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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 26/08/2015	**Recruitment status** No longer recruiting	[X] Prospectively registered [X] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 26/08/2015	**Overall study status** Ongoing	
Last Edited 20/06/2025	**Condition category** 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

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Additional identifiers

EudraCT/CTIS number
2014-004511-36

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
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

Study design
Randomized; Interventional; Design type: Treatment

Primary study design
Interventional

Secondary study design
Randomised controlled trial

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
Topic: Cancer; Subtopic: Haematological Oncology; Disease: 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

Phase
Phase II

Primary outcome measure
To evaluate whether ICD has improved clinical activity compared to CD in patients with RRMM

Secondary outcome measures
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

Overall study start date
01/09/2015

Completion date
30/06/2026

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

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
Planned Sample Size: 250; UK Sample Size: 250

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
England

United Kingdom

Wales

Study participating centre
St James Hospital (lead centre)
Leeds
United Kingdom
LS9 7TF

Study participating centre
St Bartholomew's Hospital
London
United Kingdom
EC1M 6BQ

Study participating centre

Bristol Haematology and Oncology Centre
Horfield Rd
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Bristol
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BS2 8ED

Study participating centre
The Christie NHS Foundation Trust
550 Wilmslow Rd
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United Kingdom
M20 4BX

Study participating centre
Guys & St Thomas' NHS Foundation Trust
London
United Kingdom
SE1 9RT

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

Study participating centre
Imperial College Healthcare
London
United Kingdom
SW7 9RT

Study participating centre
Nottingham University Hospital
Derby Rd
Nottingham
United Kingdom
NG7 2UH

Study participating centre
Churchill Hospital
Oxford
United Kingdom
OX3 7LE

Study participating centre
Queen Elizabeth Hospital
Queen Elizabeth Medical Centre
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United Kingdom
B15 2TH

Study participating centre
Royal Liverpool University Hospital
Prescot Street
Liverpool
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Study participating centre
The Royal Marsden NHS Foundation Trust
Downs Rd
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SM2 5PT

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

Study participating centre
Southampton General Hospital
Tremona Rd

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Study participating centre
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SA2 8QA

Study participating centre
University College London
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Study participating centre
New Cross Hospital
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Sponsor information

Organisation
University of Leeds

Sponsor details
Clinical Trials Research Unit
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LS2 9PH

Sponsor type

University/education

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

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

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?
Protocol article	protocol	02/10/2020	07/10/2020	Yes	No
Results article		01/04/2022	04/04/2022	Yes	No
HRA research summary			28/06/2023	No	No
Abstract results	P11	17/04/2022	12/09/2023	No	No
Poster results		17/04/2022	12/09/2023	No	No
Plain English results			12/02/2025	No	Yes