FLUDARABINE & CYCLOPHOSPHAMIDE
(based on LY05 Trial for mantle cell lymphoma)

INDICATION: Mantle cell lymphoma

Prior to a course of treatment

- If creatinine is raised check creatinine clearance by 24 hr urine collection – *see dose modification if Creat. Clear <60ml/min and discuss with consultant*
- Check FBC. Patient should have adequate bone marrow reserve, i.e neutrophils > 1.0, platelets >75 unless cytopaenia is due to disease, e.g marrow infiltration, splenomegaly
- Inform transfusion lab that irradiated blood products will be required
- If appropriate discuss possibility of pregnancy with female patients and need for contraception with both male and female patients. Discuss risk of infertility -offer semen cryopreservation to males.
- Written consent for course

Prior to each cycle

- Medical review of fitness for chemotherapy – exclude active infection, major changes in organ function
- Check FBC - neutrophils should be >1.0 and platelets >75
- Check creatinine – if previous fludarabine dose reduction consider gradual escalation according to renal function and haematological toxicity in earlier cycles

Fludarabine *	40mg/m^2	PO	od for 3 days
Cyclophosphamide **	250mg/m^2	PO	od for 3 days

Cyclophosphamide tablets should be taken at breakfast and fludarabine tablets at lunchtime
Note fludarabine is supplied as 10mg tablets, cyclophosphamide as 50mg tablets so round doses up or down as required

** 10mg tablets* *** 50mg tablets*

Nausea & diarrhoea are common with oral fludarabine –an **intravenous regimen** may be better tolerated

Fludarabine	25mg/m^2	IV	od for 3 days
Cyclophosphamide	250mg/m^2	IV	od for 3 days

Cyclophosphamide should be injected immediately before fludarabine for optimum effect

Repeat cycle every 28 days for up to 8 cycles

Prophylaxis for acute emesis	5HT antagonist for 3 days
Prophylaxis for delayed emesis	5HT antagonist + metoclopramide for 3-4 days (*do not use dexamethasone for anti-emetic prophylaxis)*
Other medications	Allopurinol 300mg od for 7 days with cycle 1
	Cotrimoxazole 480mg od until 6 months after completion

Dose modifications haematological toxicity (unless due to disease)

• Day 28 neuts <1.0 or plats <75	Delay treatment for up to 2 weeks & reduce dose of cyclo/fludara by 25% for subsequent cycles if counts recover *
• Neuts 0.5-1.0 or plats 50-75 despite two weeks delay	Proceed with chemotherapy at 50-75% dose *
• Day 28 neuts 0.5-1.0 or plats 50-75 despite 25% dose reduction	Reduce to 50% original doses of cyclo/fludara *
• Day 28 neuts <0.5 or plats <50	Delay until theses levels reached then proceed as above

**Growth factor support with GCSF may be appropriate in some cases - discuss with consultant*

Dose modification for renal dysfunction

• Creat. Clearance 30 – 60ml/min	50% dose fludarabine
• Creat. clearance <10ml/min	Stop fludarabine

Fludarabine & Cyclophosphamide Toxicities

Neutropenic sepsis	Nausea (moderate-severe)
Thrombocytopenia	Alopecia
Auto-immune haemolysis	Amenorrhoea & infertility (offer semen cryopreservation)
Opportunist infections	Hepatotoxicity
Diarrhoea	Encephalopathy – coma, cortical blindness (rarely)

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