

# Myeloma XII (ACCoRd trial)

<b>Submission date</b> 28/11/2016	<b>Recruitment status</b> No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol
<b>Registration date</b> 15/12/2016	<b>Overall study status</b> Ongoing	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 10/09/2024	<b>Condition category</b> Cancer	<input type="checkbox"/> Individual participant data

## Plain English summary of protocol

<http://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-looking-at-ixazomib-for-people-with-myeloma-that-has-come-back-myeloma-xii-accord>

## Contact information

### Type(s)

Scientific

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## Additional identifiers

### EudraCT/CTIS number

2016-000905-35

### IRAS number

### ClinicalTrials.gov number

### Secondary identifying numbers

32907

## Study information

**Scientific Title**

Myeloma XII (ACCoRd): A phase III study to determine the role of ixazomib as an augmented conditioning therapy in salvage autologous stem cell transplant (ASCT) and as a post-ASCT consolidation and maintenance strategy in patients with relapsed multiple myeloma

**Acronym**

ACCoRd

**Study objectives**

This trial aims to determine and compare:

1. The depth of response between standard melphalan conditioning and augmented (adding ixazomib) melphalan conditioning at second ASCT
2. The impact of adding consolidation and maintenance treatment versus no further treatment, on progression free survival

**Ethics approval required**

Old ethics approval format

**Ethics approval(s)**

North West - Greater Manchester South Research Ethics Committee, 11/10/2016, ref: 16/NW/0517

**Study design**

Randomised; Interventional; Design type: Treatment, Drug

**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 the contact details to request a patient information sheet

**Health condition(s) or problem(s) studied**

Multiple myeloma

**Interventions**

Participants are randomised in a 1:1 ratio to receive 2 cycles ITD.

ITD re-induction therapy

All participants will be registered at trial entry and will receive re-induction therapy with 4-6 cycles of ixazomib, thalidomide, and dexamethasone (ITD), as per the dosing regimen below:

Cycles 1-6 of ITD re-induction (28-day cycles)

Ixazomib: 4mg/day on days 1, 8, 15, taken orally

Thalidomide: 100mg/day on days 1-28, taken orally

Dexamethasone: 40mg/day on days 1, 8, 15, 22, taken orally

Response assessment after ITD re-induction to determine eligibility for Randomisation 1, according to International Myeloma Working Group criteria.

#### Randomisation 1

Eligible participants who reach at least stable disease after ITD re-induction will be randomised on a 1:1 basis to receive either (a) conventional autologous stem cell transplant (ASCT-con) using melphalan, or (b) augmented autologous stem cell transplant (ASCT-aug) using melphalan with ixazomib. Dosing regimens below:

ASCT-con:

Melphalan 200mg/m<sup>2</sup>/day on D-1, intravenously

ASCT on D0

ASCT-aug:

Ixazomib 4mg/day on D-4 and D-1, taken orally

Melphalan 100mg/m<sup>2</sup>/day on D-3 and D-2, intravenously

ASCT on D0

Response assessment 100 days after ASCT-con or ASCT-aug to determine eligibility for Randomisation 2, according to International Myeloma Working Group criteria.

#### Randomisation 2 (R2)

Eligible participants who reach at least minimum response 100 days after ASCT-con or ASCT-aug will be randomised on a 1:1 basis to receive either (a) ITD consolidation and ixazomib maintenance, or (b) no further therapy. If participants are randomised to receive further therapy, the dosing regimens are below:

2 cycles of ITD consolidation (28-day cycles):

Ixazomib: 4mg/day on days 1, 8, 15, taken orally

Thalidomide: 100mg/day on days 1-28, taken orally

Dexamethasone: 40mg/day on days 1, 8, 15, 22, taken orally

Ixazomib maintenance, taken until disease progression (28-day cycles):

Ixazomib: 4mg/day on days 1, 8, 15, taken orally

For participants randomised to further therapy at R2, follow-up will be done at the end of consolidation and subsequently at 3-monthly intervals (starting from 3 months post-R2). For participants randomised to no further therapy at R2, follow-up will be done at 8 weeks post-R2 and subsequently 3-monthly visits (starting from 3 months post R2) thereafter until disease progression. Following disease progression, follow-up will be done annually post-progression until death.

