FC

CLL and Low Grade NHL that is relapsing on, or refractory to, primary treatment
First-line treatment in selected patients

Drugs/Dosage:

Cyclophosphamide	150mg/m^2	PO daily	Day l to Day 5
(rounded to nearest 50mg and taken at breakfast)			
Fludarabine	24mg/m^2	PO daily	Day l to Day 5
(rounded to nearest 10mg and taken at lunchtime)			

Or, if oral route not tolerated,

Cyclophosphamide	250mg/m^2	IV daily	Days 1, 2 and 3
Fludarabine	25mg/m^2	IV daily	Days 1, 2 and 3

Administration: Cyclophosphamide tablets to be taken at breakfast time. They should be swallowed whole with plenty of water. Encourage the patient to drink plenty of fluids during the five days of oral cyclophosphamide, and for 24 hours after completed.
Fludarabine tablets to be taken at lunchtime, swallowed whole with water.

IV Cyclophosphamide should be given immediately before IV Fludarabine.
Both may be given as a bolus.

Other Drugs: Allopurinol 300mg po daily, ideally starting 24 hours before chemotherapy - review after 4 weeks
PCP prophylaxis - prescribe according to unit practice/protocol (generally until 6 months after completion of treatment, or according to CD_4 counts)
Consider aciclovir prophylaxis if history of VZV or HSV reactivation

Frequency: 4 weekly cycle for 6 - 8 cycles

Main Toxicities: myelosuppression; alopecia: opportunistic infections;
GI upset, chiefly diarrhoea (more common with oral option);
haemorrhagic cystitis; autoimmune haemolytic anaemia (fludarabine – see Comments); ovarian failure; infertility

Anti - emetics: Oral route – mildly emetogenic
IV route - moderately emetogenic

Regular Investigations:		
FBC		D1
LFTs and U&Es		D1
LDH		every other cycle **only** if elevated prior to treatment
DAT	}	baseline, and repeat if disproportionate anaemia or
Reticulocytes	}	any history of autoimmune haemolytic anaemia (AHA)
Bilirubin	}	(see Comments)

Comments: Oral treatment is preferred, if tolerated, but may produce more GI side effects (in up to 50% patients)

Reason for Update: Prepared for Network use	Approved by Chair of Network TSSG: Dr A Laurie
Version: 1	Date: 23.2.06
Supersedes: All previous versions	Review date: February 2008
Prepared by Oncology Pharmacist: S Taylor	Checked by Network Pharmacist: Jacky Turner

All patients must receive irradiated blood products for all future transfusions - inform patient and blood bank.

Patients undergoing treatment with fludarabine should be closely monitored for signs of AHA. Fludarabine should be used with caution if DAT positive in the absence of haemolysis.

In patients presenting with both leukaemia and haemolysis, the patient should usually first be treated to control haemolysis before commencing fludarabine. If the haemolysis subsequently re-occurs / worsens, then discontinuation of fludarabine is recommended.

Dose Modifications

Haematological Toxicity:

Cycle 1:
If Stage C disease (Hb < 100g/L or platelets < 100 x 10^9/L not due to autoimmune phenomena), give oral prednisolone for 3 – 4 weeks, then start treatment 1 to 2 weeks later.
For any other low initial counts thought to be disease-related, proceed with full dose treatment.

Subsequent Cycles: If a fall in counts is thought to be due to treatment, proceed as follows:
If neutrophils < 1.0 x 10^9/l or platelets < 75 x 10^9/l, defer for 1 week.
Repeat FBC and, if counts have recovered, proceed with full dose treatment.
If the counts have not recovered after 2 weeks delay, consider continuing treatment with a 50% dose reduction of both drugs.

Renal Impairment:

CrCl (ml/min)	Fludarabine Dose
> 70	Give 100%
30 – 70	Give 50%
< 30	Contra-Indicated

CrCl (ml/min)	Cyclophosphamide Dose
> 50	Give 100%
10 – 50	Give 75%
< 10	Give 50%

Patient Information: CancerBACUP leaflets for Fludarabine and Cyclophosphamide

References:
O'Brien et al; Blood (1996); 88: 480a
CLL4 trial; MRC Adult Leukaemia Working Party, 2001
www.bcshguidelines.com/pdf/NHL 200504.pdf

Reason for Update: Prepared for Network use	Approved by Chair of Network TSSG: Dr A Laurie
Version: 1	Date: 23.2.06
Supersedes: All previous versions	Review date: February 2008
Prepared by Oncology Pharmacist: S Taylor	Checked by Network Pharmacist: Jacky Turner