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A phase II randomised trial of carfilzomib, cyclophosphamide and dexamethasone (CCD) vs cyclophosphamide, velcade and dexamethasone (CVD) for first relapse or primary refractory multiple myeloma

Submission date 12/12/2012	**Recruitment status** No longer recruiting	[X] Prospectively registered [X] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 12/12/2012	**Overall study status** Completed	
Last Edited 14/01/2021	**Condition category** Cancer	

Plain English summary of protocol
http://www.cancerresearchuk.org/cancer-help/trials/a-trial-looking-carfilzomib-myeloma-muk5

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
2012-001320-36

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
12956

Study information

Scientific Title
A phase II randomised trial of carfilzomib, cyclophosphamide and dexamethasone (CCD) vs cyclophosphamide, velcade and dexamethasone (CVD) for first relapse or primary refractory multiple myeloma

Study objectives
This is a phase II randomised, controlled, parallel group, multi-centre trial of carfilzomib, cyclophosphamide and dexamethasone (CCD) vs. cyclophosphamide, bortezomib and dexamethasone (CVD) for multiple myeloma patients at first relapse or refractory to no more than 1 line of treatment. Participants will be randomised in a 2:1 ratio in favour of CCD. The proposed study will compare 8 cycles of CVD with 6 cycles of CCD, and will also assess the benefit of maintenance carfilzomib in participants in the CCD arm. Participants in the CCD arm, who have at least stable disease at the end of the initial 6 cycles of CCD, will be randomised to receive maintenance therapy with Carfilzomib or no further treatment. Participants in the CVD arm will not receive maintenance therapy. In order to compare the regimens with regard to activity, the trial has been designed to incorporate two co-primary endpoints: response and progression-free survival.

This allows the trial to:
1. Assess the activity of the regimens after a fixed period of 24 weeks of treatment, i.e. not incorporating the maintenance phase in the CCD arm
2. Compare the activity of the whole CCD regimen with and without maintenance therapy. Additionally, the whole CCD regimen without maintenance will be compared with the CVD regimen, by evaluating the longer term endpoint of progression-free survival (PFS).

The trial is designed to assess the non-inferiority of CCD as compared to CVD in terms of response and the superiority of CCD with maintenance as compared to CCD with no maintenance in terms of progression-free survival. The trial will also explore the non-inferiority of CCD with no maintenance as compared to CVD in terms of PFS.

Ethics approval required
Old ethics approval format

Ethics approval(s)
ref: 12/LO/1078

Study design
Randomised interventional phase II treatment study

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 below to request a patient information sheet

Health condition(s) or problem(s) studied
Haematological Oncology; Myeloma

Interventions
CCD, Carfilzomib, Cyclophosphamide, Dexamethasone; CVD, Cyclophosphamide, Velcade, Dexamethasone

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
CCD, Carfilzomib, Cyclophosphamide, Dexamethasone; CVD, Cyclophosphamide, Velcade, Dexamethasone

Primary outcome measure
Proportion of participants achieving at least VGPR measured at 24 weeks post initial randomisation

Secondary outcome measures
Progression-free survival

Overall study start date
01/01/2013

Completion date
30/09/2018

Eligibility

Key inclusion criteria
1. Syptomatic multiple myeloma and requiring therapy for first relapse or primary refractory disease
2. Measurable disease
3. Age = 18 years
4. Life expectancy = 6 months

5. Eastern Cooperative Oncology Group (ECOG) performance status 02
6. Adequate hepatic function, with serum ALT = 3.5 times the upper limit of normal and serum direct bilirubin = 2 mg/dL (34 µmol/L) within 14 days prior to randomisation
7. Absolute neutrophil count (ANC) = 1.0 × 10^9/L within 14 days prior to randomisation (growth factor support is not permitted)
8. Haemoglobin = 8 g/dL (80 g/L) within 14 days prior to randomisation (participants may be receiving red blood cell [RBC] transfusions in accordance with institutional guidelines)
9. Platelet count = 75 × 10^9/L (= 50 × 10^9/L if myeloma involvement in the bone marrow is > 50%) within 14 days prior to randomisation. Platelet support is not permitted.
10. Creatinine clearance (CrCl) = 15 mL/minute within 14 days prior to randomisation, either measured or calculated using a standard formula (eg, Cockcroft and Gault)
11. Written informed consent
12. Females of childbearing potential (FCBP) must agree to ongoing pregnancy testing and to practice contraception.
13. Male participants must agree to practice contraception

