Systemic Anti-Cancer Therapy Protocol

Dexamethasone, Rituximab and Cyclophosphamide (DRC)

PROTOCOL REF: MPHADRCHA
(Version No: 1.0)

Approved for use in:

- Patients with lymphoplasmacytic lymphoma/ Waldenstrom's Macrogloblinaemia
- EGOG 0 to 2

Blueteq registration not required

Dosage:

Drug	Dose	Route	Frequency
Dexamethasone	**20mg**	PO	Day 1 only
Rituximab	**375mg/m^2**	IV infusion	Day 1 only
Cyclophosphamide	**100mg/m^2 twice daily**	PO	Days 1 to 5

Maximum of 6 cycles. 21 day cycle.

Administration:

- 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
- For patients with significantly raised viscosity, rituximab may cause a transient rise in the paraprotein (and therefore viscosity) and / or a flare of paraprotein-associated symptoms such as neuropathy. In these patients, consider plasma exchange immediately before giving rituximab (or using dexamethasone and cyclophosphamide only initially, adding in the rituximab once the paraprotein is reducing/total IgM < 40g/L and viscosity <4)

- Ensure patients are well hydrated prior to starting treatment and should aim to drink 3L of fluid per day while on cyclophosphamide therapy

Anti-emetic risk:

Moderately emetogenic.

Supportive treatments:

Pre-infusion medication:

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

Supportive medication:

- Allopurinol (dose based on renal function) for the first two cycles
- Ondansetron 8mg twice daily for 5 days.
- Metoclopramide 10mg three times a day when required

Extravasation risk:

Rituximab: Non-vesicant

Refer to the Trust guidance for the prevention and management of extravasation

Interactions:

Rituximab

There are no known drug interactions with rituximab

Cyclophosphamide

There are a number of potential interactions with cyclophosphamide please consult the relevant summary of product characteristics via https://www.medicines.org.uk/emc for the full list of interactions

Treatment schedule:

Day	Drug	Dose	Route	Diluent and rate
1	**Dexamethasone**	**20mg**	**PO**	30 mins before chemotherapy
	Paracetamol	**1g**	**PO**	30 mins before chemotherapy
	Chlorphenamine	**10mg**	**IV**	30 mins before chemotherapy
	Rituximab	**375mg/m^2**	**IV**	In 500mls NaCl 0.9%. Infuse as per rituximab infusion policy.
	Cyclophosphamide	**100mg/m^2**	**PO**	Twice daily
2 to 5	**Cyclophosphamide**	**100mg/m^2**	**PO**	Twice daily

Main toxicities:

Thrombocytopenia, neutropenia, anaemia, nausea, vomiting, diarrhoea, bladder irritation, infusion related reactions, cytokine release syndrome.

Investigations and treatment plan:

	Pre	Cycle 1	Cycle 2+	Ongoing
Clinical Assessment	X			
Informed Consent	X			
SACT Assessment (including performance status and toxicity assessment)	X	X	X	
FBC	X	X	X	
U&E & LFTs & Magnesium	X	X	X	
CrCl (Cockcroft and Gault)	X			
Serum immunoglobulins/plasma viscosity	X		X	Plasma viscosity at the discretion of prescriber. Serum immunoglobulins every other cycle.
CT scan	X			Repeat after 4 cycles and at end of treatment if clinically indicated
Bone marrow biopsy	X			If clinically indicated. Repeat as clinically indicated
Hepatitis B core antibody and surface antigens and Hep C and HIV 1&2	X			
ECG/ ECHO				If clinically indicated
Blood pressure measurement	X	X	X	Continuous monitoring required while on rituximab
Temperature, respiratory rate, pulse		X	X	Continuous monitoring required while on rituximab
Height	X			
Weight	X	X	X	
Pregnancy test	X			If clinically indicated
Blood glucose	X			Repeat if clinically indicated

Dose Modifications and Toxicity Management:

Haematological toxicity:

No dose modifications required for first cycle of if cytopenias secondary to disease

Cyclophosphamide		
Neutrophils ($x10^9$/L)	Platelets ($x10^9$/L)	Dose Modification
>1.0 **and**	≥100	100%
0.5 – 1.0 **and/or**	50-100	50%
<0.5 **and/or**	<50	omit

Dosing in renal and hepatic impairment:

Cyclophosphamide		
Renal impairment	CrCl 10-30ml/min	Consider 25% dose reduction
	<10ml/min or haemodialysis	Not recommended – if unavoidable consider 50% dose reduction.
Liver impairment	Mild and moderate	No adjustment required
	Severe	Not recommended – due to risk of reduced efficacy.

References:

1. https://www.medicines.org.uk/emc rituximab (accessed April 2021)
2. https://www.medicines.org.uk/emc cyclophosphamide (accessed April 2021
3. https://www.medicines.org.uk/emc dexamethsone (accessed April 2021)
4. Krens S D, Lassche, Jansman G F G A, et al. Dose recommendations for anticancer drugs in patients with renal or hepatic impairment. Lancet Oncol 2019;20: e201–08
5. Thames Valley Strategic Clinical Network. DRC (dexamethasone + rituximab + cyclophosphamide). May 2015.