GEM-P +/- R

A salvage regimen for relapsed / refractory lymphoma

Drug/Dose:	Methylprednisolone	1000mg (fixed dose)	IV or PO Day 1 – Day 5 (5 doses)
	Gemcitabine	1000mg/m^2	IV Day 1, Day 8 and Day 15
	Cisplatin	100mg/m^2	IV Day 15
	Plus, only for patients with relapsed DLBCL and who are suitable for consolidation with an autograft transplant:		
	Rituximab	375mg/m2	IV Day 1 (administer before gemcitabine)

Administration: **Methylprednisolone** oral doses to be taken with or after breakfast.
IV doses to be reconstituted as directed, then diluted in 250 ml of 0.9% sodium chloride and infused over 30 minutes; ideally administered in the mornings.
Gemcitabine diluted in 250 ml 0.9% sodium chloride and infused over 30 minutes (and to be administered before cisplatin on Day 15)

Cisplatin:
1 litre 0.9% sodium chloride + 20mmol KCl + 10mmol $MgS0_4$ IV over 2 hours
Mannitol 20% 100 ml IV over 15 minutes
Cisplatin in 1 litre 0.9% sodium chloride IV over 3 hours
1 litre 0.9% sodium chloride + 20mmol KCl + 10mmol $MgS0_4$ IV over 2 hours
1 litre 0.9% sodium chloride + 20mmol KCl + 10mmol $MgS0_4$ IV over 2 hours

Rituximab IV in 500ml 0.9% sodium chloride, infused according to standard instructions (e.g. see R-CHOP)

Other Drugs:
Allopurinol 300mg po daily, ideally starting 24 hours before chemotherapy – review after 4 weeks
Fluconazole 100mg od as prophylaxis throughout and until neutropenia resolved
Omeprazole 20mg od (or ranitidine 150mg bd) is recommended whilst treating with steroids

Pre-medication for rituximab:

Paracetamol 1000mg	po	60 minutes pre rituximab
Chlorphenamine 10mg	IV	15 minutes pre rituximab
Dexamethasone* 8mg	IV	15 minutes pre rituximab

*IV dexamethasone may be omitted if Day 1 of methylprednisolone administered (at least 30 minutes pre if oral; at least 15 minutes pre if IV) before start of rituximab infusion

Frequency: 4 weekly cycle for 2 – 4 cycles
Review after 2 cycles

Main Toxicities: myelosuppression; neurotoxicity; ototoxicity; nephrotoxicity; erythematous rash; peripheral oedema (mild-moderate & reversible); flu-like syndrome; +/- rituximab side effects, including severe cytokine release syndrome; infertility; ovarian failure

Anti-emetics: Day 15 – highly emetogenic, including aprepitant
Day 1 and Day 8 – mildly emetogenic

Extravasation: non vesicants

Reason for Update: general review; info for rituximab added; fluconazole added	Approved by Chair of Alliance TSSG: Dr A Laurie
Version: 2	Date: 14.1.16
Supersedes: Version 1	Review date: Feb 2019
Prepared by: S Taylor	Checked by: C Tucker

Regular Investigations:	FBC	Day 1, Day 8 and Day 15
	U&Es	Day 1 and Day 15
	Mg^{2+} and Ca^{2+}	Day 15
	LFTs	Day 1 and Day 15
	LDH	Day 1
	Blood glucose monitoring	see Comments
	Blood pressure monitoring	see Comments
	Cr^{51}-EDTA or 24hr urine collection	baseline (see Comments)

Comments:

Cockcroft & Gault should not be used to predict renal function. EDTA should only be repeated if the result is borderline at the start of treatment or if there is a 30% change in serum creatinine.

Check electrolytes – additional supplementation of potassium, calcium or magnesium may be required.
Weight should be recorded prior to and at the end of cisplatin treatment, and a strict fluid balance chart should be maintained. An average urine output of at least 100ml/hr must be maintained throughout treatment, and cisplatin infusion should not be commenced unless this urine output is achieved. If the urine output is inadequate, the patient should be assessed and urine output increased by administering 500ml sodium chloride 0.9% IV +/- furosemide 20 - 40mg. Furosemide 20 – 40mg po may also be given if there is a positive fluid balance of 1.5 litres, a weight gain of 1.5kg or symptoms of fluid overload. The patient should be asked to drink 2 litres of fluid in the 24hrs following treatment, and to contact the hospital if this is impossible because of problems e.g. nausea and vomiting.

Blood glucose and blood pressure monitoring to be tailored according to individual patient needs.
Oral hypoglycaemic agents will be required if blood glucose is sustained above 12 mmol/l. Patients should also be advised to report any increase in thirst or increase in need to urinate.

Patients in whom stem cell collection is envisaged within the next 2 weeks must receive irradiated cellular blood components to prevent the possible future occurrence of graft versus host disease. Inform patient and blood bank.

Dose Modifications

Haematological Toxicity:

Day 1, Day 8 and Day 15:

Neutrophils		Platelets	Gemcitabine Dose	Cisplatin Dose (Day 15 only)
≥ 1.0 $x10^9$/l	&	≥ 75 $x10^9$/l	Give 100% dose	Give 100% dose
0.5 – 0.9 $x10^9$/l	or	50 – 74 $x10^9$/l	Give 75% dose*	Give 75% dose*
< 0.5 $x10^9$/l	or	<50 $x10^9$/l	Delay until recovered, G-CSF support if reoccurs, then 75% dose of both drugs for all subsequent cycles	

*If a dose reduction to 75% has been made one week, then the dose may be increased to 100% for the subsequent doses, providing the FBC has returned to normal limits.

Renal Impairment: NB. Cisplatin is both eliminated primarily (> 90%) in the urine and is itself nephrotoxic.

GFR (ml/min)	Cisplatin Dose
≥ 60	Give 100%
45 – 59	Give 75%
< 45	CI (consider carboplatin)

If CrCl < 30ml/min, consider gemcitabine dose reduction – clinical decision

Hepatic Impairment: If bilirubin > 27 µmol/L, initiate treatment with gemcitabine 800mg/m^2

Neurotoxicity: Seek further advice if the patient reports symptoms indicative of ototoxicity (tinnitus, deafness) or neurotoxicity (paraesthesias, difficulty with motor control).

Patient Information: Macmillan leaflets for Gemcitabine and Cisplatin +/- Rituximab

References:
Chau, I et al ; Br J Haem 2003; 120: 970 – 977
Ng, M et al ; Br J Cancer 2005 ; 92 : 1352 - 1357