ISRCTN90889843 https://doi.org/10.1186/ISRCTN90889843

Bendamustine, thalidomide, dexamethasone dose escalation study in relapsed/refractory myeloma

Submission date 18/06/2010	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 30/07/2010	**Overall study status** Completed	
Last Edited 26/10/2022	**Condition category** Cancer	

Plain English summary of protocol
https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-looking-bendamustine-chemotherapy-people-myeloma-that-has-come-back-or-is-resistant-to-treatment-muk-one

Contact information

Type(s)
Scientific

Contact name
Dr Steve Schey

Contact details
c/o Clinical Trials Research Unit
University of Leeds
Leeds
United Kingdom
LS2 9JT

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
N/A

Study information

Scientific Title
An open label, multicentre, randomised, parallel group phase II selection trial to identify the optimal starting dose of bendamustine (60 versus 100 mg/m2) when given in combination with thalidomide and dexamethasone in patients with relapsed/refractory multiple myeloma

Acronym
MUKone

Study objectives
The primary objective of this trial is to determine the optimum dose of bendamustine when combined with thalidomide and dexamethasone (BTD) in the treatment of relapsed/refractory multiple myeloma, based on response rates, tolerability and progression-free survival.

On 13/08/2012 the target number of participants was changed from 98 to 92.
On 23/08/2012 the overall trial end date was changed from 01/05/2012 to 10/07/2013.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Not provided at time of registration

Study design
Open-label multicentre randomised parallel group phase II two-stage selection trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet

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

Interventions
Arm A: Bendamustine (60), thalidomide, dexamethasone -
Bendamustine: Intravenous at 60 mg/m2/day on days 1 and 2 (30 - 60 minute infusion each day)
Thalidomide: Oral at 100 mg/day on days 1 - 28
Dexamethasone: Oral at 20 mg/day on days 1 - 4 and 15 - 18

Arm B: Bendamustine (100), thalidomide, dexamethasone -
Bendamustine: Intravenous at 100 mg/m2/day on days 1 and 2 (30 - 60 minute infusion each day)
Thalidomide: Oral at 100 mg/day on days 1 - 28
Dexamethasone: Oral at 20 mg/day on days 1 - 4 and 15 - 18

Each cycle is repeated at 28 days. Patients continue treatment until maximum response plus 2 cycles. Assuming tolerability, a minimum of 6 and maximum of 9 cycles will be given.

Patients will be followed up every 12 weeks for one year after the entry of the last patient (i.e. minimum of 1 year, maximum 2 years).

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Bendamustine, thalidomide, dexamethasone

Primary outcome measure
1. Proportion of patients achieving at least a partial response (as defined by the Modified International Working Group [IWG] Uniform Response Criteria) within six cycles of treatment, measured within 6 months of start of treatment, i.e., 18 months post-first patient
2. Proportion of patients successfully able to receive their second cycle of bendamustine within six weeks of receiving their first cycle, measured within 6 months of start of treatment, i.e., 18 months post-first patient
3. Progression-free survival, measured at 12 months post-randomisation, i.e., 24 months post first patient

Secondary outcome measures
1. Maximum response rate
2. Overall response rate
3. Response duration
4. Time to next treatment
5. Proportion of patients successfully receiving six cycles of treatment with no dose reductions or delays
6. Safety and toxicity
7. Feasibility of stem cell harvest following treatment (in eligible refractory patients)

All measured within 12 months of randomisation, i.e., within 24 months post-first patient

Overall study start date
01/09/2010

Completion date
10/07/2013

Eligibility

Key inclusion criteria

Current inclusion criteria as of 13/08/2012:
1. Aged greater than or equal to 18 years, either sex
2. Histologically confirmed multiple myeloma (MM) with measurable disease parameters requiring therapy for relapsed or refractory disease
3. Unsupported platelet count >75 x 109/L within 48 hours before registration
4. Absolute neutrophil count >1.5 x 109/L within 48 hours before registration. GCSF is permitted for no more than 7 days prior to registration.
5. Able to provide written informed consent
6. Performance status (Eastern Cooperative Oncology Group [ECOG]) 0 - 3
7. Life expectancy at least 3 months

Previous inclusion criteria until 13/08/2012:
1. Aged greater than or equal to 18 years, either sex
2. Histologically confirmed multiple myeloma (MM) with measurable disease parameters requiring therapy for relapsed or refractory disease
3. Able to provide written informed consent
4. Performance status (Eastern Cooperative Oncology Group [ECOG]) 0 - 3
5. Life expectancy at least 3 months
6. Serum bilirubin less than 1.5 times upper limit of normal
7. Serum alanine aminotransferase (ALT)/aspartate aminotransferase (AST) less than 2.5 times upper limit of normal