#### Intervention Type

Drug

#### Phase

Phase III

## **Drug/device/biological/vaccine name(s)**

Ixazomib, thalidomide, dexamethasone, melphalan

## **Primary outcome measure**

All outcome measures are measured at baseline, the end of each re-induction cycle, the end of re-induction, 100 days post-ASCT, the end of consolidation, 8 weeks post-randomisation 2, 3 monthly post randomisation-2 until disease progression and at the time of disease progression:

1. Overall response rate following ASCT, defined as the impact on Depth of Response (DoR: <VGPR vs. ≥VGPR) when salvage ASCT conditioning is augmented by the addition of a proteasome inhibitor, will be determined according to the IMWG Uniform Response Criteria for Multiple Myeloma
2. Progression-free survival, is defined as the time from randomisation to the consolidation part of the trial to first documented evidence of disease progression or death from any cause. Participants who do not progress will be censored at the last date they were known to be alive and progression free

## **Secondary outcome measures**

All outcome measures are measured at baseline, the end of each re-induction cycle, the end of re-induction, 100 days post-ASCT, the end of consolidation, 8 weeks post-randomisation 2, 3 monthly post randomisation-2 until disease progression and at the time of disease progression:

1. Overall survival is defined as the time from randomisation to the consolidation/ maintenance part of the trial post-ASCT to death from any cause or last follow-up
2. Time to disease progression is defined as time from randomisation to the consolidation/ maintenance part of the trial post-ASCT to first documented evidence of disease progression. Participants who die without disease progression will be censored in the analysis.
3. Overall response rate following re-induction will be determined according to the IMWG Uniform Response Criteria for Multiple Myeloma
4. Progression-free survival 2 is defined as the time from second randomisation to the consolidation/maintenance part of the trial post-ASCT to second documented disease progression (or the start of next line anti-myeloma treatment), or death from any cause, whichever occurs first. Participants alive and for whom a second progression after second randomisation has not been observed will be censored at the last day they were known to be alive and second progression-free.
5. Time to next line treatment is defined as the time from the date of randomisation to the date of commencement of next line treatment. Participants who do not receive next line treatment will be censored at the date of the last assessment or follow-up visit where they are known to have received no new therapy.
6. Duration of response to protocol treatment is defined from the time of achieving at least a partial response to the date of first documented evidence of disease progression. Participants who die prior to documentation of disease progression will be censored at the date of death. Participants dying from causes not primarily due to progression will also be censored at the date of death. Participants not reaching disease progression at the time of analysis will be censored at the last date known to be progression-free.
7. Engraftment kinetics will be summarised based on summaries of stem cell remobilisation protocol and success of remobilisation and stem cell harvest after the completion of ASCT for all participants
8. Rate of Minimal Residual Disease negativity is defined as the proportion of participants with minimal residual disease (MRD) as assessed by flow cytometry will be assessed at various points in trial protocol treatment
9. Toxicity and safety will be reported based on adverse events, as graded by CTCAE V4.03 and

determined by routine clinical assessments at each centre

10. Quality of Life (QoL) i.e. EORTC QLQ-C30, EORTC QLQ-MY20, and the EQ-5D will be used to measure participant-assessed QoL at registration, post re-induction, 100 days post-ASCT and annually post second randomisation until 24 months post second randomisation, or until disease progression whichever is earlier

### **Overall study start date**

01/01/2016

### **Completion date**

30/04/2027

## **Eligibility**

### **Key inclusion criteria**

1. Diagnosed with relapsed MM (with measurable disease, according to IMWG criteria) previously treated with ASCT
2. First Progressive Disease (PD) at least 12 months following first ASCT, requiring therapy
3. Eastern Cooperative Oncology Group (ECOG) Performance Status 0-2
4. Aged at least 18 years
5. Participants must have the following blood results within 14 days before registration: a. Absolute neutrophil count (ANC)  $\geq 1 \times 10^9/\text{L}$  b. Platelet count  $\geq 75 \times 10^9/\text{L}$ . If the participant has  $\geq 50\%$  bone marrow infiltration a platelet count of  $\geq 50 \times 10^9/\text{L}$  is allowed. Platelet transfusions are not allowed within 3 days before registration in order to meet these values.
6. Adequate renal function within 14 days before registration: a. Creatinine clearance  $\geq 30 \text{ ml/min}$  (calculated according to Cockcroft-Gault equation or other locally approved formula)
7. Adequate hepatobiliary function within 14 days before registration: a. Total bilirubin  $< 2 \times$  upper limit of normal (ULN) b. ALT  $< 2 \times$  ULN
8. Adequate pulmonary function within 14 days before registration: a. Adequate respiratory functional reserve (delineated by KCO/DLCO (carbon monoxide diffusion in the lung) of  $\geq 50\%$ ). No evidence of a history of pulmonary disease. If a significant history, then a review by a respiratory medicine physician is required
9. Adequate cardiac function within 12 weeks before registration: a. Left ventricular ejection fraction (LVEF)  $\geq 40\%$ . Note: repeat confirmation of cardiac function is needed if treatment is given between this assessment and registration
10. Female participants who:
  - 10.1. Are not of childbearing potential (Appendix 8), OR
  - 10.2. If they are of childbearing potential, agree to practice 2 effective methods of contraception, at the same time, from the time of signing the informed consent form until 90 days after the last dose of study drug, OR
  - 10.3. Agree to practice true abstinence when this is in line with the preferred and usual lifestyle of the subject. (Periodic abstinence [e.g. calendar, ovulation, symptothermal, post-ovulation methods] and withdrawal are not acceptable methods of contraception)
- Male participants, even if surgically sterilised (i.e. status post-vasectomy), must agree to one of the following: a. Agree to practice effective barrier contraception during the entire study treatment period and through 90 days after the last dose of study drug, OR b. Agree to practice true abstinence when this is in line with the preferred and usual lifestyle of the subject. (Periodic abstinence (e.g. calendar, ovulation, symptothermal, post-ovulation methods] and withdrawal are not acceptable methods of contraception.) Contraception for female and male participants must be in accordance with (and consent to) the Celgene-approved Thalidomide Pregnancy Prevention Programme

