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Pomalidomide Specific Targeting in Relapsed and Refractory Myeloma (MUK Seven)

Submission date 13/02/2014	**Recruitment status** Stopped	[X] Prospectively registered [ ] Protocol
Registration date 07/03/2014	**Overall study status** Stopped	[ ] Statistical analysis plan [ ] Results
Last Edited 11/05/2016	**Condition category** Cancer	[ ] Individual participant data [ ] Record updated in last year

Plain English summary of protocol

Background and study aims
Multiple myeloma is a type of bone marrow cancer. The disease is called refractory myeloma if the cancer no longer responds to treatment. If the cancer returns after treatment, it is called relapsed myeloma. Pomalidomide and dexamethasone are used as a standard treatment for patients with multiple myeloma. The new treatment being tested in this study is pomalidomide and dexamethasone with the addition of cyclophosphamide, to see if it is effective in treating patients with Relapsed and Refractory Multiple Myeloma (RRMM). A study of 250 patients is to be carried out to compare the combination of pomalidomide, cyclophosphamide and dexamethasone with pomalidomide and dexamethasone alone in patients with relapsed /refractory multiple myeloma. This study will also collect bone marrow and blood samples to study the mechanism of action of the drug and to identify markers that may be able to predict response to treatment.

Who can participate?
To enter the study patients must have received treatment with proteasome inhibitor and lenalidomide previously and have relapsed or be refractory to this treatment.

What does the study involve?
Patients are randomly allocated to receive treatment with either Pd (pomalidomide and dexamethasone) or CPD (pomalidomide, cyclophosphamide and dexamethasone) and continue treatment until disease progression or until they are unable to tolerate treatment any longer. Treatment is given for 21 days of a 28-day cycle with at least monthly visits to hospital. Bone marrow and blood samples are compulsory for the trial and are taken at the beginning, during and at the end of treatment.

What are the possible benefits and risks of participating?
The participant will be receiving a treatment that is available through normal care pathways and is known to be effective in some patients in the treatment of myeloma. Additional blood samples will be needed and therefore possibly more needle punctures will be required to take these samples. Potential side effects of the treatment will differ from patient to patient but treatment modifications and supportive care will be given to minimise any effects.

Where is the study run from?
The study is being run by the University of Leeds and is part of the Myeloma UK portfolio of myeloma trials. The trial will be run from 15 of the Myeloma UK Network NHS sites in the UK. Treatment will be given at the NHS site.

When is the study starting and how long is it expected to run for?
September 2015 to September 2017.

Who is funding the study?
University of Leeds (UK).

Who is the main contact?
Dr Martin Kaiser

Contact information

Type(s)
Scientific

Contact name
Prof Gareth Morgan

Contact details
Centre for Myeloma Research
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Sutton
United Kingdom
SM2 5PT

Additional identifiers

ClinicalTrials.gov (NCT)
NCT02406222

Clinical Trials Information System (CTIS)
2015-004508-49

Protocol serial number
HM13/10758

Study information

Scientific Title
Pomalidomide Specific Targeting in Relapsed and Refractory Myeloma (MUK Seven)

Acronym
MUK Seven

Study objectives

Current hypothesis as of 08/09/2015:
1. To compare the combination of pomalidomide, cyclophosphamide and dexamethasone with pomalidomide and dexamethasone alone.
2. Identify markers from bone marrow and blood samples to predict response to pomalidomide.

Previous hypothesis:
1. To present further safety and efficacy data of pomalidomide in relapsed/refractory myeloma in the UK.
2. Identify markers from bone marrow and blood samples to predict response to pomalidomide.

On 08/09/2015 the following changes were made to the trial record:
1. The study design was changed from 'Interventional non-randomised single arm trial' to 'Interventional randomised trial'.
2. The overall trial start date was changed from 01/08/2014 to 01/09/2015.
3. The overall trial end date was changed from 01/02/2016 to 01/09/2017.

