11) and have a negative urine pregnancy test at screening. Male participants must use an effective barrier method of contraception if sexually active with a female of childbearing potential. For both male and female participants, effective methods of contraception must be used throughout the trial and for at least 12 months following the last dose of trial treatment
9. Required laboratory values are required at registration and within 14 days prior to randomisation:
9.1. Platelet count ≥50x109/L. Platelet count of 30-50 is acceptable if bone marrow aspirate or trephine shows tumour replacement of >50%. Platelet support is permitted within 14 days prior to randomisation, although platelet transfusions to help participants meet eligibility criteria are not allowed within 72 hours prior to the blood sample to confirm protocol eligibility
9.2. Absolute neutrophil count ≥1.0 x 109/L. Growth factor support is not permitted within 14 days prior to randomisation
9.3. Haemoglobin ≥ 80 g/L. Blood support is permitted
9.4. Alanine transaminase (ALT) and / or aspartate transaminase (AST) ≤3 x upper limit of normal
9.5. Creatinine clearance ≥ 20 ml/min (using Cockcroft Gault formula)
9.6. Bilirubin ≤1.5 x upper limit of normal. Suspected Gilberts syndrome patients must have a total bilirubin ≤3 x upper limit of normal

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
All

Total final enrolment
66

Key exclusion criteria

Current exclusion criteria as of 23/06/2022:
1. The following participants will be excluded:
1.1. Those with non-measurable disease
1.2. Those with a solitary bone or solitary extramedullary plasmacytoma
1.3. Plasma cell leukaemia
2. Participants with a history of malignancy (other than myeloma) within 5 years before the date of registration (exceptions are squamous and basal cell carcinomas of the skin, carcinoma in situ of the cervix or breast, or other non-invasive lesion that, in the opinion of the investigator, with concurrence with the Chief Investigator, is considered cured with minimal risk of recurrence within 5 years)
3. Participants with a known or underlying uncontrolled concurrent illness that, in the investigator's opinion, would make the administration of the study drug hazardous or circumstances that could limit compliance with the study, including, but not limited to the following:
3.1. Acute or chronic graft versus host disease
3.2. Uncontrolled hypertension
3.3. Symptomatic congestive heart failure
3.4. Unstable angina pectoris
3.5. Myocardial infarction within past 6 months
3.6. Uncontrolled cardiac arrhythmia (CTCAE grade >2)
3.7. Active symptomatic fungal, bacterial, and/or viral infection including known active HIV or known viral (A, B or C) hepatitis
3.8. Psychiatric or social conditions that may interfere with participant compliance
3.9. Uncontrolled (i.e., clinically unstable) infection requiring parenteral antibiotics, antivirals, or antifungals within one week prior to first dose; however, prophylactic use of these agents is acceptable even if parenteral
3.10. Ocular herpes simplex
3.11. Any other condition (including laboratory abnormalities) that in the opinion of the Investigator places the participant at unacceptable risk for adverse outcome if he/she were to participate in the study
4. Participants who have previously received Selinexor or any other selective inhibitor of Nuclear Export (SINE) compound
5. Previous anti-tumour therapies including investigational medicinal products at any dose within 28 days before the start of protocol treatment. (NB: Prednisone up to a dose of 175 mg per week may be given between screening and the beginning of treatment if medically required but should be stopped before trial treatment starts. Other steroids are not permitted. Bisphosphonates for bone disease are also permitted)
6. Participants with a history of a refractory nausea, diarrhoea, vomiting, malabsorption, gastrointestinal surgery or other procedures or conditions that might, in the opinion of the Investigator, interfere with the absorption or swallowing of the study drug(s)
7. Female participants who are lactating or have a positive pregnancy test at screening
8. Known allergy or intolerance to any of the study medications, their analogues, or excipients in the various formulations of any agent that would prevent participant receiving these as directed in the protocol.
9. Major surgery within 14 days prior to randomisation
10. Radiotherapy within 7 days prior to randomisation for palliative pain control or therapeutic radiotherapy within 14 days prior to randomisation
11. Myeloma involving the Central Nervous System

Previous exclusion criteria:
1. The following participants will be excluded:
1.1. Those with non-measurable disease