11. If female and of childbearing potential (see Appendix 8), must have a negative pregnancy test performed by a healthcare professional in accordance with the Celgene Thalidomide Pregnancy Prevention Programme
12. Patients agree not to receive other clinical trials treatment, including investigational medicinal products (IMPs) not included in this trial, within 30 days of trial registration and throughout the duration of the trial, until disease progression
13. Able to provide written informed consent

**Participant type(s)**

Patient

**Age group**

Adult

**Lower age limit**

18 Years

**Sex**

Both

**Target number of participants**

Planned Sample Size: 406; UK Sample Size: 406

**Key exclusion criteria**

1. Received prior second line therapy for their relapsed disease other than local radiotherapy, therapeutic plasma exchange, or dexamethasone (up to a maximum of 200mg is allowed but not within 30 days prior to registration). Radiotherapy sufficient to alleviate or control pain of local invasion is permitted, but must not be within 14 days before registration. Patients who have received hemi-body radiation or similar since relapse will not be eligible
2.  $\geq$ Grade 2 peripheral neuropathy within 14 days before registration
3. Known HIV or Hepatitis B/C seropositivity
4. Known resistance, intolerance or sensitivity to any component of the planned therapies
5. Any medical or psychiatric condition which, in the opinion of the investigator, contraindicates the participant's participation in this study
6. Previous or concurrent malignancies at other sites (excluding completely resected non-melanoma skin cancer or carcinoma in situ of any type, such as cervical cancer)
7. Pregnant, lactating or breast feeding female participants
8. Failure to have fully recovered (i.e. less than or equal to Grade 1 toxicity) from the reversible effects of prior chemotherapy.
9. Major surgery within 14 days before registration
10. Central nervous system involvement with myeloma
11. Ongoing or active infection requiring systemic antibiotic therapy or other serious infection within 14 days before registration
12. Evidence of current uncontrolled cardiovascular conditions, including uncontrolled hypertension, uncontrolled cardiac arrhythmias, symptomatic congestive heart failure, unstable angina, or myocardial infarction within the past 6 months
13. Systemic treatment, within 14 days before the first dose of ixazomib with strong CYP3A inducers (e.g. rifampin, rifapentine, rifabutin, carbamazepine, phenytoin, phenobarbital), or use of Ginkgo biloba or St. John's wort
14. Known gastrointestinal (GI) disease or GI procedure that could interfere with the oral absorption or tolerance of ixazomib, including difficulty swallowing

15. Patients that have previously been treated with ixazomib or participated in a study with ixazomib whether treated with ixazomib or not

**Date of first enrolment**

20/03/2017

**Date of final enrolment**

31/05/2022

## **Locations**

**Countries of recruitment**

England

Northern Ireland

Scotland

United Kingdom

**Study participating centre**

**St James's University Hospital**

Beckett Street

Leeds

United Kingdom

LS9 7TF

**Study participating centre**

**Addenbrookes Hospital**

Hills Road

Cambridge

United Kingdom

CB2 0QQ

**Study participating centre**

**Arrowe Park Hospital**

Arrowe Park Road

Upton

Birkenhead

Wirral

United Kingdom

CH49 5PE

**Study participating centre**

**Barnsley Hospital**

Gawber Road  
Barnsley  
United Kingdom  
S75 2EP

**Study participating centre**

**Basingstoke and North Hampshire Hospital**

Aldermaston Road  
Basingstoke  
United Kingdom  
RG24 9NA

**Study participating centre**

**Beatson West of Scotland Cancer Centre**

Great Western Road  
Glasgow  
United Kingdom  
G12 0YN

**Study participating centre**

**Belfast City Hospital**

Lisburn Road  
Belfast  
United Kingdom  
BT9 7AB

**Study participating centre**

**Birmingham Heartlands Hospital**

Bordesley Green E  
Birmingham  
United Kingdom  
B9 5SS

**Study participating centre**

**Blackpool Victoria Hospital**

Whinney Heys Road  
Blackpool  
United Kingdom  
FY3 8NR

**Study participating centre**

**Bradford Royal Infirmary**

Duckworth Lane

Bradford

United Kingdom

BD9 6RJ

**Study participating centre**

**Bristol Haematology and Oncology Centre**

Horfield Road

Bristol

United Kingdom

BS2 8ED

**Study participating centre**

**Calderdale Royal Hospital**

Salterhebble

Halifax

United Kingdom

HX3 0PW

**Study participating centre**

**Chesterfield Royal Infirmary**

Chesterfield Road

Calow

Chesterfield

United Kingdom

S44 5BL

**Study participating centre**

**Countess of Chester**

The Countess Of Chester Health Park

Liverpool Road

Chester

United Kingdom

CH2 1UL

**Study participating centre**

**Darent Valley Hospital**

Darent Wood Road  
Dartford  
United Kingdom  
DA2 8DA

**Study participating centre****Derriford Hospital**

Derriford Road  
Plymouth  
United Kingdom  
PL6 8DH

**Study participating centre****Freeman Hospital**

Freeman Road  
High Heaton  
Newcastle upon Tyne  
United Kingdom  
NE7 7DN

**Study participating centre****Good Hope Hospital**

Rectory Road  
Sutton Coldfield  
United Kingdom  
B75 7RR

**Study participating centre****Grantham and District Hospital**

101 Manthorpe Road  
Grantham  
United Kingdom  
NG31 8DG

**Study participating centre****Huddersfield Royal Infirmary**

Acre Street  
Lindley

Huddersfield  
United Kingdom  
HD3 3EA

**Study participating centre**

**Ipswich Hospital**  
Heath Road  
Ipswich  
United Kingdom  
IP4 5PD

**Study participating centre**

**James Cook University Hospital**  
Marton Road  
Middlesbrough  
United Kingdom  
TS4 3BW

**Study participating centre**

**John Radcliffe Hospital**  
Headley Way  
Oxford  
United Kingdom  
OX3 9DU

**Study participating centre**

**King's Mill Hospital**  
Mansfield Road  
Sutton-in-Ashfield  
United Kingdom  
NG17 4JL

**Study participating centre**

**Leicester Royal Infirmary**  
Infirmary Square  
Leicester  
United Kingdom  
LE1 5WW

**Study participating centre**  
**Lincoln County Hospital**  
Greetwell Road  
Lincoln  
United Kingdom  
LN2 5QY

**Study participating centre**  
**Maidstone Hospital**  
Hermitage Lane  
Maidstone  
United Kingdom  
ME16 9QQ

**Study participating centre**  
**Milton Keynes General Hospital**  
Standing Way  
Eaglestone  
Milton Keynes  
United Kingdom  
MK6 5LD

**Study participating centre**  
**Monklands Hospital**  
Monkscourt Avenue  
Airdrie  
United Kingdom  
ML6 0JS

**Study participating centre**  
**Ninewells Hospital**  
NHS Tayside  
Dundee  
United Kingdom  
DD1 9SY

**Study participating centre**  
**Norfolk & Norwich University Hospital**  
Colney Lane

Norwich  
United Kingdom  
NR4 7UY

**Study participating centre**  
**North Tyneside General Hospital**  
Rake Lane  
North Shields  
United Kingdom  
NE29 8NH

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

**Study participating centre**  
**Pilgrim Hospital**  
Sibsey Road  
Boston  
United Kingdom  
PE21 9QS

**Study participating centre**  
**Pinderfields General Hospital**  
Aberford Road  
Wakefield  
United Kingdom  
WF1 4DG

**Study participating centre**  
**Queen Elizabeth Hospital Birmingham**  
Mindelsohn Way  
Birmingham  
United Kingdom  
B15 2TH