Ethics approval required
Old ethics approval format

Ethics approval(s)
MRES Committee London – Surrey Borders – REC approval pending

Study design
Interventional randomised trial

Primary study design
Interventional

Study type(s)
Treatment

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

Interventions
Current interventions as of 08/09/2015:
Patients will be randomised to receive treatment with either Pd (pomalidomide and dexamethasone) or CPD (pomalidomide, cyclophosphamide and dexamethasone). All treatment cycles will consist of 28 days and participants will receive treatment with pomalidomide and dexamethasone until they progress or are unable to tolerate treatment any longer.

Previous interventions:
Participants will receive treatment with oral pomalidomide and dexamethasone, this will be given to the participant to take at home. 4 mg of Pomalidomide will be taken daily on days 1-21 of the 28 day cycle, 40 mg of dexamethasone will be taken on days 1, 8, 15 and 22 only. The participant will see their doctor at hospital at least once a month.

Participants will receive treatment with pomalidomide and dexamethasone until they progress or are unable to tolerate treatment any longer.

Intervention Type

Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Pomalidomide, dexamethasone, cyclophosphamide

Primary outcome(s)
Current primary outcome measures as of 08/09/2015:
Progression free survival, from randomisation until disease progression

Previous primary outcome measures:
Safety and toxicity, as assessed by adverse reactions throughout the trial

Key secondary outcome(s))
Current secondary outcome measures as of 08/09/2015:
1. Response to treatment defined as achieving at least a partial response during treatment. Maximal response will be defined as the proportion of participants achieving a response as their maximum response to treatment. Time to response will be measured from randomisation to the maximal response achieved. Duration of response will be from the time of achieving at least a partial response until disease progression.
2. Safety and toxicity, as assessed by adverse reaction throughout the trial.

Previous secondary outcome measures:
1. Response to treatment defined as achieving at least a partial response during treatment. Maximal response will be defined as the proportion of participants achieving a response as their maximum response to treatment. Time to response will be measured from registration to the maximal response achieved. Duration of response will be from the time of achieving at least a partial response until disease progression.
2. Progression-free survival will be calculated from registration until disease progression or death. Overall survival will be calculated from registration to death.

Completion date
01/09/2017

Reason abandoned (if study stopped)
Change of design resulted in a new trial being submitted to REC/MHRA.

Eligibility

Key inclusion criteria
Current inclusion criteria as of 08/09/2015:
1. Diagnosed with symptomatic multiple myeloma and have measurable disease
2. Participants must require therapy for relapsed or refractory disease
3. Participants must have received ≥ 2 treatment lines of anti-myeloma therapy
4. Participants must have received prior treatment with both lenalidomide and proteasome inhibitor, either as single agents or in combination regimens
5. All participants must have failed treatment with either lenalidomide or proteasome inhibitor in one of the following three ways:
5.1. Documented progressive disease on or within 60 days of completing treatment with

lenalidomide and/or proteasome inhibitor
5.2. In case of prior response [≥ partial response (PR)] to lenalidomide or proteasome inhibitor, participants must have relapsed within 6 months after stopping treatment with lenalidomide and /or proteasome inhibitor-containing regimens
5.3. Participants who have not had a ≥ minimal response (MR) despite receiving at least 4 cycles of treatment or who have developed intolerance/toxicity after a minimum of two cycles of lenalidomide- and/or proteasome inhibitor-containing regimen
6. Participants must have received adequate prior alkylator therapy in one of the following three ways:
6.1. As part of a stem cell transplant
6.2. A minimum of 4 consecutive cycles of an alkylator based therapy
6.3. Progression on treatment with an alkylator; provided that the participant received at least two cycles of an alkylator-containing therapy.
7. Life expectancy of at least 3 months
8. Eastern Cooperative Oncology Group (ECOG) performance status score of 0, 1, or 2
9. Required laboratory values: within 14 days of day 1 of treatment
9.1. Absolute neutrophil count (ANC) ≥ 1.0 x 109/L (growth factor support is permitted)
9.2. Platelet count ≥ 30 x 109/L (platelet transfusion is permitted
9.3. Creatinine Clearance > 30 mL/min
9.4. Corrected serum calcium ≤3.5 mmol/L
9.5. Haemoglobin ≥ 8 g/dL (blood transfusion support is permitted)
9.6. Aspartate aminotransferase (AST) or Alanine aminotransferase (ALT) < 3.0 x upper limit of normal (ULN)
9.7. Serum total bilirubin < 17µmol/l
10. Participants must consent to provide a bone marrow sample
11. Able to give informed consent and willing to follow trial protocol
12. Aged 18 years or over
13. Females of childbearing potential (FCBP) must agree to utilise one reliable form of contraception for 28 days prior to starting trial treatment, during the trial and for 28 days after trial treatment discontinuation and even in case of dose interruption, and must agree to regular pregnancy testing during this timeframe.
14. Females must agree to abstain from breastfeeding during trial participation and 28 days after trial drug discontinuation
15. Males must agree to use a latex condom during any sexual contact with FCBP during the trial, including during dose interruptions and for 28 days following discontinuation from this trial even if he has undergone a successful vasectomy
16. Males must also agree to refrain from donating semen or sperm while on pomalidomide including during any dose interruptions and for 28 days after discontinuation from this trial
17. All participants must agree to refrain from donating blood while on trial

Previous inclusion criteria:
1. Diagnosed with symptomatic multiple myeloma and have measurable disease
2. Participants must require therapy for relapsed or refractory disease
3. Participants must have received ≥ 2 treatment lines of anti-myeloma therapy
4. Participants must have received prior treatment with both lenalidomide and bortezomib, either as single agents or in combination regimens
5. All participants must have failed treatment with either lenalidomide or bortezomib in one of the following three ways:
5.1. Documented progressive disease on or within 60 days of completing treatment with lenalidomide and/or bortezomib
5.2. In case of prior response [≥ partial response (PR)] to lenalidomide or bortezomib, participants must have relapsed

within 6 months after stopping treatment with lenalidomide and/or bortezomib-containing regimens
5.3. Participants who have not had a ≥ minimal response (MR) despite receiving at least 4 cycles of treatment or who have developed intolerance/toxicity after a minimum of two cycles of lenalidomide- and/or bortezomib-containing regimen
6. Participants must have received adequate prior alkylator therapy in one of the following three ways:
6.1. As part of a stem cell transplant
6.2. A minimum of 4 consecutive cycles of an alkylator based therapy
6.3. Progression on treatment with an alkylator; provided that the participant received at least two cycles of an alkylator-containing therapy.
7. Life expectancy of at least 3 months
8. Eastern Cooperative Oncology Group (ECOG) performance status score of 0, 1, or 2
9. Required laboratory values: within 14 days of day 1 of treatment
9.1. Absolute neutrophil count (ANC) ≥ 1.0 x 109/L (growth factor support is permitted)
9.2. Platelet count ≥ 30 x 109/L (platelet transfusion is permitted
9.3. Creatinine Clearance > 30 mL/min
9.4. Corrected serum calcium ≤3.5 mmol/L
9.5. Haemoglobin ≥ 8 g/dL (blood transfusion support is permitted)
9.6. Aspartate aminotransferase (AST) or Alanine aminotransferase (ALT) < 3.0 x upper limit of normal (ULN)
9.7. Serum total bilirubin < 2.0 mg/dL, or <3.0 x ULN for participants with hereditary benign hyperbilirubinemia
10. Participants must consent to provide a bone marrow sample
11. Able to give informed consent and willing to follow trial protocol
12. Aged 18 years or over
13. Females of childbearing potential (FCBP) must agree to utilise one reliable form of contraception for 28 days prior to starting trial treatment, during the trial and for 28 days after trial treatment discontinuation and even in case of dose interruption, and must agree to regular pregnancy testing during this timeframe.
14. Females must agree to abstain from breastfeeding during trial participation and 28 days after trial drug discontinuation
15. Males must agree to use a latex condom during any sexual contact with FCBP during the trial, including during dose interruptions and for 7 days following discontinuation from this trial even if he has undergone a successful vasectomy
16. Males must also agree to refrain from donating semen or sperm while on pomalidomide including during any dose interruptions and for 7 days after discontinuation from this trial
17. All participants must agree to refrain from donating blood while on trial

