# ESHAP

Relapsed or refractory intermediate or high grade Non-Hodgkins Lymphoma, or relapsed Hodgkins 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 – 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 – 5** | Corticosteroid eye drops e.g. prednisolone 0.5% | One drop | To each eye | Every 4 hours, increasing to 2 hourly if eyes become sore |

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

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| 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 (optional, but useful for reducing problems with fluid retention)<br>Cisplatin as above over 23 hours, concurrent with:<br>1 litre 0.9% Sodium Chloride + 20mmol KCl + 10mmol $MgS0_4$ IV |
| 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.

**Other Drugs:** Allopurinol 300mg po daily, ideally starting 24 hours before chemotherapy – review after 3 weeks
Fluconazole as prophylaxis throughout and until neutropenia resolved
Use of proton pump inhibitor or $H_2$ receptor antagonist (eg ranitidine) is recommended whilst treating with steroids
G-CSF primary prophylaxis may be considered, according to ASCO guidelines and local practice



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| Reason for Update: Prepared for Network use | Approved by Chair of Network TSSG: Dr A Laurie |
| Version: 1 | Date: 9.2.06 |
| Supersedes: All previous versions | Review date: February 2007 |
| Prepared by Oncology Pharmacist: S Taylor | Checked by Network Pharmacist: Jacky Turner |

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|---|---|
| Frequency: | Usually 2 cycles to achieve remission, followed by a 3rd cycle for harvesting if remission achieved<br>Every 3 – 4 weeks, according to blood recovery |
| Main Toxicities: | myelosuppression; neuropathy; ototoxicity; nephrotoxicity; cytarabine syndrome, including conjunctivitis; mucositis; alopecia; steroid side effects; ovarian failure; infertility |
| Anti- emetics: | Highly emetogenic (dexamethasone IV not required 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 Course 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.

**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: 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 60% dose |
| < 45 | Give 50% dose |
| < 30 | Consider alternative |

| CrCl (ml/min) | Cisplatin Dose |
|---|---|
| > 60 | Give 100% |
| 50 – 60 | Give 75% |
| 40 – 50 | Give 50% |
| < 40 | Contra-indicated |

| CrCl (ml/min) | Etoposide Dose |
|---|---|
| 60 | Give 85% |
| 45 | Give 80% |
| 30 | Give 75% |

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 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 |

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

Patient Information: CancerBACUP leaflet for ESHAP

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