SACT PROTOCOL

The Clatterbridge Cancer Centre NHS Foundation Trust

Systemic Anti Cancer Therapy Protocol

Mini-CHOP +/- Rituximab Non-Hodgkin's Lymphoma

PROTOCOL REF: MPHAMICHHA
(Version No: 2.0)

Approved for use in:

- Patients over the age of 80 or patients under the age of 80 with significant co-morbidities with non-hodgkin's lymphoma (NHL). Rituximab should only be added if CD20+ disease (B-cell NHL).

Blueteq application is not required.

Dosage:

Drug	Dose	Route	Frequency
+/- Rituximab	**375mg/m^2**	IV	Day 1
Cyclophosphamide	**400mg/m^2**	IV	Day 1
Doxorubicin	**25mg/m^2**	IV	Day 1
Vincristine	**1mg**	IV	Day 1
Prednisolone	**40mg/m^2**	Oral	Once daily on days 1 to 5

Cycle frequency:

R-Mini-CHOP

- Every 21 days for 3-6 cycles, depending on the stage of disease

Mini-CHOP

- Every 21 days for 6 cycles

Administration +/- counselling:

- Due to the long retention time of rituximab in B cell depleted patients, women of childbearing potential should use effective contraceptive methods during and for 12 months following treatment with rituximab.
- Doxorubicin may impart a red colour to the urine. Patients should be cautioned that this does not pose any health hazards.

Emetogenic risk:

Moderately emetogenic

Supportive treatments:

Pre-infusion medication:

- Paracetamol tablet 1gram oral (PO)
- Chlorphenamine injection 10mg intravenous (IV)
- Ensure oral steroids have been taken at least 30 minutes prior to rituximab

Supportive medication:

- Allopurinol 300mg once daily for the first two cycles.
- Ondansetron 8mg twice daily (BD) for 5 days.
- Metoclopramide 10mg three times a day when required.
- Docusate Sodium 200mg twice daily when required
- Filgrastim 48 or 30 million units (dose dependent on weight) by subcutaneous injection once daily for 5 days starting on day 5.
- Aciclovir 400mg twice daily and co-trimoxazole 480mg once daily are not generally required but may be given at the discretion of the prescriber.

Extravasation risk:

- Rituximab: Non-vesicant
- Cyclophosphamide: Non-vesicant
- Doxorubicin: Vesicant
- Vincristine: Vesicant

Refer to the CCC policy for the 'Prevention and Management of Extravasation Injuries'

Dosing in renal and hepatic impairment:

Renal		
Cyclophosphamide	**Creatinine clearance (mL/min)**	**Dose Adjustment**
	10 - 29	75%
	<10 or haemodialysis	Not recommended. Consider 50% dose
Doxorubicin	No dose adjustment needed	
Vincristine	No dose adjustment needed	
Rituximab	No dose adjustment needed	

Hepatic		
Cyclophosphamide	No dose adjustment needed	
Doxorubicin	**Bilirubin (µmol/L)**	**Dose Adjustment**
	20 – 50	50% dose
	51 – 86	25% dose
	>86	Omit
Vincristine	>51	50% dose
Rituximab	No dose adjustment needed	

Interactions:

- Mould active azoles (e.g. posaconazole) should be avoided in combination with vincristine as there is an increased risk of neurotoxicity. Fluconazole can be given but signs of neurotoxicity should be monitored.
- Phenytoin given with vincristine and/or doxorubicin may reduce blood levels of the anticonvulsant and to increase seizure activity. Therapeutic drug monitoring (TDM) for phenytoin would be advised.
- Concomitant administration of inhibitors of CYP450 and/or P-glycoprotein might lead to increased plasma concentrations of doxorubicin and thereby increased toxicity.
- Clozapine may increase the risk/severity of the haematologic toxicity of doxorubicin
- Doxorubicin may reduce oral bioavailability of digoxin.

For more detailed interaction information please refer to the individual drug SPCs.

Treatment Schedule:

If lymphocytes ≥25x10^9/L prior to first dose then split rituximab dose as per table below:

Day	Drug	Dosage	Route	Diluent and Rate
1	**Paracetamol**	1g	PO	At least 30 minutes before rituximab
	Chlorphenamine	10mg	IV	
	Prednisolone	40mg/m^2	IV	Once daily day 1 to 5 **Take 30 mins prior to rituximab on day 1**
	Rituximab	100mg	IV	**≤450mg** in 250mL 0.9% sodium chloride **≥500mg** in 500mL 0.9% sodium chloride Rate as per rituximab infusion guideline
2	**Paracetamol**	1g	PO	At least 30 minutes before rituximab
	Chlorphenamine	10mg	IV	
	Prednisolone	40mg/m^2	PO	Once daily day 1 to 5 **Take 30 mins prior to rituximab on day 2**
	Rituximab	375mg/m^2 (minus 100mg)	IV	**≤450mg** in 250mL 0.9% sodium chloride **≥500mg** in 500mL 0.9% sodium chloride Rate as per rituximab infusion guideline
	Ondansetron	8mg	IV	In 100mL sodium chloride 0.9% over 15-30 minutes.
	Cyclophosphamide	400mg/m^2	IV	In 250mL sodium chloride 0.9% over 30 mins
	Doxorubicin	25mg/m^2	IV	In 100mL sodium chloride 0.9% over 30 mins
	Vincristine	1mg	IV	In 50mL Sodium Chloride 0.9% over 5-10 minutes. **Intravenous Use only. Fatal if given by any other route**

