

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

Intermediate dose Cyclophosphamide-Bortezomib-Dexamethasone protocol

This protocol is for patients with Mayo Stage II or early/fitter stage III

Please see full dose protocol for stage I patients and low dose protocol for Advanced stage III

	Day 1	Day 8	Day 15	Day 22	Day 29
Bortezomib 1.3mg/m ² sc ^{a,b}	*	*	*	*	
Cyclophosphamide 350mg/m ² PO (max 500mg) ^c	*	*	*	*	
Dexamethasone 20mg PO/IV ^d	*	*	*	*	

^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 1.6mg/m² if tolerated and 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

^c Dose modify in renal failure (if eGFR <30 ml/min, reduce to 250 mg/m² or as per local guidelines)

^d Dexamethasone should be given as 20 mg on day 1 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.
- 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 to treatment 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

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- 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.