GDP +/- R

A salvage regimen for relapsed / refractory lymphoma
(as recommended by NICE NG52, 2016)

Drug/Dose:	Gemcitabine	1000mg/m^2	IV Day 1 and Day 8
	Cisplatin	75mg/m^2	IV Day 1
	Dexamethasone	40mg	po Days 1, 2, 3 & 4

Plus, only for patients with relapsed DLBCL and who are suitable for consolidation with an autograft transplant:
Rituximab 375mg/m^2 IV Day 1 (administer before gemcitabine; on Cycle 1 for day case patients, give rituximab on Day 1 and GDP on Day 2)

Administration: **Dexamethasone** to be taken with or after breakfast.
Gemcitabine diluted in 250 ml 0.9% sodium chloride and infused over 30 minutes (and to be administered before cisplatin on Day 1)

Cisplatin: 1 litre 0.9% sodium chloride + 20mmol KCl + 10mmol $MgSO_4$ 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 $MgSO_4$ IV over 2 hours
500ml Sodium Chloride 0.9% IV **or** 500mls – 1 litre water orally over 1 hour

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 3 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 dexamethasone administered at least 30 minutes before start of rituximab infusion

Frequency: 3 weekly cycle
Review after 2 cycles - responding patients may be considered for high-dose chemotherapy and ASCT; otherwise, continue up to a total of 6 cycles, unless disease progression or unacceptable toxicity

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

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

Reason for Update: new, following NICE guidance NG52	Approved by Chair of Alliance TSSG: Dr A Laurie
Version: 1	Date: 28/11/16
Supersedes: none (Gem-P protocol to stay as well for now)	Review date: December 2018
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Extravasation:	non vesicants	
Regular Investigations:	FBC	Day 1 & Day 8
	U&Es & LFTs	Day 1
	Mg^{2+} and Ca^{2+}	Day 1
	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: Delay cycle if neutrophils < 1.0 x 10^9/l or platelets < 100 x 10^9/l.

Day 8:

Neutrophils		Platelets	Gemcitabine Dose
≥ 1.0 x10^9/l	&	≥ 100 x10^9/l	Give 100% dose
0.5 – 0.99 x10^9/l	or	50 – 99 x10^9/l	Give 75% of Day 1 dose
< 0.5 x10^9/l	or	≤ 50 x10^9/l	Omit the Day 8 gemcitabine **or** delay until neutrophils > 0.5 and platelets > 50

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:
Crump, M et al; JCO 2014; 32 (31): 3490 – 3496
Kuruvilla, J et al; Cancer 2006; 106: 353 – 360
Baetz, T et al; Annals of Oncology 2003; 14: 1762–1767