Patient Name: **Patient Number:** **DOB:** **Consultant:** **Allergies:**	**Kent and Medway SACT protocol** **R-IVE** Relapsed or Refractory Non-Hodgkin's Lymphoma Disease Modification Cycle No….. Repeat every 21 days For 2 cycles and then assess response.	Date calculated		Protocol No. HAEM-NHL-084
		Height (m)		Written/Checked by: M.Archer O.Okuwa K.Miller
		Weight (kg)		Authorising Consultant: R.Gale
		Surface area (m^2)		Date written:18/05/19 Finalised:10/06/20 Date of review: Version No: v1

- Virology status to be checked prior to cycle 1.
- Baseline MUGA/ECHO where clinically indicated.
- ECG baseline.
- FBC, U&E and LFTs at baseline and before each cycle. Monitor between cycles as clinically indicated.
- BP baseline and as clinically indicated.
- Neuts <1 and plts <100 delay cycle for 1 week and commence when levels have recovered to neuts >1 and plts >100.
- Pre-hydration is recommended (3litres of sodium chloride 0.9% over 18 hours).
- Weight should be recorded once daily and a strict fluid balance chart should be maintained. If there is a weight increase of 2kg, a positive fluid balance of 2 litres, or symptoms of fluid overload, furosemide 20-40mg po should be given.
- Urine should be dipstick tested for signs of haematuria and increase MESNA if blood detected. (ref http://www.londoncancer.org/media/75898/140214-London-Cancer-Mesna-Guideline-v1.pdf)
- Use rituximab infusion monitoring record.
- Infusion rates: first infusion – Initiate at 50 mg/hr. Increase at 50mg/hr increments every 30mins to 400mg/hr. max. Subsequent infusions – Initiate infusion at 100mg/hr. Increase rate at 100mg/hr increments every 30mins to 400mg/hr max.
- Consider reduction of cell load by other means prior to Rituximab infusion if high tumour load and consider decreasing infusion speed.
- Ensure pre-medication of Rituximab with chlorphenamine, hydrocortisone & paracetamol. Monitor Rituximab infusion closely (complete monitoring form), watch for signs of dyspnoea, fever, rigors. If such symptoms occur stop infusion and seek medical advice. Infusion may be recommenced at half the previous rate, once symptoms have subsided. Anaphylaxis drugs must be available when treating with Rituximab
- Consider withdrawing any anti-hypertensives 12 hours before treatment with Rituximab.
- Patients with a high tumour burden or with a high number of lymphocytes (>25 x 10^9/l) who may be at higher risk of especially severe cytokine release syndrome, should only be

treated with extreme caution. These patients should be very closely monitored throughout the first infusion. Consideration should be given to the use of a reduced infusion rate for the first infusion in these patients or a split dosing over two days during the first cycle.

- **Dose Modifications:**
  - **Hepatic impairment:**
    Epirubicin: Bilirubin 24-51µmol/L give 50% dose, if bilirubin 51-85µmol/L give 25% dose and if bilirubin >85µmol/L omit dose.
    Etoposide: Bilirubin 26-51µmol/L or AST 60-180 units give 50%; bilirubin > 51µmol/L or AST > 180 units clinical decision.
    Ifosfamide: Bilirubin >17umol/L or ALP > 2.5ULN is a clinical decision.
  - **Renal impairment:**
    Ifosfamide: CrCl 40-59 ml/min give 70% dose; CrCl < 40 ml/min clinical decision.
    Etoposide: CrCl 15-50mL/min dose at 75%; CrCl <15mL/min clinical decision, consider 50% dose reduction.
- **Neurotoxicity:** Ifosfamide may cause a reversible encephalopathy at high doses. This usually manifests as decreased rousability and disorientation often leading to somnolence. In severe cases this can progress to irreversible encephalopathy and death. Symptoms may develop within 2 hours of initiation or up to 28 days after treatment; the usual onset is within 24-96 hours after the initiation of ifosfamide and disappears within 48-72 hours of discontinuing ifosfamide.
- **Skin reactions:** Severe skin reactions such as Toxic Epidermal Necrolysis (Lyell's Syndrome) and Stevens-Johnson syndrome, some with fatal outcome, have been reported with rituximab. Treatment should be permanently discontinued if this is suspected.
- **Drug interactions:**
  Avoid concomitant use of ciclosporin and aprepitant.
- Live vaccines should not be administered during treatment.

