

# Velcade™ (bortezomib) combination chemotherapy in AL amyloidosis

<b>Submission date</b> 30/07/2010	<b>Recruitment status</b> Stopped	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 30/07/2010	<b>Overall study status</b> Stopped	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
<b>Last Edited</b> 27/03/2019	<b>Condition category</b> Cancer	<input type="checkbox"/> Individual participant data <input type="checkbox"/> Record updated in last year

## 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

### Contact name

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### Contact details

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## Additional identifiers

### EudraCT/CTIS number

2009-014906-33

### IRAS number

### ClinicalTrials.gov number

### Secondary identifying numbers

## 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 successfully 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

### Study design

Multicentre randomised interventional treatment trial

### Primary study design

Interventional

## Secondary study design

Randomised controlled trial

## Study setting(s)

Hospital

## Study type(s)

Treatment

## Participant information sheet

Not available in web format, please use the contact details below to request a patient information sheet

## 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/m<sup>2</sup> intravenous (IV) Days 1, 4, 8, 11 (increase to 1.3 mg/m<sup>2</sup> if well tolerated)

Doxorubicin 18 mg/m<sup>2</sup> 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/m<sup>2</sup> IV Days 1, 4, 8, 11 (increase to 1.3 mg/m<sup>2</sup> if well tolerated)

Cyclophosphamide 350 mg/m<sup>2</sup> 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 measure

1. Clonal response of the underlying plasma cell dyscrasia

2. Safety and toxicity of PAD and CVD

All assessed at 3 or 7 months.

## Secondary outcome measures

1. Improvement in amyloidotic organ function
  2. Overall survival
  3. Cost effectiveness
- All assessed at 7 months.

**Overall study start date**

01/12/2010

**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

**Age group**

Adult

**Lower age limit**

18 Years

**Sex**

Both

**Target number of participants**

Planned sample size: 52; UK sample size: 52

**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  $50 \times 10^9/l$ )
9. Neutropaenia (neutrophil count less than  $1 \times 10^9/l$ )
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/m<sup>2</sup>
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**

England

United Kingdom

**Study participating centre**

Cancer Research UK & UCL Cancer Trials Centre

London

United Kingdom

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## **Sponsor information**

**Organisation**

University College London (UCL) (UK)

**Sponsor details**

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**Sponsor type**

University/education

**Website**

<http://www.ucl.ac.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****Publication and dissemination plan**

Not provided at time of registration

**Intention to publish date****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?
<a href="#">HRA research summary</a>			28/06/2023	No	No