FLUDARABINE & CYCLOPHOSPHAMIDE (based on the MRC CLL4)

INDICATION: CLL, lymphoplasmacytic lymphoma

Prior to a course of treatment

- If creatinine is raised check creatinine clearance – *see dose modification*
- 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
- 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
- Inform transfusion lab that irradiated blood products will be required
- 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 *(see dose modification)*
- Check creatinine – consider gradual dose escalation according to renal function and haematological toxicity in earlier cycles

Fludarabine *	24mg/m^2	PO	od for 5 days
Cyclophosphamide **	150mg/m^2	PO	od for 5 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 in 100ml Nsaline	IV over 30mins	od for 3 days
Cyclophosphamide	250mg/m^2	IV bolus	od for 3 days

Cyclophopshamide 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 5 days
Prophylaxis for delayed emesis	5HT antagonist + metoclopramide for 3-4 days *(do not use dexamethasone for antiemetic 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

• Creatinine clearance 30-60ml/min	50% fludarabine
• Creatinine 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)

Written by Dr MP Macheta, Consultant Haematologist

Date July 2013

Review date July 2015