

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

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

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

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Additional identifiers

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

Primary study design

Interventional

Study design

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

Study type(s)

Treatment

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(s)

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

Key secondary outcome(s)

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

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 $>75 \times 10^9/L$ within 48 hours before registration
4. Absolute neutrophil count $>1.5 \times 10^9/L$ 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

Healthy volunteers allowed

No

Age group

Adult

Lower age limit

18 Years

Sex

All

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 $40 \times 10^9/L$ within 14 days before enrolment
6. Patient has an absolute neutrophil count less than $1.0 \times 10^9/L$ 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

United Kingdom

England

Study participating centre

University of Leeds

Leeds

United Kingdom

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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

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

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