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MUK six

Submission date	Recruitment status	[_] Prospectively registered
19/12/2012	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
19/12/2012	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
21/05/2021	Cancer	

Plain English summary of protocol
http://www.cancerresearchuk.org/cancer-help/trials/a-trial-of-panobinostat-with-bortezomib-thalidomide-and-dexamethasone-for-myeloma-that-has-come-back-or-no-longer-responding-to-treatment-muk-six

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
2012-000842-36

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
13613

Study information

Scientific Title
A Phase I/IIa trial of VTD-panobinostat treatment and panobinostat maintenance in relapsed and relapsed/refractory multiple myeloma patients

Study objectives
This is an open label, multi-centre, phase I/IIa trial to firstly identify the maximum tolerated dose (MTD) of VTD-panobinostat in eligible participants with relapsed or relapsed and refractory multiple myeloma. A rolling six dose escalation design36 is proposed to determine the MTD and recommended dose (RD) of VTD-Pano. An expansion phase will then be incorporated to estimate the response rate (partial response or better) within 16 cycles of therapy at the RD. Safety will be assessed throughout the trial.

Ethics approval required
Old ethics approval format

Ethics approval(s)
First MREC, 11/07/2012, ref: 12/LO/0965

Study design
Non-randomised interventional study

Primary study design
Interventional

Secondary study design
Non randomised study

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
Haematological Oncology; Disease: Myeloma

Interventions
Dexamethasone will be administered for 16 cycles on days 1, 2, 8 and 9
Panobinostat will be administered alongside Velcade, Thalidomide and Dexamethasone for 16 cycles of induction therapy, each lasting 21 days.
Participants will then receive 12 months of panobinostat monotherapy maintenance.

Thalidomide will be administered daily for 16 cycles
Velcade will be administered in a regimen alongside panobinostat, thalidomide and dexamethasone

Intervention Type
Drug

Phase
Phase I/II

Drug/device/biological/vaccine name(s)
Dexamethasone, panobinostat, thalidomide, velcade

Primary outcome measure
Dose limiting toxicities measured within the first cycle of treatment (21 days)

Secondary outcome measures
Response - proportion of participants achieving at least a partial response within 16 cycles of VTD-Pano

Overall study start date
10/12/2012

Completion date
01/06/2014

Eligibility

Key inclusion criteria
1. Patients with a previous diagnosis of multiple myeloma based on IMWG 2003 definitions:
1.1. Monoclonal immunoglobulin (M component) on electrophoresis, and on immunofixation of serum or of total 24 hour urine
1.2. Bone marrow (clonal) plasma cells =10% or biopsy proven plasmacytoma
1.3. Related organ or tissue impairment (CRAB symptoms, anemia, hypercalcemia, lytic bone lesions, renal insufficiency, hyperviscosity, amyloidosis or recurrent infections)
2. Relapsed or relapsed-and-refractory myeloma who have received 14 prior lines and now require further treatment
3. Able to give informed consent and willing to follow study protocol
4. Aged 18 years or over
5. ECOG Performance Status = 2
6. Required laboratory values within 14 days of registration:
6.1. Absolute neutrophil count = 1.0 x 109/L. Growth factor support is not permitted within 14 days prior to eligibility assessment
6.2. Platelet count = 100 x 109/L. Platelet support is not permitted within 14 days prior to eligibility assessment
6.3. Haemoglobin = 8.0g/dL. Blood transfusion support is permitted
6.4. Bilirubin = 2 x upper limit of normal (ULN)
6.5. AST and/or ALT = 2.5 x ULN; except in subjects with known hepatic involvement, where AST and/or ALT = 5.0 x ULN
6.6. Serum creatinine = 2.0 x ULN

6.7. Corrected calcium = 2.8 mmol/L
7. Anticipated survival of at least 3 months
8. Evaluable disease per modified IWG criteria, utilising the following assessments as appropriate:
8.1. Serum M protein = 10g/l
8.2. Urine M protein = 200mg/24 hours
8.3. Serum free light chain assay: involved FLC level = 100mg/l. Provided serum FLC ratio is abnormal
9. Female subjects of childbearing potential must have a negative pregnancy test at baseline and agree to use dual methods of contraception for the duration of the study and must continue to do so for 3 months after the end of treatment. Male subjects must agree to use a barrier method of contraception for the duration of the study if sexually active with a female of childbearing potential and must continue to do so for 3 months after the end of treatment.
10. Male or female participants

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
UK Sample Size: 54

Key exclusion criteria
1. Pregnant (positive pregnancy test) or breastfeeding women
2. Non-secretory multiple myeloma
3. Previous anti-tumour therapies, including prior experimental agents or approved anti-tumour small molecules and biologics, within 28 days before the start of protocol treatment. Steroid therapy is permitted (maximum 160mg dexamethasone or equivalent), but must be stopped 48 hours prior to study drug administration. Bisphosphonates for bone disease and radiotherapy for palliative intent are also permitted.
4. Concurrent or previous malignancies (<12 months post end of treatment) at other sites with the exception of appropriately treated localised epithelial skin or cervical cancer, or incidental histologic findings of prostate cancer (TMN stage T1a or 1b). Patients with histories (=12 months) of other tumours may be entered
5. Poorly controlled or serious medical or psychiatric illness that, in the Investigators opinion, is likely to interfere with participation and/or compliance in this clinical study
6. Patients with significant cardiovascular disease (e.g. history of congestive heart failure requiring therapy, presence of severe valvular heart disease, presence of an atrial or ventricular arrhythmia requiring treatment, uncontrolled hypertension, a history of QTc abnormalities)
7. Active symptomatic fungal, bacterial, and/or viral infection including known active HIV or known viral (A, B, or C) hepatitis
8. Gastrointestinal disorders that may interfere with absorption of the study drug
9. Patients who have been refractory to prior bortezomib, i.e. did not achieve at least an MR, or

who have progressed on therapy or within 60 days of last dose
10. Participants with peripheral neuropathy CTC grade 2 or higher or grade 1 with pain within 14 days prior to registration
11. Any history of known hypersensitivity to any of the study medication or excipients

Date of first enrolment
10/12/2012

Date of final enrolment
01/06/2014

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
University of Leeds
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Sponsor information

Organisation
University of Leeds (UK)

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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

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

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Plain English results				No	Yes
Results article	results	01/12/2016		Yes	No
HRA research summary			28/06/2023	No	No