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Carfilzomib in combination with doxorubicin and dexamethasone (CAD) therapy in transplant eligible relapsed myeloma patients

Submission date 02/12/2010	**Recruitment status** Stopped	[ ] Prospectively registered [ ] Protocol [ ] Statistical analysis plan [ ] Results [ ] Individual participant data [ ] Record updated in last year
Registration date 12/05/2011	**Overall study status** Stopped	
Last Edited 26/11/2012	**Condition category** Cancer	

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
HM10 9644

Study information

Scientific Title
An open label, multicentre, phase I/II dose escalation trial of carfilzomib in combination with doxorubicin and dexamethasone (CAD) therapy in transplant eligible relapsed myeloma patients

Acronym
MUK 02

Study objectives
During the dose finding phase, the primary objective of this trial is to determine the maximum tolerated dose (MTD) of carfilzomib in combination with doxorubicin and dexamethasone (CAD). In the dose expansion phase the primary objective will be to estimate the response rate to four cycles of CAD therapy at MTD identified in the dose finding stage in transplant eligible relapsed myeloma patients.

Within the extension phase there are also the following secondary objectives:
1. Assess the safety and toxicity of CAD therapy
2. Assess the feasibility to mobilise stem cells following CAD therapy
3. Estimate maximum response to therapy
4. Estimate time to maximum response to therapy
5. Estimate progression free survival following CAD therapy
6. Assess the feasibility of delivering CD maintenance

Ethics approval required
Old ethics approval format

Ethics approval(s)
Not provided at time of registration

Study design
Open label multicentre phase I/II dose escalation trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Multiple myeloma

Interventions
Dose escalation:

Dose level 1
Carfilzomib 20mg/m2 on days 1 and 2 of cycle 1 only, 27mg/m2 on days 8-9 and 15-16 of cycle 1 and all subsequent doses. Adriamycin® (doxorubicin) 9.0 mg/m2 days 1, 2, 15 and 16. dexamethasone 40mg days 1, 2, 8, 9, 15 and 16

Dose level 2
Carfilzomib 20mg/m2 on days 1 and 2 of cycle 1 only, 36mg/m2 on days 8-9 and 15-16 of cycle and all subsequent doses. Adriamycin® (doxorubicin) 9.0 mg/m2 days 1, 2, 15 and 16. dexamethasone 40mg days 1, 2, 8, 9, 15 and 16

Dose level 3
Carfilzomib 20mg/m2 on days 1 and 2 of cycle 1 only, 45mg/m2 on days 8-9 and 15-16 of cycle 1

and all subsequent doses. Adriamycin® (doxorubicin) 9.0 mg/m2 days 1, 2, 15 and 16. dexamethasone 40mg days 1, 2, 8, 9, 15 and 16

Patients will receive four cycles of CAD and will be given the option of a further four cycles of consolidation therapy. Patients will then receive carfilzomib and dexamethasone maintenance therapy until disease progression and will be followed up every 2 months.

26/11/2012: Please note that this trial was never started.

Intervention Type
Drug

Phase
Phase I/II

Drug/device/biological/vaccine name(s)
Carfilzomib, doxorubicin, dexamethasone

Primary outcome(s)
The primary endpoints for the dose escalation phase is dose limiting toxicities within the first cycle of treatment (28 days). In the dose expansion phase, the primary endpoint will be the proportion of patients achieving at least a partial response after four cycles of CAD.

Key secondary outcome(s))
1. The proportion of patients for whom stem cell cell mobilisation is possible following CAD therapy
2. Safety and toxicity
3. Maximum response rate within four cycles of CAD
4. Maximum response rate within four cycles of CAD, consolidation therapy and maintenance therapy (i.e. maximum response to therapy)
5. Time to maximum response to therapy (i.e. within four cycles of CAD, consolidation therapy and maintenance therapy)
6. Progression-free survival
7. Feasibility of CD-maintenance therapy

Completion date
01/04/2016

Reason abandoned (if study stopped)
Lack of funding/sponsorship

Eligibility

Key inclusion criteria
1. Able to give informed consent and willing to follow study protocol
2. Aged over 18 years, either sex
3. Patients with relapsed myeloma requiring therapy
4. Transplant eligible
5. Adequate renal function (creatinine clearance greater than or equal to 30 ml/min) within 14 days prior to study entry

6. Adequate liver function (alanine aminotransferase [ALT]/aspartate aminotransferase [AST] less than 3 x upper limit of normal [ULN]) within 14 days prior to study entry
7. Adequate bone marrow reserve (haemoglobin [Hb] greater than 8.0 g/dL, absolute neutrophil count [ANC] greater than 1.0 x 10^9/L, platelets [Plts] greater than 75 x 10^9/L) within 14 days prior to study entry
8. Female subjects of child-bearing potential must have a negative pregnancy test within 24 hours prior to starting therapy and agree to use dual methods of contraception for the duration of the study. Male subjects must agree to use a barrier method of contraception for the duration of the study if sexually active with a female of child-bearing potential.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Unable to tolerate an aggressive fluid hydration regimen (e.g. due to pre-existing pulmonary, cardiac or renal impairment)
2. Received an investigational medicinal product at any dose within 28 days of study entry (registration)
3. Concurrent or previous malignancies (less than 12 months post end of treatment) at other sites, with the exception of appropriately treated localised epithelial skin or cervical cancer. Patients with histories (greater than or equal to 12 months) of other tumours may be entered.
4. Seropositive for human immunodeficiency [HIV], or active hepatitis A, B or C infection
5. Any history of hypersensitivity to any of the study medications or excipients
6. Patients with active uncontrolled infections
7. Patients with peripheral neuropathy Common Toxicity Criteria (CTC) grade 3 or higher within 14 days prior to study entry
8. Poorly controlled or serious medical or psychiatric illness that, in the Investigator's opinion, is likely to interfere with participation and/or compliance in this clinical study
9. Pregnant or breast feeding

Date of first enrolment
01/04/2011

Date of final enrolment
01/04/2016

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Haemato-Oncology Unit
Sutton
United Kingdom
SM2 5PT

Sponsor information

Organisation
University of Leeds (UK)

ROR
https://ror.org/024mrxd33

Funder(s)

Funder type
Charity

Funder Name
Myeloma UK (UK)

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes