NATIONAL AMYLOIDOSIS CENTRE
DIVISION OF MEDICINE
UCL

Professor PN Hawkins PhD FRCP FRCPath FMedSci
Tel: 020 7433 2815 (PA 2816) Email: p.hawkins@ucl.ac.uk
Dr JD Gillmore MD PhD FRCP
Tel: 020 7433 2726 Email: j.gillmore@ucl.ac.uk
Dr HJ Lachmann MD FRCP
Tel: 020 7433 2804 Email: h.lachmann@ucl.ac.uk
Dr AD Wechalekar MD FRCP FRCPath
Tel: 020 7433 2758 Email: a.wechalekar@ucl.ac.uk
Dr CJ Whelan MD MRCP
Tel: 020 7433 2875 Email: c.whelan@ucl.ac.uk

General Enquiries Tel: 020 7433 2725
Clinical Secretaries Tel: 020 7433 2811/2798/2772
Pathology Coordinator Tel: 020 7433 2753
Fax: ++44 (0)20 7433 2817

Low dose Cyclophosphamide-Bortezomib-Dexamethasone protocol

This protocol is for patients with Advanced Mayo Stage III (defined as NTproBNP >1000 pMol/L and some patients with SBP <100 mm of Hg)

Please see full dose protocol for stage I patients and intermediate dose protocol for stage II/Early stage III

	Day 1	Day 8	Day 15	Day 22	Day 29
Bortezomib 1.0mg/m^2 sc[a,b]	*	*	*	*	
Cyclophosphamide 350mg/m^2 PO (max 500mg) [c]	*	*	*	*	
Dexamethasone 20mg PO/IV [d]	*	*	*	*	

This protocol should be initiated under cardiac monitoring for the first dose of bortezomib (24-48 hrs from day 1)

[a] Use bortezomib IV if there is marked abdominal wall oedema due to uncertain absorption from oedematous sites
[b] Consider increase in the dose of bortezomib to 1.3mg/m^2 from day 8 onwards if day 1 dose is well tolerated. If SBP <90 mm of Hg, please consider addition of oral midodrine 2.5 mg BD (increase as needed to maximum of 20 mg TDS) to support the blood pressure before commencing therapy and to allow for adequate diuresis. In selected patients depending on tolerance, if there is less than a partial response by end of cycle 1 or less than a very good partial response by end of cycle 2, bortezomib dose can be further increased in 1.6mg/m^2
[c] Dose modify in renal failure (if eGFR <30 ml/min, reduce to 250 mg/m^2 or as per local guidelines)

[d] Dexamethasone should be given as 20 mg on day 1 and 8 of cycle 1 and, depending on tolerance, should be increased to 20 mg on days 1,2, 8,9, 15, 16, 22, 23

The cycle is repeated every 35 days

- All patients will receive a minimum of three cycles of CVD in the absence of unacceptable toxicity or poor tolerability.
- Discontinuation of chemotherapy (with close monitoring for relapse) should be considered among patients who experience severe adverse events as soon as they achieve a CR or VGPR
- Response should be assessed at the end of each cycle:
  - Patients who achieve a complete response or VGPR will continue for one more cycle after achieving response (e.g. if patient has achieved CR or VGPR at cycle 1 or 2, they will finish three cycles and stop. If they achieve CR or plateau after cycle 3, they will receive one more cycle after achieving CR or plateau).
  - Patients who achieve a partial response but not a VGPR (defined as dFLC <40 mg/L) by end of cycle 2 should be considered for dose increase in bortezomib.

- Patients with ongoing reduction in dFLC should continue until they achieve VGPR or complete response or to a maximum of 8 cycles.
- Patients who have not responded by end of cycle 2 will need regime modification after discussion with the NAC or as per local practice.

Prophylactic Medicines

All patients should receive prophylaxis as per local guidance or as suggested below:

a. Oral acyclovir 400 mg twice daily with **dose modified according to renal function** or appropriate alternative. Acyclovir should be continued for three months after the last dose of bortezomib.
b. Oral Lansoprazole 15 mg once daily or Omeprazole 20mg once daily or appropriate alternative
c. Oral Co-trimoxazole 480 mg twice daily given three times weekly (unless contraindicated). Prophylaxis to be continued for the duration of chemotherapy.

Antiemetics should be administered as per local protocols.