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Velcade™ (bortezomib) combination chemotherapy in AL amyloidosis

Submission date 30/07/2010	**Recruitment status** Stopped	[X] Prospectively registered [ ] Protocol [ ] Statistical analysis plan [ ] Results [ ] Individual participant data [ ] Record updated in last year
Registration date 30/07/2010	**Overall study status** Stopped	
Last Edited 27/03/2019	**Condition category** Cancer	

Plain English summary of protocol
https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-looking-bortezomib-with-chemotherapy-for-amyloidosis-reveal

Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
2009-014906-33

Protocol serial number
8441

Study information

Scientific Title
A pilot study of relapsed or refractory patients using Velcade™ (bortezomib) combination chemotherapy in AL amyloidosis

Acronym
REVEAL

Study objectives
The trial aims to assess the efficacy, safety and tolerability of two bortezomib-based combination chemotherapy regimens in patients with AL amyloidosis who have relapsed (disease has been succesfully treated but has returned) or have inadequate response to front line treatment (disease has responded partly but not enough to improve the amyloid related organ function) or are refractory (disease has not responded at all to prior treatment).

Background:
AL amyloidosis is a multisystem disorder resulting from the accumulation of abnormal protein deposits called amyloid deposits in various organs of the body, causing impairment of organ function. The deposited proteins are formed by light chains secreted by abnormal plasma cells (a type of blood cell). Treatment of AL amyloidosis involves chemotherapy to kill the abnormal plasma cell, thus reducing the abnormal light chains, in the hope of slowing down or halting amyloid deposition, and preserving organ function. Bortezomib, used as a single agent, has been shown to be an effective agent for treating myeloma and amyloidosis and combining it with other drugs appears to increase the rapidity and completeness of response i.e. a quick and long-lasting remission in myeloma. The current study would be the first study of such combinations in relapsed or refractory AL amyloidosis.

Specific aims of research:
The study will compare two bortezomib-dexamethasone-chemotherapy combinations, one with adriamycin (PAD) and one with cyclophosphamide (CVD), in a randomised multicentre parallel phase II design.

Outline of research plan:
The patients will be identified and consented at the UK National Amyloidosis Centre and will be treated at regional haematology centres (RHCs). They will be given 3 cycles of chemotherapy and will be assessed for response thereafter. Those who have only a partial response will continue to a maximum of six cycles.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Central London REC 4 pending as of 13/08/2010, ref: 10/H0715/30

Primary study design
Interventional

Study design
Multicentre randomised interventional treatment trial

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Topic: National Cancer Research Network; Subtopic: Haematological Oncology; Disease: Leukaemia (acute), Leukaemia (acute lymphoblastic)

Interventions
PAD or CVD (maximum of 6 x 21 day cycles):

1. PAD:
Bortezomib 1.0 mg/m2 intravenous (IV) Days 1, 4, 8, 11 (increase to 1.3 mg/m2 if well tolerated)
Doxorubicin 18 mg/m2 IV Days 1, 8
Dexamethasone 20 mg orally (po) Days 1, 4, 8, 11 (increase to 40 mg if well tolerated)

2. CVD:
Bortezomib 1.0 mg/m2 IV Days 1, 4, 8, 11 (increase to 1.3 mg/m2 if well tolerated)
Cyclophosphamide 350 mg/m2 po Days 1, 8, 15
Dexamethasone 20 mg po Days 1, 4, 8, 11 (increase to 40 mg if well tolerated)

Follow-up length: 7 months
Study entry: single randomisation only

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Bortezomib, adriamycin, cyclophosphamide

Primary outcome(s)
1. Clonal response of the underlying plasma cell dyscrasia
2. Safety and toxicity of PAD and CVD
All assessed at 3 or 7 months.

Key secondary outcome(s)
1. Improvement in amyloidotic organ function
2. Overall survival
3. Cost effectiveness
All assessed at 7 months.

Completion date
31/05/2013

Reason abandoned (if study stopped)
Objectives no longer viable

Eligibility

Key inclusion criteria

1. Aged 18 years or greater, either sex
2. Systemic AL amyloidosis who fulfil all the following criteria:
2.1. Measurable clonal disease in the serum as defined by either a serum paraprotein of greater than 7 g/L or the abnormal component of the serum free light chain greater than 75 mg/L (abnormal ratio only in case of renal failure)
2.2. Amyloid related organ dysfunction or organ syndrome
3. Following prior chemotherapy or prior autologous stem cell transplant, evidence of either:
3.1. Clonal disease relapse
3.2. Refractory clonal disease
3.3. Inadequate clonal response (defined as less than a 90% reduction in serum clonal markers)
4. Capable of providing written informed consent

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
All

Key exclusion criteria
1. Overt symptomatic non-amyloid manifestations of multiple myeloma
2. Amyloidosis of unknown or non-AL type
3. Localised AL amyloidosis (in which amyloid deposits are limited to a typical single organ, for example the bladder or larynx, in association with a clonal proliferative disorder within that organ)
4. Trivial or incidental AL amyloid deposits in the absence of a significant amyloid related organ syndrome (e.g., isolated carpal tunnel syndrome)
5. Allogeneic stem cell transplantation
6. Solid organ transplantation
7. Severe peripheral neuropathy or autonomic neuropathy causing significant functional impairment
8. Thrombocytopaenia (platelet count less than 50 x 10^9/l)
9. Neutropaenia (neutrophil count less than 1 x 10^9/l)
10. Liver involvement by amyloid causing bilirubin greater than 2 times or alkaline phosphatase greater than 4 times upper limit of normal
11. Estimated glomerular filtration rate (eGFR) less than 20 ml/min but not on dialysis (patients on dialysis are not excluded)
12. Ejection fraction less than 40%
13. New York Heart Association (NYHA) class IV heart failure
14. Eastern Cooperative Oncology Group (ECOG) performance status greater than 3
15. Estimated life expectancy of less than 3 months
16. Active hepatitis B or C or human immunodeficiency virus (HIV) infection

17. Previous cumulative anthracycline dose of greater than 200 mg/m2
18. Previous treatment with bortezomib combined with anthracycline and/or alkylator and/or immunomodulatory drugs (ImiD)
19. Concurrent active malignancies, except surgically removed basal cell carcinoma of the skin or other in situ carcinomas
20. Pregnant, lactating or unwilling to use adequate contraception
21. Intolerance/sensitivity to any of the study drugs

Date of first enrolment
01/12/2010

Date of final enrolment
31/05/2013

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Cancer Research UK & UCL Cancer Trials Centre
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Sponsor information

Organisation
University College London (UCL) (UK)

ROR
https://ror.org/02jx3x895

Funder(s)

Funder type
Charity

Funder Name

Cancer Research UK (CRUK) (UK) - Clinical Trials Advisory and Awards Committee (CTAAC) grant (ref: C23725/A11440)

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?
HRA research summary			28/06/2023	No	No