Mini-BEAM +/- R

Relapsed or refractory, intermediate or high grade Non-Hodgkin's Lymphoma or Hodgkin's disease, suitable for subsequent PBSCH and autograft
MDTs should carefully assess patient suitability with respect to tertiary centre criteria for high dose treatment, prior to starting salvage therapy

Drugs/Dosage/Administration:

Day	Drug	Dose	Administration	Frequency
1	Carmustine *	60mg/m^2	IV in 500ml 0.9% sodium chloride over 60 minutes (** with antihistamine cover)	single dose
2 – 5 (4 days)	Cytarabine	100mg/m^2/dose (total 8 doses)	IV in 100ml 0.9% sodium chloride over 30 minutes	12 hourly
2 – 5 (4 days)	Etoposide	75mg/m^2/day	IV in 500ml 0.9% sodium chloride over 60 mins	once daily
6	Melphalan	30mg/m^2	IV in 100 - 250ml 0.9% sodium chloride over 30 minutes	single dose
Plus, funding only for patients with relapsed DLBCL and who are suitable for consolidation with an autograft transplant:				
1	Rituximab	375mg/m^2	IV in 500ml 0.9% sodium chloride, infused according to standard instructions (e.g. see R-CHOP)	single dose, to be administered before carmustine

* When carmustine is unavailable, substitute with lomustine 40mg/m^2 po (only available as 40mg capsules) as a single dose on Day 1[1]

Other Drugs:

**Chlorphenamine 10mg IV 30 minutes before carmustine infusion
Allopurinol 300mg po daily, ideally starting 24 hours before chemotherapy – review after 3 weeks
Fluconazole 100mg po od as prophylaxis throughout until neutropenia resolved
G-CSF primary prophylaxis, according to Alliance guidelines for G-CSF;
G-CSF mobilisation for harvesting to start on Day 7

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

Frequency: 1 - 2 cycles may be used, with the second cycle given only once neutrophils > 1.0 x 10^9/L and platelets > 75 x 10^9/L

Main Toxicities: prolonged (> 7 days) myelosuppression, with risk of infections and haemorrhage; alopecia; mucositis; pulmonary toxicity (see Comments); +/- rituximab side effects, including severe cytokine release syndrome; ovarian failure; infertility

Reason for Update: general review, info for rituximab added; fluids and infusion rates reviewed for each cytotoxic	Approved by Chair of Alliance TSSG: Dr A Laurie
Version: 5	Date: 12.1.16
Supersedes: Version 4	Review date: Feb 2019
Prepared by: S Taylor	Checked by: C Tucker

Anti- emetics: highly emetogenic: Day 1* and Day 6; moderately emetogenic: Days 2 – 5

(*further dexamethasone not required on Day 1, if rituximab included and dexamethasone has already been administered pre rituximab)

Extravasation: melphalan and carmustine are vesicants

Regular Investigations:		
	FBC	alternate days until thrombocytopenia or neutropenia occur, then daily to recovery
	U&Es	Day 1, Day 3 and Day 5
	Mg^{2+} and Ca^{2+}	Day 1
	LFTs	Day 1
	LDH	Day 1
	Cr^{51}-EDTA or 24hr urine collection	baseline if concerned
	CXR	baseline

Comments: Carmustine-associated pulmonary toxicity may occur within 3 years of therapy and appears to be dose related, with total cumulative doses of 1200-1500mg/m² being associated with increased likelihood of lung fibrosis. Risk factors include smoking, the presence of a respiratory condition, pre-existing radiographic abnormalities, sequential or concomitant thoracic irradiation and association with other agents that cause lung damage.

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 **Important note** - because this regimen is used in the context of salvage therapy for potentially curable patients, any dose reductions *must be confirmed by the treating Consultant and/or tertiary centre.* The dose modifications outlined below are not mandatory but are intended to guide discussion and decision making.

Haematological Toxicity: Proceed once neutrophils > 1.0 x 10^9/L and platelets > 75 x 10^9/L.
If low counts are thought to be due to marrow infiltration, discuss with Consultant.
Delay in count recovery after treatment should be managed according to local protocols / practice.

Renal Impairment:

CrCl (ml/min)	Carmustine Dose
60	Give 80%
45	Give 75%
< 30	Clinical decision

CrCl (ml/min)	Etoposide Dose
> 50	Give 100%
15 – 50	Give 75%
< 15	Give 50%

CrCl (ml/min)	Melphalan Dose
30 – 50	Give 50%
< 30	Clinical decision

CrCl (ml/min)	Lomustine Dose
45 – 60	Give 75%
30 - 45	Give 50%
< 30	Not recommended

Hepatic Impairment:

Bilirubin (µmol/L)	Cytarabine Dose
> 34	Give 50% dose

Creatinine clearance is the strongest predictor of etoposide clearance. There is conflicting information about dose reduction with hepatic impairment. Use the table below but, if in doubt, discuss with Consultant.

Bilirubin (µmol/l)		AST (units/l)	Etoposide Dose
26 – 51	**or**	60 - 180	Give 50% dose
> 51	**or**	> 180	Clinical decision

Lomustine: Lack of information - consider a dose reduction.

Patient Information: Macmillan leaflets for Carmustine (or Lomustine), Etoposide, Cytarabine, Melphalan +/- Rituximab

References:
Chopra, R et al; Br J Haem 1992; 81: 197 – 202
Girouard C et al; Ann Oncol 1997; 8: 675 – 680
[1]two thirds of the carmustine dose, as accepted practice