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
UK Sample Size: 300

Total final enrolment
300

Key exclusion criteria
1. Non-secretory multiple myeloma
2. Extramedullary plasmacytoma (without evidence of myeloma)
3. Received therapy for their first relapsed or primary refractory disease other than local radiotherapy, therapeutic plasma exchange, or dexamethasone up to a maximum of 200mg
4. Pregnant or lactating females
5. Major surgery within 21 days prior to randomisation
6. Acute active infection requiring treatment (systemic antibiotics, antivirals, or antifungals) within 14 days prior to randomisation
7. Known human immunodeficiency virus infection
8. Active hepatitis B or C infection
9. Unstable angina or myocardial infarction within 4 months prior to randomization, NYHA Class III or IV heart failure, uncontrolled angina, history of severe coronary artery disease, severe uncontrolled ventricular arrhythmias, sick sinus syndrome, or electrocardiographic evidence of acute ischemia or Grade 3 conduction system abnormalities unless participant has a pacemaker
10. Uncontrolled hypertension or uncontrolled diabetes within 14 days prior to randomisation
11. Previous or concurrent active malignancy within the past 3 years with the exception of:

11.1 Adequately treated basal cell carcinoma, squamous cell skin cancer, or thyroid cancer
11.2. Carcinoma in situ of the cervix or breast
11.3. Prostate cancer of Gleason Grade 6 or less with stable prostate-specific antigen levels
11.4. Cancer considered cured by surgical resection or unlikely to impact survival during the duration of the study, such as localised transitional cell carcinoma of the bladder or benign tumours of the adrenal or pancreas
12. Significant neuropathy (Grades 34, or Grade 2 with pain) within 14 days prior to randomisation
13. Patients with haemorrhagic cystitis
14. Known history of hypersensitivity to any of the study medications or excipients
15. Participants undergoing active treatment for infiltrative lung disease
16. Contraindication to any of the required concomitant drugs or supportive treatments, including hypersensitivity to all anticoagulation and antiplatelet options, antiviral drugs, or intolerance to hydration due to pre-existing pulmonary or cardiac impairment
17. Contraindication to IV hydration programme
18. Participants with pleural effusions requiring thoracentesis or ascites requiring paracentesis within 14 days prior to randomisation
19. Any other clinically significant medical disease or condition that, in the Investigators opinion, may interfere with protocol adherence or a participants ability to give informed consent

Date of first enrolment
01/01/2013

Date of final enrolment
31/12/2015

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
University of Leeds
Leeds
United Kingdom
LS2 9NG

Sponsor information

Organisation
University of Leeds (UK)

Sponsor details

Woodhouse Lane
Leeds
England
United Kingdom
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Sponsor type
University/education

Website
http://www.leeds.ac.uk/

ROR
https://ror.org/024mrxd33

Funder(s)

Funder type
Charity

Funder Name
Myeloma UK ref: CD11/06

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
Planned publication in Q1 2021.

Intention to publish date
31/03/2021

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be stored in a non-publically available repository, the MUK 5 Clinical Macro Database hosted by the University of

Leeds. The sharing of pseudo-anonymised data will be evaluated on completion of a data access request that should be sent to medctco@leeds.ac.uk and will be reviewed by the trial management group in the first instance. Only requests that have a methodologically sound proposal and whose proposed use of the data has been approved by the independent trial steering committee will be considered. Requests must be fully funded, have appropriate ethical approval and if approved undertake a data-sharing agreement. Consent has been obtained from participants for use of this data in future research.

IPD sharing plan summary

Stored in repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article	protocol	17/05/2016		Yes	No
Abstract results	results presented at ASH	07/12/2017		No	No
Basic results		12/01/2021	12/01/2021	No	No
HRA research summary			28/06/2023	No	No