ISRCTN58227268 https://doi.org/10.1186/ISRCTN58227268

# Cyclophosphamide and dexamethasone in combination with Ixazomib, in relapsed or refractory multiple myeloma (RRMM) patients who have relapsed after treatment with thalidomide, lenolidomide and bortezomib

| | | |
|---|---|---|
| **Submission date**<br>26/08/2015 | **Recruitment status**<br>No longer recruiting | [X] Prospectively registered<br>[X] Protocol<br>[_] Statistical analysis plan<br>[X] Results<br>[_] Individual participant data |
| **Registration date**<br>26/08/2015 | **Overall study status**<br>Completed | |
| **Last Edited**<br>28/05/2026 | **Condition category**<br>Cancer | |

**Plain English summary of protocol**
https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-of-cyclophosphamide-dexamethasone-and-ixazomib-for-myeloma-muk-8

## Contact information

**Type(s)**
Scientific

**Contact name**
Dr S N Roberts

**Contact details**
Leeds Institute of Clinical Trials Research
Level 10 Worsley Building
University of Leeds
Leeds
United Kingdom
LS2 9JT
-
ctru_mukseven@leeds.ac.uk

## Additional identifiers

**ClinicalTrials.gov (NCT)**
NCT02461888

### Clinical Trials Information System (CTIS)
2014-004511-36

### Integrated Research Application System (IRAS)
167060

### Central Portfolio Management System (CPMS)
19412

# Study information

### Scientific Title
A randomised Phase II trial of cyclophosphamide and dexamethasone in combination with Ixazomib, in relapsed or refractory multiple myeloma (RRMM) patients who have relapsed after treatment with thalidomide, lenolidomide and bortezomib.

### Acronym
MUK Eight

### Study objectives
The aim of this study is to run a phase II trial of cyclophosphamide and dexamethasone in combination with Ixazomib (MLN9708), in relapsed or refractory multiple myeloma (RRMM) patients who have relapsed after treatment with thalidomide, lenalidomide and bortezomib.

### Ethics approval required
Old ethics approval format

### Ethics approval(s)
North West-Liverpool East, 12/06/2015, ref: 15/NW/0416

### Primary study design
Interventional

### Study design
Randomized; Interventional; Design type: Treatment

### Study type(s)
Treatment

### Health condition(s) or problem(s) studied
Myeloma

### Interventions
Participants will be randomised to receive either ICD (ixazomib, cyclophosphamide and dexamethasone) or CD (cyclophosphamide and dexamethasone). All cycles of treatment consist of 28 days and treatment will continue until disease progression death, unacceptable toxicity or withdrawal of consent, whichever is sooner.

### Intervention Type

Other

### Primary outcome(s)
To evaluate whether ICD has improved clinical activity compared to CD in patients with RRMM

### Key secondary outcome(s)
1. To further evaluate the clinical activity of ICD with regard to additional secondary endpoints
2. To determine the safety and toxicity profile of ICD
3. To determine the cost-effectiveness of ICD compared to CD
4. To determine quality of life with ICD
5. To assess the impact of baseline Charlson index score on
6. Outcomes and deliverability of treatment

### Completion date
10/03/2026

## Eligibility

### Key inclusion criteria
1. Able to give informed consent and willing to follow study protocol assessments
2. Aged 18 years or over
3. Participants with confirmed MM based on IMWG criteria, 2009
4. Measurable disease with at least one of the following:
4.1. Paraprotein >5g/L or 0.5 g/l for IgD subtype;
4.2. Serum-free light chains >100mg/L with abnormal radio for light chain only myeloma;
4.3. Bence Jones protein >200mg/L
5. Participants with relapsed or relapsed refractory myeloma and now require further treatment following exposure to thalidomide, lenalidomide and bortezomib regardless of response to these
6. ECOG Performance Status = 2
7. Required laboratory values within 14 days prior to Randomisation:
7.1. -Platelet count =50x109/L. Platelet count of 30-50 is acceptable if bone marrow aspirate shows tumour replacement of >50%. Platelet support is permitted within 14 days prior to randomisation although platelet transfusions to help patients meet eligibility criteria are not allowed within 72 hours prior to the blood sample to confirm protocol eligibility
7.2. -Absolute neutrophil count =1.0 x 109/L. Growth factor support is not permitted within 14 days prior to randomisation
7.3. Haemoglobin > 9 g/dL. Blood support is permitted
-7.4. ALT and / or AST =3 x upper limit of normal
7.5. -Creatinine clearance = 30 ml/min (using Cockcroft Gault formula)
7.6. -Bilirubin =1.5 x upper limit of normal
8. Female participants should avoid becoming pregnant and male participants should avoid impregnating a female partner. Both non-sterilised and sterilised females and males of reproductive age should use effective methods of contraception during the entire trial treatment (including treatment breaks) and up to 90 days after the last dose of trial treatment
9. Post-allograft patients may be included if >12 months from transplant

### Participant type(s)
Patient

### Healthy volunteers allowed

No

## Age group
Mixed

## Lower age limit
18 Years

## Upper age limit
100 Years

## Sex
All

## Total final enrolment
112

## Key exclusion criteria
1.Those with non-measurable disease, a solitary bone or solitary extramedullary plasmacytoma, Plasma cell leukaemia
2. Prior malignancy other than those treated with surgery.
3. Participants with a known or underlying uncontrolled concurrent illness that, in the investigators 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: acute or chronic graft versus host disease, uncontrolled hypertension, symptomatic congestive heart failure, unstable angina pectoris, myocardial infarction within past 6 months, uncontrolled cardiac arrhythmia, renal failure, psychiatric or social conditions that may interfere with participant compliance, or 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. Patients who have previously received Ixazomib or MLN9708 in a trial. Previous experimental agents or approved anti-tumour treatment within 30 days before the date of randomisation.
5. A maximum of 160mg of dexamethasone (in 40mg blocks) 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 and radiotherapy for palliative intent are also permitted.
6. Participants with a history of a refractory nausea, diarrhoea, vomiting, malabsorption, gastrointestinal surgery or other procedures that might, in the opinion of the Investigator, interfere with the absorption or swallowing of the study drug(s)
7. Peripheral neuropathy of = grade 2 (or grade 1 with pain) severity (as per NCI-CTCAEv4.0)
8. Gastrointestinal disorders that may interfere with absorption of the study drug
9. Active symptomatic fungal, bacterial, and/or viral infection including known active HIV or known viral (A, B or C) hepatitis
10. Female patients who are lactating or have a positive pregnancy test during the screening period
11. Known allergy to any of the study medications, their analogues, or excipients in the various formulations of any agent
12. Systemic treatment, within 14 days before the first dose of Ixazomib, with strong inhibitors of CYP1A2 (fluvoxamine, enoxacin, ciprofloxacin), strong inhibitors of CYP3A (clarithromycin, telithromycin, itraconazole, voriconazole, ketoconazole, nefazodone, posaconazole) or strong CYP3A inducers (rifampin, rifapentine, rifabutin, carbamazepine, phenytoin, phenobarbital), or

use of Ginkgo biloba or St. John’s wort
13. Major surgery within 14 days prior to the date of randomisation
14. Radiotherapy within 7 days for palliative pain control or therapeutic radiotherapy within 14 days prior to randomisation
15. Myeloma involving the Central Nervous System

### Date of first enrolment
01/10/2015

### Date of final enrolment
01/09/2017

## Locations

### Countries of recruitment
United Kingdom

England

Wales

### Study participating centre
**St James Hospital (lead centre)**
Beckett St, Harehills
Leeds
England
LS9 7TF

### Study participating centre
**St Bartholomew’s Hospital**
W Smithfield
London
England
EC1M 6BQ

### Study participating centre
**Bristol Haematology and Oncology Centre**
Horfield Rd
Avon
Bristol
England
BS2 8ED

**Study participating centre**
**The Christie NHS Foundation Trust**
550 Wilmslow Rd
Manchester
England
M20 4BX

**Study participating centre**
**Guys & St Thomas' NHS Foundation Trust**
Westminster Bridge Road
London
England
SE1 9RT

**Study participating centre**
**Birmingham Heartlands Hospital**
Bordesley Green East
Bordesley Green
Birmingham
England
B9 5SS

**Study participating centre**
**Imperial College Healthcare NHS Trust**
The Bays
St Marys Hospital
South Wharf Road
London
England
W2 1BL

**Study participating centre**
**Nottingham University Hospital**
Derby Rd
Nottingham
England
NG7 2UH

**Study participating centre**
**Churchill Hospital**
Old Road

Headington
Oxford
England
OX3 7LE

**Study participating centre**
**Queen Elizabeth Hospital**
Queen Elizabeth Medical Centre
Birmingham
England
B15 2TH

**Study participating centre**
**Royal Liverpool University Hospital**
Prescot Street
Liverpool
England
L7 8XP

**Study participating centre**
**The Royal Marsden NHS Foundation Trust**
Downs Rd
Sutton
England
SM2 5PT

**Study participating centre**
**Royal Hallamshire Hospital**
Glossop Rd
Sheffield
England
S10 2SJ

**Study participating centre**
**Southampton General Hospital**
Tremona Rd
Southampton
England
SO16 6YD

**Study participating centre**
**Singleton Hospital**
Sketty Ln
Sketty
Swansea
Wales
SA2 8QA

**Study participating centre**
**University College London**
250 Euston Road
London
England
NW1 2PG

**Study participating centre**
**New Cross Hospital**
Wednesfield Rd
Wolverhampton
England
WV10 0QP

# Sponsor information

**Organisation**
University of Leeds

**ROR**
https://ror.org/024mrxd33

# Funder(s)

**Funder type**
Charity

**Funder Name**
Myeloma UK

**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
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

### Study outputs

| Output type | Details | Date created | Date added | Peer reviewed? | Patient-facing? |
|---|---|---|---|---|---|
| Results article | | 01/04/2022 | 04/04/2022 | Yes | No |
| Results article | | 01/04/2022 | 07/08/2025 | Yes | No |
| Protocol article | | 02/10/2020 | 07/10/2020 | Yes | No |

| | | | | |
|---|---|---|---|---|
| Abstract results | 17/04/2022 | 12/09/2023 | No | No |
| HRA research summary | | 28/06/2023 | No | No |
| Plain English results | | 12/02/2025 | No | Yes |
| Poster results | 17/04/2022 | 12/09/2023 | No | No |