If lymphocytes <25x10^9/L prior to first dose and all subsequent doses:

Day	Drug	Dosage	Route	Diluent and Rate
1	**Paracetamol**	1g	PO	At least 30 minutes before rituximab
	Chlorphenamine	10mg	IV	
	Prednisolone	40mg/m^2	PO	Once daily day 1 to 5 **Take 30 mins prior to rituximab on day 1**
	Rituximab	375mg/m^2	IV	**≤450mg** in 250mL 0.9% sodium chloride **≥500mg** in 500mL 0.9% sodium chloride Rate as per rituximab infusion guideline
	Ondansetron	8mg	IV	In 100mL sodium chloride 0.9% over 15-30 minutes
	Cyclophosphamide	400mg/m^2	IV	In 250mL sodium chloride 0.9% over 30 mins

	Doxorubicin	25mg/m^2	IV	In 100mL sodium chloride 0.9% over 30 mins
	Vincristine	1mg	IV	In 50mL Sodium Chloride 0.9% over 5-10 minutes. **Intravenous Use only. Fatal if given by any other route**

Main toxicities:

Rituximab
Infusion related reactions, hypersensitivity reactions, tumour lysis syndrome, thrombocytopenia, neutropenia, infections, hepatitis B reactivation
CHOP
Thrombocytopenia, neutropenia, anaemia, nausea, vomiting, diarrhoea, constipation, peripheral neuropathy and jaw pain (vincristine), haemorrhagic cystitis and bladder irritation (cyclophosphamide) and cardiac toxicity (doxorubicin).

Investigations and treatment plan:

	Pre	Cycle 1	Cycle 2 +	Ongoing
Informed Consent	X			
Clinical Assessment (inc SACT assessment, PS and toxicity grading)	X	X	X	Every cycle
Blood pressure	X	X	X	Continuous monitoring required if on rituximab
Temperature, respiratory rate, pulse		X	X	Continuous monitoring required if on rituximab
FBC, U&E, LFTs and bone profile	X	X	X	Every cycle
CrCl (Cockcroft and gault)	X			Every cycle
HbA1C	X			Repeat as clinically indicated
Serum Immunoglobulins	X			Repeat as clinically indicated
CT or PET CT Scan	X			Interim and end of treatment scans as indicated
Bone Marrow	X			Repeat as clinically indicated
ECG and ECHO or MUGA Scan	X			Echo should be done prior to anthracyclines unless this would lead to delaying treatment in an acutely unwell patient
Hepatitis B core antibody and surface antigens & Hep C & HIV 1+2	X			
Pregnancy test	X			Where appropriate
Height	X			
Weight	X	X	X	Every cycle

Dose Modifications and Toxicity Management:

Haematological toxicity:

No dose modification required for cycle 1.

Subsequent cycles to proceed if:

ANC ≥ 1.0 x 10^9/L	Platelets ≥ 100 x 10^9/L

Haematological Dose Modifications	
Neutrophils (x10^9/L)	**Modification**
<1 on day of treatment	Delay cycle by 1 week. Discuss use of G-CSF or dose reductions for further cycles with consultant
Any febrile neutropenia following any cycle of CHOP	All subsequent cycles should be given with GCSF support. Consider dose reduction.
Febrile neutropenic episode despite GCSF support	Reduce doses of cyclophosphamide and doxorubicin, discuss with consultant
Platelets (x10^9/L)	**Modification**
<100 on day of treatment	Delay cycle by 1 week.
Second delay due to thrombocytopenia	Reduce doses of cyclophosphamide and doxorubicin, discuss with consultant

These haematological guidelines assume that patients are well with good performance status, that other acute toxicities have resolved and the patient has not had a previous episode of neutropenic sepsis.

Non- Haematological toxicity:

Infusion Related Reactions

Rituximab	
Cytokine release syndrome	Monitor patients closely. Patients who develop evidence of severe reactions, especially severe dyspnea, bronchospasm or hypoxia should have infusion interrupted immediately. The patient should then be evaluated for evidence of TLS including appropriate laboratory tests and, for pulmonary infiltration, with a chest x-ray. The infusion should not be restarted until complete resolution of all symptoms, and normalization of laboratory values and chest x-ray findings. At this time, the infusion can be initially resumed at not more than one-half the previous rate. If the

	same adverse reaction occurs for a second time, the decision to stop the treatment should be seriously considered on a case by case basis. Mild or moderate infusion-related reactions usually respond to a reduction in the rate of infusion. The infusion rate may be increased upon improvement of symptoms.

Neurotoxicity

Vincristine	
Grade	**Modification**
Grade 2 motor weakness or grade 3 sensory toxicity	Give 50% vincristine
Higher grades of neurological toxicity	Omit vincristine

References:

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7. NICE Guideline NG52: ''*Non-Hodgkin's lymphoma: diagnosis and management"*, National Institute for Health and Clinical Excellence, July 2016

Circulation/Dissemination

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Date document posted on the Intranet	NA

Version History

		Author name and designation	Summary of main changes
V1.0	February 2021	**Aileen McCaughey – Advanced Pharmacist Haemato-oncology**	**Protocol created**
V2.0	February 2024	**Jade Marsh – Advanced Pharmacist Haemato-oncology**	**Changed to new protocol template, slight changes to dose modifications in hepatic/renal section**