1.2. Those with a solitary bone or solitary extramedullary plasmacytoma
1.3. Plasma cell leukaemia
2. Participants with a history of malignancy (other than myeloma) within 5 years before the date of randomisation (exceptions are squamous and basal cell carcinomas of the skin, carcinoma in situ of the cervix or breast, or other non-invasive lesion that, in the opinion of the investigator, with concurrence with the Chief Investigator, is considered cured with minimal risk of recurrence within 5 years)
3. Participants with a known or underlying uncontrolled concurrent illness that, in the investigator's opinion, would make the administration of the study drug hazardous or circumstances that could limit compliance with the study, including, but not limited to the following:
3.1. Acute or chronic graft versus host disease
3.2. Uncontrolled hypertension
3.3. Symptomatic congestive heart failure
3.4. Unstable angina pectoris
3.5. Myocardial infarction within past 6 months
3.6. Uncontrolled cardiac arrhythmia
3.7. Active symptomatic fungal, bacterial, and/or viral infection including known active HIV or known viral (A, B or C) hepatitis
3.8. Psychiatric or social conditions that may interfere with participant compliance
3.9. Uncontrolled (i.e., clinically unstable) infection requiring parenteral antibiotics, antivirals, or antifungals within one week prior to first dose; however, prophylactic use of these agents is acceptable even if parenteral
3.10. Any other condition (including laboratory abnormalities) that in the opinion of the Investigator places the participant at unacceptable risk for adverse outcome if he/she were to participate in the study
4. Participants who have previously received Selinexor
5. Previous anti-tumour therapies including investigational medicinal products at any dose within 28 days before the start of protocol treatment. (NB: Prednisone up to a dose of 175 mg per week may be given between screening and the beginning of treatment if medically required but should be stopped before trial treatment starts. Bisphosphonates for bone disease are also permitted)
6. Participants with a history of a refractory nausea, diarrhoea, vomiting, malabsorption, gastrointestinal surgery or other procedures or conditions that might, in the opinion of the Investigator, interfere with the absorption or swallowing of the study drug(s)
7. Female participants who are lactating or have a positive pregnancy test at screening
8. Known allergy or intolerance to any of the study medications, their analogues, or excipients in the various formulations of any agent
9. Major surgery within 14 days prior to randomisation
10. Radiotherapy within 7 days prior to randomisation for palliative pain control or therapeutic radiotherapy within 14 days prior to randomisation
11. Chemotherapy or immunotherapy or any other anticancer therapy within 2 weeks prior to Cycle 1 Day 1 or radio-immunotherapy 4 weeks prior to Cycle 1 Day 1 (except steroids in the doses outlined above)
12. Myeloma involving the Central Nervous System

Date of first enrolment
20/06/2018

Date of final enrolment
30/05/2021

Locations

Countries of recruitment
United Kingdom

England

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

Study participating centre
St Bart's Hospital
West Smithfield
London
United Kingdom
EC1A 7BE

Study participating centre
Hammersmith Hospital - Imperial
Imperial College Healthcare NHS Trust
Du Cane Road
London
United Kingdom
W12 0HS

Study participating centre
Royal Stoke University Hospital
Cancer Clinical Trials
Cancer Centre
Newcastle Road
Stoke-on-Trent
United Kingdom
ST4 6QG

Study participating centre
Royal Hallamshire Hospital
Glossop Road

Sheffield
United Kingdom
S10 2JF

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

Study participating centre
Worthing Hospital - University Hospitals Sussex
Lyndhurst Road
Worthing
United Kingdom
BN11 2DH

Study participating centre
St Richards Hospital - University Hospitals Sussex
Spitalfield Lane
Chichester
United Kingdom
PO19 6SE

Study participating centre
Birmingham Heartlands Hospital
Bordesley Green East
Birmingham
United Kingdom
B9 5SS

Study participating centre
Guys & St Thomas Hospital
Guy's Hospital
Great Maze Pond
London
United Kingdom
SE1 9RT

Study participating centre
Royal Bournemouth Hospital
Clinical Trial Office
Castle Lane East
Bournemouth
United Kingdom
BH7 7DW

Study participating centre
Clatterbridge Cancer Centre
Clatterbridge Road
Wirral
United Kingdom
CH63 4JY

Study participating centre
Norfolk and Norwich University Hospital
Colney Lane
Norwich
United Kingdom
NR4 7UY

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

Sponsor information

Organisation
University of Leeds

ROR
https://ror.org/024mrxd33

Funder(s)

Funder type
Charity

Funder Name
Myeloma UK; Grant Codes: HM17/95228

Alternative Name(s)
Myeloma United Kingdom

Funding Body Type
Government organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
De-identified individual participant data datasets generated and/or analysed during the current study will be available upon request from the Clinical Trials Research Unit, University of Leeds (contact CTRU-DataAccess@leeds.ac.uk in the first instance). Data will be made available at the end of the trial, i.e. usually when all primary and secondary endpoints have been met and all key analyses are complete. Data will remain available from then on for as long as CTRU retains the data.
CTRU makes data available by a 'controlled access' approach. Data will only be released for legitimate secondary research purposes, where the Chief Investigator, Sponsor and CTRU agree that the proposed use has scientific value and will be carried out to a high standard (in terms of scientific rigour and information governance and security), and that there are resources available to satisfy the request. Data will only be released in line with participants' consent, all applicable laws relating to data protection and confidentiality, and any contractual obligations to which the CTRU is subject. No individual participant data will be released before an appropriate agreement is in place setting out the conditions of release. The agreement will govern data retention, usually stipulating that data recipients must delete their copy of the released data at the end of the planned project.
The CTRU encourages a collaborative approach to data sharing, and believe it is best practice for researchers who generated datasets to be involved in subsequent uses of those datasets. Recipients of trial data for secondary research will also receive data dictionaries, copies of key trial documents and any other information required to understand and reuse the released datasets.
The conditions of release for aggregate data may differ from those applying to individual participant data. Requests for aggregate data should also be sent to the above email address to discuss and agree suitable requirements for release.

IPD sharing plan summary

Available on request, Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article	version 1.0	26/10/2022	27/10/2022	Yes	No
Basic results			28/10/2024	No	No
HRA research summary			28/06/2023	No	No