

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

<b>Submission date</b> 05/03/2018	<b>Recruitment status</b> No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol
<b>Registration date</b> 21/03/2018	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 28/10/2024	<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-of-selinexor-cyclophosphamide-and-prednisolone-for-myeloma-muk-twelve#undefined>

## Contact information

### Type(s)

Scientific

### Contact name

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## 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

**Study design**

Randomised; Interventional; Design type: Treatment, Drug

**Primary study design**

Interventional

**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  $\geq 5\text{g/L}$
  - 4.2. Serum free light chains  $\geq 100\text{mg/L}$  with abnormal ratio for light chain only myeloma
  - 4.3. Bence Jones protein  $\geq 200\text{mg/24h}$
5. Participants with relapsed or relapsed refractory myeloma who have received  $\geq 2$  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  $\leq 2$
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  $\geq 50 \times 10^9/\text{L}$ . 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  $\geq 1.0 \times 10^9/\text{L}$ . Growth factor support is not permitted within 14 days prior to randomisation
  - 9.3. Haemoglobin  $\geq 80 \text{ g/L}$ . Blood support is permitted
  - 9.4. Alanine transaminase (ALT) and / or aspartate transaminase (AST)  $\leq 3 \times$  upper limit of normal
  - 9.5. Creatinine clearance  $\geq 20 \text{ ml/min}$  (using Cockcroft Gault formula)
  - 9.6. Bilirubin  $\leq 1.5 \times$  upper limit of normal. Suspected Gilberts syndrome patients must have a total bilirubin  $\leq 3 \times$  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/024mrx33>

## **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](mailto: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?
<a href="#">Protocol article</a>		26/10/2022	27/10/2022	Yes	No
<a href="#">Basic results</a>	version 1.0		28/10/2024	No	No
<a href="#">HRA research summary</a>			28/06/2023	No	No