Myeloma XII (ACCoRd trial)

Submission date	Recruitment status No longer recruiting	[X] Prospectively registered		
28/11/2016		[X] Protocol		
Registration date	Overall study status	Statistical analysis plan		
15/12/2016	Ongoing	[X] Results		
Last Edited	Condition category	[] Individual participant data		
10/09/2024	Cancer			

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

Clinical Trials Information System (CTIS)

2016-000905-35

Protocol serial number

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

Study type(s)

Treatment

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/m2/day on D-1, intravenously ASCT on D0

ASCT-aug:

Ixazomib 4mg/day on D-4 and D-1, taken orally Melphalan 100mg/m2/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(s)

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

Key secondary outcome(s))

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

Completion date

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) $\geq 1 \times 109 / L$ b.Platelet count $\geq 75 \times 109 / L$. If the participant has $\geq 50\%$ bone marrow infiltration a platelet count of $\geq 50 \times 109 / L$ 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 ≥30ml/min (calculated according to Cockcroft-Gault equation or other locally approved formula)
- 7. Adequate hepatobiliary function within 14 days before registration: a. Total bilirubin $<2 \times 10^{-2}$ upper limit of normal (ULN) b. ALT $<2 \times 10^{-2}$ 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 ≥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) ≥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

All

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. ≥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

United Kingdom

England

Northern Ireland

Scotland

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

Darenth Wood Road Dartford United Kingdom DA2 8DA

Study participating centre Derriford Hospital Dessifeed Bood

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

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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

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Study participating centre Milton Keynes General Hospital

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Study participating centre Monklands Hospital

Monkscourt Avenue Airdrie United Kingdom ML6 0JS

Study participating centre Ninewells Hospital

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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

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Combe Park Bath United Kingdom BA1 3NG

Study participating centre Russells Hall Hospital

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Study participating centre Salisbury District Hospital

Odstock Road Salisbury United Kingdom SP2 8BJ

Study participating centre Stepping Hill Hospital

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Study participating centre St Bartholomew's Hospital

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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
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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

ROR

https://ror.org/024mrxd33

Funder(s)

Funder type Charity

Funder Name

Cancer Research UK

Alternative Name(s)

CR_UK, Cancer Research UK - London, Cancer Research UK (CRUK), 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

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?
Results article		06/09/2024	10/09/2024	Yes	No
Protocol article	protocol	07/03/2018		Yes	No
HRA research summary			26/07/2023		No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes