SACT PROTOCOL

The Clatterbridge Cancer Centre NHS Foundation Trust

Systemic Anti Cancer Therapy Protocol

RITUXIMAB (SINGLE AGENT) MULTIPLE INDICATIONS

PROTOCOL REF: MPHARISAHA
(Version No. 2.0)

Approved for use in:

- CD20 positive indolent lymphomas *(check funding status for specific indications)*
- CD20 positive lymphoma in patients not fit for more intensive therapy *(check funding status for specific indication)*
- Epstein-Barr virus (EBV) reactivation as part of active lymphoma requiring chemotherapy
- Rituximab naïve Waldenstroms Macroglobulinaemia *(NHSE baseline commissioning)*
- Post-transplant Lymphoproliferative Disorder (PTLD) *(NHSE baseline commissioning)*
- Epstein-Barr virus (EBV) reactivation following stem cell transplant *(NHSE baseline commissioning)*
- Chronic graft versus host disease after stem cell transplantation *(NHSE Baseline Commissioning)*
- IgM related paraproteinemic nephropathy *(NHSE Baseline Commissioning)*
- Immune cytopenias
- Management of toxicity associated with immune-oncology (IO) chemotherapy

Blueteq not required

Dosage:

Single Dose

Drug	Dose	Route	Frequency
Rituximab	**375mg/m^2**	IV infusion	Day 1 only

Cycle length every 28 days. Maximum 4 cycles.

Weekly Dosing

Drug	Dose	Route	Frequency
Rituximab	**375mg/m^2**	IV infusion	Day 1, 8, 15 and 22

Cycle length 28 days. Single cycle only.

A further 4 doses may be given every four weeks, or at weekly intervals, at the discretion of the clinician for the treatment of indolent lymphomas

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.
- Reactivation of Hepatitis B can occur if rituximab is administered to people previously exposed to Hepatitis B. Virology screening including Hepatitis B Core Antibody and Surface Antigen should be carries out and confirmed as negative prior to administration of rituximab. Any positive or equivocal result should be discussed with Consultant.
- Infusion related reactions (IRR) are a common side effect of rituximab. The infusion rate should be titrated slowly during the first infusion and the patient monitored closely for signs of IRR. Ensure pre-medications administered prior to every dose of rituximab.

Emetogenic risk

Mildly emetogenic

Supportive treatments:

Rituximab pre-infusion medicines:

- Paracetamol PO 1g
- Chlorphenamine IV bolus 10mg
- Hydrocortisone sodium succinate IV bolus 100mg

Supportive medicines:

- Consider allopurinol oral 300mg once daily for first cycle, if risk of tumour lysis applicable.

- Consider co-trimoxazole 480mg once daily oral at clinician discretion

Extravasation risk:

Rituximab: non-vesicant

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

Dosing in renal and hepatic impairment:

Renal
No dose recommendation required
Hepatic
No dose recommendation required

Interactions:

Rituximab: No significant drug interactions

Treatment schedule:

If lymphocytes ≥25x10^9/L then consider splitting the first dose (100mg in 100mL sodium chloride 0.9% over 2 hours on day 1 and then the remainder of the dose in 250mL or 500mL sodium chloride 0.9% as per standard infusion rates on day 2). If no IRR then subsequent doses can be given in one infusion.

Day	Drug	Dose	Route	Diluent and rate
1	**Paracetamol**	**1g**	**PO**	30 mins prior to rituximab
Or	**Chlorphenamine**	**10mg**	**IV**	Bolus dose over 3-5 minutes. 30 minutes prior to rituximab
1, 8, 15 & 22	**Hydrocortisone**	**100mg**	**IV**	Bolus dose over 3-5 minutes. 30 minutes prior to rituximab
	Rituximab	**375mg/m²**	**IV**	**≤450mg** 250mL sodium chloride 0.9% **≥500mg** 500mL sodium chloride 0.9% Rate as per rituximab infusion guideline.

Main toxicities:

Rituximab
Infusion related reactions, cytokine release syndrome. Severe cytokine release syndrome is characterised by severe dyspnoea, often accompanied by bronchospasm and hypoxia, in addition to fever, chills, rigors, urticaria, and angioedema. Hepatitis B reactivation

Investigations and treatment plan:

	Pre	Day 1	Ongoing
Informed Consent	X		
Clinical Assessment	X		As clinically indicated or at the end of treatment
SACT Assessment (including PS and toxicity assessment)	X	x	Every cycle. Repeat prior to each dose of rituximab as indicated
FBC	X	x	Every cycle. Repeat prior to each dose of rituximab as indicated
U&E & LFTs & Magnesium	X	x	Every cycle. Repeat prior to each dose of rituximab as indicated
CrCl (C-G)	X	x	Every cycle. Repeat prior to each dose of rituximab as indicated
Imaging	x		If clinically indicated
Blood pressure	X	x	Continuous monitoring required if on Rituximab
Temperature, respiratory rate, pulse		x	Continuous monitoring required if on Rituximab
Weight	X	x	Every cycle
Height	X		
Hepatitis B core antibody and surface antigens & Hep C & HIV 1+2	X		
Pregnancy test	X		If clinically indicated

Dose Modifications and Toxicity Management:

Haematological toxicity:

Subsequent cycles can proceed if-

ANC ≥ 1.5 x 10^9/L	Platelets ≥ 75 x 10^9/L

Note therapy can proceed if values are below these levels if cytopenias known to be secondary to disease.

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:

See section entitled 'Dosing in Renal and Hepatic Impairment'

Infusion Related Reactions

Non-Haematological toxicities:	
Rituximab	
Infusion-related Reactions	Severe infusion-related reactions with fatal outcome can have an onset ranging within 30 minutes to 2 hours after starting the first rituximab infusion. They can be characterised by pulmonary events and in some cases included rapid tumour lysis and features of tumour lysis syndrome (TLS) in addition to fever, chills, rigors, hypotension, urticaria, and angioedema. Severe cytokine release syndrome may occur. 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 normalisation 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.

	Anaphylactic and other hypersensitivity reactions may occur. In contrast to cytokine release syndrome, true hypersensitivity reactions typically occur within minutes after starting infusion. 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

References:

1. https://www.medicines.org.uk/emc rituximab (accessed July 2023)
2. 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.
3. Ganne V, Siddiqi N, Kamaplath B, et al. Humanized anti-CD20 monoclonal antibody (Rituximab) treatment for post-transplant lymphoproliferative disorder. *Clin Transplant*, 2003. Vol 17 (5). Page 417-422
4. Oertel SH, Verschuuren E, Reinke P, et al. Effect of anti-CD 20 antibody rituximab in patients with post-transplant lymphoproliferative disorder (PTLD). *Am J Transplant*, 2005. Vol 5(12). Page 2901-2906
5. McLaughlin P, Grillo-López AJ, Link BK, Levy R, