ESHAP +/- R

Relapsed or refractory, intermediate or high grade Non-Hodgkin's Lymphoma or Hodgkin's disease
For patients suitable for subsequent PBSCH and autograft, peripheral blood stem cells may be harvested off the back of this regimen
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 – 4 (4 doses)	Cisplatin	25mg/m^2/day	IV in 1000ml 0.9% sodium chloride over 23 hours (Line 1)	once daily
1 – 5 (5 doses)	Methylprednisolone	500mg/day	IV in 100ml 0.9% sodium chloride over 30 minutes (Line 2)	once daily
1 ONLY	Cytarabine	2000mg/m^2 (Age > 70, give cytarabine 1000mg/m^2)	IV in 500ml 0.9% sodium chloride over 2 hours (Line 2)	single dose
1 – 4 (4 doses)	Etoposide	40mg/m^2/day	IV in 250ml 0.9% sodium chloride over 1 hour (Line 2)	once daily
1 – 6	Corticosteroid eye drops e.g. Maxidex	one drop	to each eye	every 4 hours, increasing to 2 hourly if eyes become sore
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 Day 1 chemotherapy

Aggressive hydration required with cisplatin (via Line 1), as follows:

Day 1 only, pre cisplatin: 1 litre 0.9% sodium chloride + 20mmol KCl IV over 2 hours

Daily on Days 1 – 4: Mannitol 20% 100ml IV over 15 - 30 minutes (useful for reducing problems with fluid retention)
Cisplatin as above over 23 hours,
concurrent with 1 litre 0.9% sodium chloride + 20mmol KCl + 10mmol $MgS0_4$ IV over 23 hours

Day 5: The patient should be asked to drink 2 litres of fluid in the 24hrs following completion of cisplatin

A double lumen CVC is advised, but treatment may be given using a single lumen CVC/PICC and a peripheral cannula.

Reason for Update: overdue general review; info for rituximab added	Approved by Chair of Alliance TSSG: Dr A Laurie
Version: 4	Date: 15.1.16
Supersedes: Version 3	Review date: Feb 2019
Prepared by: S Taylor	Checked by: C Tucker

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
G-CSF primary prophylaxis, according to Alliance Guidelines for G-CSF

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 15 minutes before start of rituximab infusion

Frequency: Usually 2 cycles to achieve remission, followed by a 3rd cycle for harvesting if remission achieved
Every 3 – 4 weeks, according to blood recovery

Main Toxicities: myelosuppression; neuropathy; ototoxicity; nephrotoxicity; alopecia; cytarabine syndrome, including conjunctivitis; mucositis; steroid side effects; +/- rituximab side effects, including severe cytokine release syndrome; ovarian failure; infertility

Anti- emetics: highly emetogenic (anti-emetic dexamethasone not required on days 1 - 5 if Day 1 methylprednisolone given before cisplatin starts)

Extravasation: non-vesicants

Regular Investigations:

FBC	alternate days until neutropenia or thrombocytopenia occur, then daily to recovery
U&Es	D1, D3 and D5
Mg^{2+} and Ca^{2+}	D1, D3 and D5
LFTs	D1
LDH	D1
Blood glucose	D1, D3 and D5 of first cycle, then as indicated
Cr^{51}-EDTA or 24hr urine collection	baseline (see Comments)
ECG (ejection fraction if concerned)	baseline

Comments: For patients on Cycle 1 whose Cr^{51}-EDTA / 24 hour urine result is not yet available, Cockcroft & Gault may be used to predict GFR. Cisplatin dose should be adjusted if necessary once results available. Repeat Cr^{51}-EDTA / 24 hour urine only if the result is borderline at the start of treatment or if there is a 30% change in serum creatinine.

Check electrolytes – additional supplements of magnesium, potassium or calcium may be required.

Weight should be recorded daily during 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 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.

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 may be 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: N.B. The requirement for dose modifications for cytarabine in renal impairment is not absolute. If CrCl < 60ml/min, please discuss individual case with Consultant.

CrCl (ml/min)	Cytarabine Dose
> 60	Give 100% dose
46 - 60	Give 60% dose
31 - 45	Give 50% dose
< 30	Consider alternative

CrCl (ml/min)	Cisplatin Dose
≥ 60	Give 100%
45 – 59	Give 75%
< 45	Contra-indicated

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

Hepatic Impairment: Creatinine clearance is the strongest predictor of etoposide clearance. There is conflicting information about dose reduction with hepatic impairment. Use the table below, but discuss with Consultant before any dose reductions are made.

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

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

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

Patient Information: Macmillan leaflet for ESHAP +/- Rituximab

References: Velasquez et al; JCO 1994; 12 (6): 1169 – 1176
Aparicio, J et al; Ann Oncol 1999; 10 (5): 593 – 595