References: KMCC proforma HAEM-NHL-020v1 HAEM-NHL-027v2; SPC accessed on line 24/05/2019; Derby-Burton Local Cancer Network R-IVE protocol NO: HCCPG B53; Cheshire & Merseyside protocol R +/- IVE; St Lukes cancer alliance protocol IVE +/- R; BNF accessed on line; the North London Cancer Network Dosage Adjustment for Cytotoxics in Hepatic and Renal Impairment

Repeat every 21 days

Day	Drug	Dose	Route	Infusion Duration	Administration Details	Batch No	Nurses Sign	Start Time	Stop Time
Day 1 …/…/…	Paracetamol	1000mg	PO	stat					
	Chlorphenamine	10mg	IV	1 min	by slow IV infusion				
	Hydrocortisone	100mg	IV	stat					
	Commence Rituximab at least 30 mins – 1 hour after pre-medication.								
	RITUXIMAB (Truxima) 375mg/m²		IV	see notes	Sodium Chloride 0.9% 500ml				
Day 2 …/…/…	Ondansetron	<75yrs 16mg >/=75yrs 8mg	IV	15 min	In 50ml Sodium chloride 0.9%				
	Dexamethasone	8mg	IV	stat					
	EPIRUBICIN 50mg/m²		IV	Slow bolus	Through the side of a fast running Sodium chloride 0.9% intravenous infusion.				
	ETOPOSIDE 200mg/m²		IV	2 hours	Sodium Chloride 0.9% 1L Maximum concentration 0.4mg/ml.				
	MESNA 1800mg/m²		IV	Infuse over 15 mins pre ifosfamide and mesna	Sodium Chloride 0.9% 250ml				
	IFOSFAMIDE (to run concurrently with MESNA) **3000mg/m²**		IV	22 hours	Sodium chloride 0.9% 1L				
	MESNA 3000mg/m²		IV	22 hours	Sodium chloride 0.9% 1L				
Prescribers signature & date:					**Pharmacists clinical screen & date:**	**Final release signature & date:**			

Day	Drug	Dose	Route	Infusion Duration	Administration Details	Batch No	Nurses Sign	Start Time	Stop time
Day 3 …/…/…	Ondansetron	<75yrs 16mg >/=75yrs 8mg	IV	15 min	In 50ml Sodium chloride 0.9%				
	Dexamethasone	8mg	IV						
	ETOPOSIDE 200mg/m²		IV	2 hours	Sodium Chloride 0.9% 1L. Maximum concentration 0.4mg/ml.				
	IFOSFAMIDE (to run concurrently with MESNA) **3000mg/m²**		IV	22 hours	Sodium chloride 0.9% 1L				
	MESNA 3000mg/m²		IV	22 hours	Sodium chloride 0.9% 1L				
Day 4 …/…/…	Ondansetron	<75yrs 16mg >/=75yrs 8mg	IV	15min	In 50ml Sodium chloride 0.9%				
	Dexamethasone	8mg	IV						
	ETOPOSIDE 200mg/m²		IV	2 hours	Sodium chloride 0.9% 1L. Maximum concentration 0.4mg/ml.				
	IFOSFAMIDE (to run concurrently with MESNA) **3000mg/m²**		IV	22 hours	Sodium chloride 0.9% 1L				
	MESNA 3000mg/m²		IV	22 hours	Sodium chloride 0.9% 1L				
Day 5 …/…/…	**MESNA 5400mg/m2**		IV	12 hours	Sodium chloride 0.9% 1L				
Prescribers signature & date:					**Pharmacists clinical screen & date:**	**Final release signature & date:**			

TTO Medica-tion	Drug	Dose	Route	Directions	Date	Quantity	Disp	Check
	Allopurinol	300mg	PO	OD for 3 weeks. Review after cycle 1. Take with or just after food, or a meal. Take with a full glass of water				
	Metoclopramide	10mg	PO	Up to TDS regularly for 3 days, then 10mg up to TDS PRN (28 tabs)				
	Co-trimoxazole	480mg	PO	BD Mondays, Wednesdays, Fridays. Space the doses evenly throughout the day. Keep taking this medicine until the course is finished, unless you are told to stop.				
	Aciclovir	400mg	PO	BD. Space the doses evenly throughout the day. Keep taking this medicine until the course is finished, unless you are told to stop.				
	Fluconazole	100mg	PO	OD				
	Chlorhexidine mouthwash	10ml	TOP	QDS from Day 1 of chemotherapy.				
	Filgrastim	300 mcg or consider dose of 480 mcg if patient > 80kg	SC	OD from Day 7 for 5 days.				
	Lansoprazole	30mg	PO	OD. Take 30 to 60 minutes before food. Swallow this medicine whole. Do not chew or crush. Do not take indigestion remedies 2 hours before or after you take this medicine.				
Prescribers signature & date:				**Pharmacists clinical screen & date:**	**Final release signature & date:**			

References:

https://www.uhdb.nhs.uk/download.cfm?doc=docm93jijm4n2953.pdf&ver=4582 derby/burton protocol
https://stlukescanceralliance.co.uk/wp-content/uploads/2015/10/IVE-V4-1.16.pdf St Lukes
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http://www.londoncancer.org/media/75878/London-Cancer-Methylene-Blue-Guideline-v1.pdf