**Study participating centre**  
**Queen's Hospital**  
Belvedere Road  
Burton-on-Trent  
United Kingdom  
DE13 0RB

**Study participating centre**  
**Royal Alexandra Hospital**  
Corsebar Road  
Paisley  
United Kingdom  
PA2 9PN

**Study participating centre**  
**Royal Derby Hospital**  
Uttoxeter Road  
Derby  
United Kingdom  
DE22 3NE

**Study participating centre**  
**Royal Hallamshire Hospital**  
Glossop Road  
Sheffield  
United Kingdom  
S10 2JF

**Study participating centre**  
**Royal Hampshire County Hospital**  
Romsey Road  
Winchester  
United Kingdom  
SO22 5DG

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

**Study participating centre**  
**Royal Marsden Hospital**  
Fulham Road  
Chelsea  
London  
United Kingdom  
SW3 6JJ

**Study participating centre**  
**Royal Stoke University Hospital**  
Newcastle Road  
Stoke-on-Trent  
United Kingdom  
ST4 6QG

**Study participating centre**  
**Royal United Hospital**  
Combe Park  
Bath  
United Kingdom  
BA1 3NG

**Study participating centre**  
**Russells Hall Hospital**  
Pensnett Road  
Dudley  
United Kingdom  
DY1 2HQ

**Study participating centre**  
**Salisbury District Hospital**  
Odstock Road  
Salisbury  
United Kingdom  
SP2 8BJ

**Study participating centre**

**Stepping Hill Hospital**

Poplar Grove  
Hazel Grove  
Stockport  
United Kingdom  
SK2 7JE

**Study participating centre****St Bartholomew's Hospital**

W Smithfield  
London  
United Kingdom  
EC1A 7BE

**Study participating centre****St George's Hospital**

Blackshaw Road  
Tooting  
London  
United Kingdom  
SW17 0QT

**Study participating centre****St Helens Hospital**

Marshalls Cross Road  
St. Helens  
United Kingdom  
WA9 3D

**Study participating centre****St Helier Hospital**

Wrythe Lane  
Sutton  
Carshalton  
United Kingdom  
SM5 1AA

**Study participating centre****Southampton General Hospital**

Tremona Road  
Southampton

United Kingdom  
SO16 6YD

**Study participating centre**  
**Sunderland Royal Hospital**  
Kayll Road  
Sunderland  
United Kingdom  
SR4 7TP

**Study participating centre**  
**The Beatson West of Scotland Cancer Centre**  
1053 Great Western Road  
Glasgow  
United Kingdom  
G12 0YN

**Study participating centre**  
**The Christie**  
550 Wilmslow Road  
Manchester  
United Kingdom  
M20 4BX

**Study participating centre**  
**Torbay Hospital**  
Newton Road  
Torquay  
United Kingdom  
TQ2 7AA

**Study participating centre**  
**Tunbridge Wells Hospital**  
Tonbridge Road  
Tunbridge Wells  
United Kingdom  
TN2 4QJ

**Study participating centre**

**University College London Hospital**  
235 Euston Road  
London  
United Kingdom  
NW1 2BU

**Study participating centre**  
**University Hospital Aintree**  
Longmoor Lane  
Liverpool  
United Kingdom  
L9 7AL

**Study participating centre**  
**University Hospital Ayr**  
Dalmellington Road  
Ayr  
United Kingdom  
KA6 6DX

**Study participating centre**  
**University Hospital Crosshouse**  
Kilmarnock Road  
Crosshouse  
Kilmarnock  
United Kingdom  
KA2 0BE

**Study participating centre**  
**Worcestershire Royal Hospital**  
Charles Hastings Way  
Worcester  
United Kingdom  
WR5 1DD

## **Sponsor information**

**Organisation**  
University of Leeds

## **Sponsor details**

-

Leeds  
England  
United Kingdom  
LS2 9JT

## **Sponsor type**

University/education

## **ROR**

<https://ror.org/024mrx33>

## **Funder(s)**

### **Funder type**

Charity

### **Funder Name**

Cancer Research UK

### **Alternative Name(s)**

CR\_UK, Cancer Research UK - London, CRUK

### **Funding Body Type**

Private sector organisation

### **Funding Body Subtype**

Other non-profit organizations

### **Location**

United Kingdom

### **Funder Name**

Takeda Development Center Americas, Inc.

## **Results and Publications**

### **Publication and dissemination plan**

Planned publication in a high-impact peer-reviewed journal, 12 months after the trial ends.

### **Intention to publish date**

30/04/2028

**Individual participant data (IPD) sharing plan**

The current data sharing plans for the current study are unknown and will be made available at a later date.

**IPD sharing plan summary**

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>	protocol	07/03/2018		Yes	No
<a href="#">HRA research summary</a>			26/07/2023	No	No
<a href="#">Results article</a>		06/09/2024	10/09/2024	Yes	No