DT-PACE

This protocol must be used in conjunction with the Celgene Pregnancy Prevention Plan

INDICATION: Relapsed or refractory multiple myeloma

Prior to a course of treatment

- Double lumen Hickman line
- Assess cardiac function by history & exam, ECG and CXR. If there is evidence of cardiac disease or risk factors or prior anthracyclines perform a MUGA scan or echo. If LVEF< 50% doxorubicin may be inappropriate – *discuss with consultant*.
- Clinical assessment for neuropathy – do not use thalidomide if there is neuropathy of severity grade3 (severe sensory loss or paraesthesiae interfering with ADLs, weakness interfering with ADLs) or grade 4 (sensory loss causing disability, or paralysis)
- Patient must be counselled about the risk of birth defects with foetal exposure. A completed prescription authorisation form must accompany each prescription.
- Check FBC – neutrophils must be > 1.0, platelets >75 unless due to marrow infiltration
- Check U&Es, creat, LFTs– *see dose modifications*
- Written consent for course

Prior to each cycle

- Medical review of fitness for chemotherapy – exclude active infection, major changes in organ function.
- Patient must be counselled about the risk of birth defects with foetal exposure. See Celgene Pregnancy Prevention Programme. A completed prescription authorisation form must accompany each prescription.
- Clinical assessment for neuropathy – do not use thalidomide if there is neuropathy of severity grade3 (severe sensory loss or paraesthesiae interfering with ADLs, weakness interfering with ADLs) or grade 4 (sensory loss causing disability, or paralysis)
- Request irradiated blood products from day -7 if PBSC harvesting is planned
- Check FBC, U&Es, creat, LFTs – delay treatment until neuts > 1.0 x 10^9/l and platelets > 100 x 10^9/l

Day 1	Start thalidomide	400mg od PO nocte	(50mg capsules)
	Thalidomide to be continued throughout treatment		
	Dexamethasone	40mg od PO	(2mg tablets)
	Cisplatin	10mg/m^2 continuous IV infusion	*see note 2*
	Etoposide	40mg/m^2 continuous IV infusion	*see note 1*
	Doxorubicin	10mg/m^2 continuous IV infusion	*see note 1*
	Cyclophosphamide	400mg/m^2 IV bolus	
Day 2	Dexamethasone	40mg od PO	(2mg tablets)
	Cisplatin	10mg/m^2 continuous IV infusion	*see note 2*
	Etoposide	40mg/m^2 continuous IV infusion	*see note 1*
	Doxorubicin	10mg/m^2 continuous IV infusion	*see note 1*
	Cyclophosphamide	400mg/m^2 IV bolus	

Day 3	Dexamethasone	40mg od PO	(2mg tablets)
	Cisplatin	10mg/m^2 continuous IV infusion	*see note 2*
	Etoposide	40mg/m^2 continuous IV infusion	*see note 1*
	Doxorubicin	10mg/m^2 continuous IV infusion	*see note 1*
	Cyclophosphamide	400mg/m^2 IV bolus	
Day 4	Dexamethasone	40mg od PO	(2mg tablets)
	Cisplatin	10mg/m^2 continuous IV infusion	*see note 2*
	Etoposide	40mg/m^2 continuous IV infusion	*see note 1*
	Doxorubicin	10mg/m^2 continuous IV infusion	*see note 1*
	Cyclophosphamide	400mg/m^2 IV bolus	
Day 5	GCSF	daily sc od until neutrophils > 1.0 x 10^9/l for 2 consecutive days (10mcg/kg sc od if PBSC harvest planned)	

Note 1: Daily dose of etoposide and doxorubicin combined in 1.0L N saline and infused over 24 hours

Note 2: Cisplatin made in 1.0L Nsaline with 20mmol/l KCl and 10mmol/l $MgSO_4$ and infused over 24 hours

Repeat cycle every 4 – 6 weeks for 2 – 6 cycles in total

Other medications

Allopurinol 300mg od (100mg if Cr Cl < 20ml.min)

Fluconazole 50mg od

Acyclovir 400mg bd

Cotrimoxazole 480mg od

Consider anti-bacterial prophylaxis according to local policy

H_2 antagonist or PPI

Chlorhexidine mouthwash 10ml qds

Prophylactic dose LMWH (when platelets > 50 x 10^9/l) if not on warfarin

Cisplatin dose modifications renal impairment

Cr Cl > 60ml/min	100% dose
Cr Cl 50-60ml/min	75% dose
Cr Cl 40-50ml/min	50% dose
Cr Cl < 40ml/min	Omit cisplatin

Etoposide dose modification for renal impairment

GFR > 50ml/min	100% dose
GFR 10-50ml/min	75% dose
GFR < 10ml/min	50% dose

Etoposide dose modification for hepatic toxicity

Bilirubin 26-51umol/l or AST 60-180u/l	50% dose
Bilirubin > 51umol/l or AST > 180u/l	Omit

Doxorubicin dose modification for hepatic toxicity

Bilirubin 26-51umol/l	50% dose
Bilirubin 51-85umol/l	25% dose
Bilirubin >85umol/l	Omit
AST 2-3 x ULN	75% dose
AST > 3 x ULN	50% dose

Management of neuropathy secondary to thalidomide

	Sensory	**Motor**
Grade 1	Loss of deep tendon reflexes, mild paraesthesias but not interfering with function	Asymptomatic weakness on exam only
Grade 2	Sensory alteration or paraesthesias interfering with function but not ADLs	Symptomatic weakness interfering with function but not ADLs
Grade 3	Severe sensory loss or paraesthesias interfering with ADLs	Weakness interfering with ADLs; bracing or assisitance to walk required
Grade 4	Disability	Severe weakness/disability e.g paralysis

Grade 3 or 4 toxicity	Stop thalidomide until symptoms resolve; consider reintroducing at 50mg od and escalation up to 200mg if tolerated
Grade 2 toxicity	Stop thalidomide until toxicity resolves to less than grade 1then restart at 50% dose
Grade 1 toxicity	Reduce dose by 50%

DT-PACE Toxicities

Neutropenic sepsis	Thrombocytopenia and bleeding
Rash	Venous thromboembolism
Sedation	Constipation
Rash	Tremor
Oedema	Renal failure
Sensory and motor neuropathy	Tinnitus and hearing loss
Cardiomyopathy, arrythmias	Gastric ulceration
Personality and mood changes	

Reference; Lee C et al. DT-PACE: an effective, novel combination chemotherapy with thalidomide for previously treated patients with myeloma. J Clin Oncol 2003;21(14); 2732-2739

LSCCN HAEMATOLOGY PROTOCOLS

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