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
92 (95 patients recruited by end of recruitment on 13/07/2012)

Total final enrolment
94

Key exclusion criteria
Current exclusion criteria as of 13/08/2012:
1. Pregnancy, lactation or women of child-bearing potential unwilling to use adequate and highly effective method of contraception whilst receiving treatment and for 12 months after treatment has finished as defined by the Thalidomide Pregnancy Prevention Programme
2. Patients with non-secretory MM
3. Relapsed on previous bendamustine therapy
4. Serum bilirubin >2.0 times ULN within 14 days before registration
5. Serum ALT/AST > 2.5 times ULN within 14 days before registration
6. Patient has a calculated or measured creatinine clearance less than 10 mL/minute within 14 days before enrolment

7. Patient has greater than or equal to grade 2 peripheral neuropathy within 14 days before enrolment
8. Any history of hypersensitivity to any of the study medications or excipients
9. Seropositive for human immunodeficiency virus (HIV), or active hepatitis A, B or C infection
10. Previous or concurrent malignancies at other sites, with the exception of appropriately treated localised epithelial skin or cervical cancer. Patients with histories (greater than or equivalent to 12 months) of other cured tumours may be entered.
11. Serious medical or psychiatric illness likely to interfere with participation in this clinical study
12. Uncontrolled or severe cardiovascular disease including myocardial infarction within 6 months of enrolment, New York Heart Association (NYHA) class III or IV heart failure, uncontrolled angina, clinically significant pericardial disease, or cardiac amyloidosis
13. Subjects who have received an investigational medicinal product within 28 days of study entry
14. Steroid treatment totally greater than 160mg dexamethasone, or equivalent, in the 14 days prior to registration
15. Major surgery less than 30 days before start of treatment
16. Yellow fever vaccination within 3 months before registration
17. Current infections, especially involving leukocytopenia

Previous exclusion criteria until 13/08/2012:
1. Pregnancy, lactation or women of child-bearing potential unwilling to use adequate and highly effective method of contraception whilst receiving treatment and for 12 months after treatment has finished as defined by the Thalidomide Pregnancy Prevention Programme
2. Subjects with evidence of clinically unstable disease, as determined by medical history, clinical laboratory tests, electrocardiogram (ECG) results, and physical examination that, in the Investigator's opinion, preclude entry into the study
3. Any history of hypersensitivity to any of the study medications or excipients
4. Patients with non-secretory MM
5. Patient has a platelet count less than 40 x 10^9/L within 14 days before enrolment
6. Patient has an absolute neutrophil count less than 1.0 x 10^9/L within 14 days before enrolment
7. Patient has a calculated or measured creatinine clearance less than 10 mL/minute within 14 days before enrolment
8. Patient has greater than or equal to grade 2 peripheral neuropathy within 14 days before enrolment
9. Seropositive for human immunodeficiency virus (HIV), or active hepatitis A, B or C infection
10. Serious medical or psychiatric illness likely to interfere with participation in this clinical study
11. Previous or concurrent malignancies at other sites, with the exception of appropriately treated localised epithelial skin or cervical cancer. Patients with remote histories (greater than 5 years) of other cured tumours may be entered.
12. Poorly controlled hypertension or diabetes mellitus or other serious medical or psychiatric conditions that could interfere with adherence to or completion of this study
13. Uncontrolled or severe cardiovascular disease including myocardial infarction within 6 months of enrolment, New York Heart Association (NYHA) class III or IV heart failure, uncontrolled angina, clinically significant pericardial disease, or cardiac amyloidosis
14. Subjects who have received an investigational medicinal product within 30 days of study entry

Date of first enrolment
27/01/2012

Date of final enrolment

25/06/2012

Locations

Countries of recruitment
England

United Kingdom

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

Sponsor information

Organisation
University of Leeds (UK)

Sponsor details
c/o Dr Neville Young
Quality Assurance Manager - Clinical Trials
University of Leeds and Leeds Teaching Hospitals NHS Trust
Research & Development
34 Hyde Terrace
Leeds
England
United Kingdom
LS2 9LN

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
Not provided at time of registration

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	01/08/2015		Yes	No
Plain English results			26/10/2022	No	Yes