BORTEZOMIB-DEXAMETHASONE (Myeloma IX Relapse Protocol)

INDICATION : Myeloma

Prior to a course of treatment

- Check creatinine clearance – *see dose modification*.
- Assess cardiac function by history and exam with ECG, CXR. Consider MUGA scan if abnormal. Note bortezomib is contraindicated if severe cardiac impairment.
- Assess for peripheral neuropathy –may worsen on therapy; contraindicated if ≥ Grade 3 sensory
- Check FBC – neutrophils must be > 0.5, platelets >25 unless due to marrow infiltration
- Check LFTs – *see dose modification.*
- If appropriate discuss possibility of pregnancy with female patients and need for contraception with both male and female patients. Discuss potential for infertility - offer semen cryopreservation to male patients
- Written consent for course

Prior to each cycle

- Medical review of fitness for chemotherapy – exclude active infection, major changes in organ function.
- Check FBC, U&Es, creat, LFTs – *see dose modification*. *Discuss with consultant* if renal or hepatic function have changed change significantly.
- Encourage patient to drink 3 L fluid daily

Prior to each dose

- Reassess for peripheral neuropathy – *see dose modifications*
- Check FBC - give blood product and GCSF support as necessary during the cycle.

Bortezomib	1.3mg/m^2 od	IV bolus	days 1, 4, 8 and 11 **or** twice a week **but** allow at least 72hrs between each dose *(state dates on prescription)*
Dexamethasone	20mg od	PO	days 1-2, 4-5, 8-9 and 11-12

Repeat cycle every 21 days

- Plan to give at least 2 cycles to assess response
- If CR is achieved give an additional 2 cycles up to a maximum of 8 cycles
- If there is partial or marginal response give an additional 2 cycles after plateau up to max. 8 cycles
- If patient fails to reach at least a minimal response after 4 cycles consider stopping bortezomib - *discuss with consultant*

Anti-emetic prophylaxis	Metoclopramide
Other medications	Allopurinol 300mg od (100mg if Cr.Cl <20ml/min) for cycle 1 Acyclovir 400mg qds recommended

Dose modification for neutropenia (unless due to disease)

• Neutrophils <0.5 or platelets <25 on day 1 of cycle	Stop until > 1.0 then restart at 1.0 mg/m^2 if initially 1.3mg/m^2 or 0.7 mg/m^2 if initially 1.0mg/m^2 **OR** GCSF prophylaxis
• No resolution of neutropenia or recurs at 0.7mg/m^2	Consider stopping treatment – *discuss with consultant*

Dose modification for thrombocytopenia (unless due to disease)

• Platelets <25 on day 1 of cycle	Stop until >25 then restart at 1.0 mg/m^2 if initially 1.3mg/m^2 or 0.7 mg/m^2 if initially 1.0mg/m^2 **OR** Support with platelet transfusion
• No resolution of thrombocytopenia or recurs at 0.7mg/m^2	Consider stopping treatment – *discuss with consultant*

Dose modifications for peripheral neuropathy

• Grade 1 (but no pain) i.e loss of tendon reflexes or paraesthesiae but not interfering with function	No change
• Grade 1 with pain or Grade 2, i.e objective sensory loss or paraesthesia interfering with function but not activities of daily living	Reduce to 1.0mg/m^2
• Grade 2 with pain or Grade 3, i.e sensory loss or paraesthesia interfering with activities of daily living	Withhold until symptoms resolve, then restart at 0.7mg/m^2 at once a week. If symptoms fail to resolve within 2 weeks – stop treatment
• Grade 4, i.e permanent sensory loss that interferes with function	Discontinue bortezomib

Modification for renal dysfunction

- If < 30ml/min *discuss with consultant*. Note that the incidence of serious adverse effects increases with mild-moderate renal impairment. Patients have been treated safely when the creatinine clearance is<30ml/min and on dialysis but monitor carefully for toxicities if renal function is impaired.

Modification for liver dysfunction

- The major route of bortezomib excretion is hepatic and there is limited on the use of bortezomib in patients with hepatic impairment. If bilirubin >30μmol/L use with caution, monitor closely for toxicity and consider dose reduction – *discuss with consultant*

Dose modification for diarrhoea

• If ≥ grade 3 diarrhoea, i.e increase of ≥ 7 stools/day over baseline, incontinence, hospitalization with >24 hrs IV fluids	Reduce dose to 1.0mg/m^2, then 0.7mg/m^2 if symptoms persist

Bortezomib Toxicities

Thrombocytopenia	Nausea
Neutropenic sepsis	Fatigue
Fluid retention & cardiac failure	Diarrhoea, constipation & ileus
Peripheral neuropathy (may be painful)	Hypotension
Fatigue, malaise, weakness	

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