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
Current exclusion criteria as of 08/09/2015:
1. Unable or unwilling to give a bone marrow sample for laboratory analysis.
2. Previous therapy with pomalidomide
3. Hypersensitivity to thalidomide, lenalidomide, cyclophosphamide or dexamethasone
4. Participants with non-secretory multiple myeloma
5. Peripheral neuropathy ≥ Grade 3
6. Participants who have received an allogeneic bone marrow or allogeneic peripheral blood stem cell transplant
7. Participants who are planning for a stem cell transplant
8. Previous anti-tumour therapies including investigational medicinal products at any dose within 28 days before the start of treatment (or 5 half-lives whichever is longer). Bisphosphonates for bone disease and radiotherapy for palliative intent are permitted
9. Chronic use of steroids or any other immunosuppressive therapy
10. Participants with any one of the following:
10.1. Uncontrolled congestive heart failure
10.2. Myocardial infarction within 12 months prior to starting trial treatment
10.3. Unstable or poorly controlled angina pectoris, including Prinzmetal variant angina pectoris.
11. Participants with gastrointestinal disease that may significantly alter absorption of pomalidomide
12. Participants unable or unwilling to undergo antithrombotic prophylactic treatment
13. Pregnant or breastfeeding females
14. Participants known to be seropositive for Human Immunodeficiency Virus (HIV) or active infectious hepatitis A, B or C
15. Any conditions including the presence of laboratory abnormalities, which places the participant at unacceptable risk if they were to participate in the trial.
16. Participants with a history of other malignancies within 5 years before the date of study entry

Previous exclusion criteria:
1. Unable or unwilling to give a bone marrow sample for laboratory analysis.
2. Previous therapy with pomalidomide
3. Hypersensitivity to thalidomide, lenalidomide, or dexamethasone
4. Participants with non-secretory multiple myeloma
5. Peripheral neuropathy ≥ Grade 3
6. Participants who have received an allogeneic bone marrow or allogeneic peripheral blood stem cell transplant
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11. Participants with gastrointestinal disease that may significantly alter absorption of pomalidomide
12. Participants unable or unwilling to undergo antithrombotic prophylactic treatment

13. Pregnant or breastfeeding females
14. Participants known to be seropositive for Human Immunodeficiency Virus (HIV) or active infectious hepatitis A, B or C
15. Any conditions including the presence of laboratory abnormalities, which places the participant at unacceptable risk if they were to participate in the trial.

Date of first enrolment
01/09/2015

Date of final enrolment
01/09/2017

Locations

Countries of recruitment
United Kingdom

England

Northern Ireland

Scotland

Wales

Study participating centre
Royal Marsden NHS Foundation Trust
Sutton
United Kingdom
SM2 5PT

Study participating centre
St Bartholomew's Hospital
United Kingdom
EC1M 6BQ

Study participating centre
Guys & St Thomas' NHS Foundation Trust
United Kingdom
SE1 9RT

Study participating centre

Birmingham Heartlands Hospital
United Kingdom
B9 5SS

Study participating centre
St James Hospital
Leeds
United Kingdom
LS9 7TF

Study participating centre
Churchill Hospital
Oxford
United Kingdom
OX3 7LE

Study participating centre
Queen Elizabeth Hospital
Birmingham
United Kingdom
B15 2GW

Study participating centre
Royal Hallamshire Hospital
United Kingdom
S10 2SJ

Study participating centre
University College London
United Kingdom
NW1 2PG

Study participating centre
Beatson Oncology Centre
United Kingdom
G11 6NT

Study participating centre
Belfast City Hospital
United Kingdom
BT9 7AB

Study participating centre
Leicester Royal Infirmary
United Kingdom
LE1 5WW

Study participating centre
Ninewells Hospital
United Kingdom
DD1 9SY

Study participating centre
University Hospital of Wales
United Kingdom
CF14 4XW

Sponsor information

Organisation
University of Leeds (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

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not expected to be made available