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Vorinostat in combination with bortezomib and dexamethasone in patients with relapsed and relapsed refractory multiple myeloma

Submission date 31/10/2011	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 01/03/2012	**Overall study status** Completed	
Last Edited 30/05/2025	**Condition category** Cancer	

Plain English summary of protocol
https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-looking-at-vorinostat-bortezomib-and-dexamethasone-for-myeloma-that-has-come-back-muk-four

Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
2011-005361-20

ClinicalTrials.gov (NCT)
NCT01720875

Protocol serial number
HM11/10041

Study information

Scientific Title
A Phase II trial of vorinostat in combination with bortezomib and dexamethasone in patients with relapsed and relapsed refractory multiple myeloma

Study objectives
Aim:
To assess the overall response rate of patients with relapsed or refractory and refractory multiple myeloma after induction treatment with vorinostat in combination with bortezomib and dexamethasone.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Not provided at time of registration

Study design
Open-label multi-centre single-arm Phase II trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Relapsed or relapsed and refractory multiple myeloma

Interventions
All trial participants will receive the same treatment regimen as follows:

Cycles 1- 8 (21-day cycle):
1. Bortezomib: 1.3 mg/m2 IV on days 1,4, 8 and 11
2. Dexamethasone: 20 mg PO on days 1, 2, 4, 5, 8, 9, 11 and 12
3. Vorinostat: 400 mg PO on days 1-14

Maintenance (28-day cycle):
Vorinostat: 400 mg PO on 1-7 and 15-21

Maintenance will continue until disease progression or intolerance

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)

Vorinostat, bortezomib, dexamethasone

Primary outcome(s)
Proportion of patients achieving at least a partial response (PR) within 8 cycles of protocol treatment, as defined by modified International Working Group (IWG) criteria

Key secondary outcome(s))
1. Safety, toxicity and tolerability
2. Progression-free survival
3. Proportion of patients achieving at least a very good partial response (VGPR) within 8 cycles of treatment
4. Maximum response of patients to treatment overall and after 8 treatment cycles
5. Time to maximum response
6. Quality of life

Completion date
01/03/2013

Eligibility

Key inclusion criteria
1. Able to give informed consent and willing to follow study protocol and quality of life assessments
2. Aged 18 years or over
3. Subjects with multiple myeloma diagnosed according to standard criteria, who require further treatment due to relapse or non-response after at least one but not more than three prior lines of treatment
4. Patients with measurable extramedullary plasmacytomas are allowed if they fulfil the above inclusion criteria
5. No prior Histone deacetylases (HDAC) inhibitor treatment. Patients who have received compounds with HDAC inhibitor-like activity, such as valproic acid, as anti-tumour therapy must not be enrolled in this study. (Patients who have received such compounds for other indications, e.g. valproic acid for epilepsy, may enrol after a 30-day washout period.)
6. Eastern Cooperative Oncology Group (ECOG) Performance Status ≤2
7. Required laboratory values within 21 days of registration
7.1. Absolute neutrophil count ≥1.0 x 10e9/L
7.2. Platelet count ≥75 x 10e9/L
7.3. Haemoglobin >9 g/dL
7.4. Bilirubin ≤1.5 x upper limit of normal
7.5. ALT and/or AST ≤2.5 x upper limit of normal
7.6. Serum creatinine ≤2.0 x upper limit of normal
7.7. Corrected calcium ≤2.8 mmol/L
8. Life expectancy of at least 3 months
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 child-bearing potential and must continue to do so for 3 months after the end of treatment
10. Patient is able to swallow capsules and is able to take or tolerate oral medications on a continuous basis

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
16

Key exclusion criteria
1. Pregnant or breastfeeding females
2. 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 to stop rapid relapse during this period is permitted, but must be stopped 7 days prior to study drug administration. Bisphosphonates for bone disease and radiotherapy for palliative intent are also permitted.
3. Previous or concurrent active malignancies (<12 months post end of treatment) at other sites with the exception of appropriately treated localised epithelial skin or cervical cancer. Patients with histories (≥12 months) of other tumours may be entered
4. Patients considered to be refractory to prior bortezomib treatment (defined below) or unable to tolerate treatment with bortezomib.
4.1. Relapse on or within 60 days after the last dose of a bortezomib-containing regimen
4.2. No clinical response (≤SD/NC) on a bortezomib-containing regimen
4.3. Peripheral neuropathy of ≥ grade 2 severity
4.4. Patient has plasma cell leukaemia defined as the presence of more than 20% plasma cells in the peripheral blood and/or an absolute plasma cell count of ≥2000/μL
4.5. Patient has uncontrolled concurrent illness or circumstances that could limit compliance with the study, including, but not limited to the following: acute or chronic graft versus host disease, uncontrolled hypertension, symptomatic congestive heart failure, unstable angina pectoris, myocardial infarction within past 6 months, uncontrolled cardiac arrhythmia, renal failure, psychiatric or social conditions that may interfere with patient compliance, or any other condition (including laboratory abnormalities) that in the opinion of the Investigator places the patient at unacceptable risk for adverse outcome if he/she were to participate in the study.
4.6. Patients with significant cardiovascular disease (e.g. acute diffuse infiltrative pulmonary disease, pericardial disease, a 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 or with QTC interval > 480 msecs
4.7. Active symptomatic fungal, bacterial, and/or viral infection, including known active HIV or known viral (A, B, or C) hepatitis
5. Unable to take corticotherapy at study entry
6. Patient with prior allogeneic bone marrow transplant

7. Patient has known hypersensitivity to any components of bortezomib (such as boron, mannitol) or vorinostat
8. Patient has known central nervous system (CNS) metastases and/or carcinomatous meningitis
9. Patient has a history of a gastrointestinal surgery or other procedures that might, in the opinion of the Investigator, interfere with the absorption or swallowing of the study drug(s)

Date of first enrolment
01/03/2012

Date of final enrolment
01/03/2013

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Haemato-Oncology Unit
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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?
Results article	results	03/12/2015		Yes	No
Results article		01/03/2021	31/03/2021	Yes	No
Plain English results			30/05/2025	No	Yes