(R)-DHAP

INDICATION: Relapsed and refractory lymphoma

Prior to a course of treatment

- Check FBC, U&Es, creatinine, calculated GFR and LFTs (*see dose modification)*
- Check hepatitis B and C serology
- Patient should have adequate bone marrow reserve before commencing treatment, i.e neuts >1.0, platelets >100, unless due to marrow infiltration, splenomegaly - *if not discuss with consultant*
- ECG, and consider echocardiogram or MUGA scan - patient must have adequate cardiac function to cope with large volumes of fluid required.
- If appropriate discuss possibility of pregnancy with female patients and need for contraception with both male and female patients. Discuss risk of infertility - offer semen cryopreservation to male patients
- Written consent for course

Prior to each cycle

- Medical review of fitness for chemotherapy – exclude active infection, major changes in organ function
- Repeat creatinine clearance and LFTs prior to each cycle *(see dose modifications.* Note that if there has been significant nephrotoxicity with earlier cycles consider changing cisplatin to carboplatin dosed according to area under the curve as per template for R-ICE.
- FBC, U&Es, creat, Ca, Mg - neuts must be > 1.0, plats >50 *(see dose modifications)*.
- If PBSC harvest planned inform transfusion lab that further blood products must be irradiated beginning from 7 days prior to harvest until completion. Liaise with transplant CNS to ensure results of virology are known and NBS is aware of planned PBSC mobilisation. Note NBS demand the virology results checked in their own laboratories and may refuse to process the harvest if the results are not known
- Assess venous access or arrange for insertion of femoral line following cycle 2/3 with a view to apheresis

Day 1	Rituximab	IV in 375mg/m^2 in 0.5L N saline (*see protocol for rituximab)*
	Rituximab may be given on day - 1 or day – 2	
	Cisplatin and hydration	
T – 3.0hr	1.0L Nsaline (+20mmol KCL+10mmol $MgSO_4$) over 2hr	
T - 1hr	Mannitol 10% 0.5L over 1hr - *check urine output >100ml/hr*	
T = 0 [a]	Cisplatin 100mg/m^2 by continuous 12hr IV infusion in 3.0L N saline	
	(*total dose should be divided into 3 doses each in 1.0L over 4hrs)*	
T = 0-4hrs	1.0L Nsaline (+20mmol KCL+10mmol $MgSO_4$) over 4hrs	
T = 4-10hrs	1.0L dextrose-saline (+20mmol KCL+10mmol $MgSO_4$) over 6hrs	
	Maintain urine output of at least 100ml/hr – give frusemide 20-40mg iv if necessary	
	Dexamethasone phosphate	40mg od IV over 15mins or PO

Day 2	Dexamethasone phosphate	40mg od IV over 15mins or PO	
Day 3	Cytarabine	2g/m^2 IV over 3hrs in 1.0L Nsaline	
	Hydration with 1.0L dextrose-saline over 9hrs		
	Cytarabine	2g/m^2 IV over 3hrs in 1.0L Nsaline	
	Dexamethasone phosphate	40mg od IV over 15mins or PO	
Day 4	Dexamethasone phosphate	40mg od IV over 15mins or PO	
From day 6	GCSF	5mcg/kg SC od *	Continue until neuts have passed through the nadir and > 0.5

* *If PBSCH planned after cycle 3 use GCSF 10mcg/kg od from day 6 and continue until harvesting completed*

Repeat cycle every 21 days for 2 - 6 cycles

If stem cell harvest is planned start counting peripheral blood CD34 count when WBC >1.0 x 10^9/L

Prophylaxis for acute emesis	5HT antagonist
Prophylaxis for delayed emesis	5HT antagonist & metoclopramide
Other medications	Prednisolone 0.5% eye drops each eye tds days 2-8
	Allopurinol 300mg od for 5 days with cycle 1
	Omeprazole 20mg od for 7 days
	Anti-infective prophylaxis according to local policy

Dose modification for haematological toxicity

- There are no dose reductions in subsequent cycles but neuts must be > 1.0, plats >50 prior to each cycle – if treatment is delayed by ≥ 2 weeks further treatment may be inappropriate – *discuss with consultant*

Dose modification for neurological toxicity

- In case of grade 1 toxicity to cisplatin (sensory or motor polyneuritis, constipation, visual or auditory changes) reduce dose to 75mg/m^2 per cycle.
- If toxicity increases despite reduced dosage, discontinue cisplatin permanently.

Dose modification for renal dysfunction

- Creatinine clearance > 60ml/min — 100% dose cisplatin
- Creatinine clearance 40 – 60ml/min — 50% dose cisplatin
- Creatinine clearance < 40ml/min — Replace cisplatin with carboplatin
- If renal impairment is severe (creat. clear <30ml/min) use cytarabine with caution (increased risk of cerebellar toxicity) – *discuss with consultant*

Dose modification for liver dysfunction (unless due to disease)

- There is limited information – clinical decision.

R-DHAP Toxicities	
Neutropenic sepsis & thrombocytopenia	Nausea& vomiting (moderate - severe)
Mucositis, gastritis, oesophagitis	Amenorrhoea & infertility (offer semen cryopreservation)
Alopecia	Conjunctivitis (cytarabine)
Peripheral neuropathy & ototoxicity	Nephrotoxicity, hypokalaemia, hypocalcaemia & hypomagnesaemia
Rash (cytarabine)	Cerebral & cerebellar dysfunction (cytarabine)
Hyperglycaemia	Fever, chills, hypotension, rigors & anaphylaxis (rituximab) – usually first dose only
Stevens-Johnson syndrome (rituximab)	Cytokine-release syndrome (rituximab, potentially fatal)

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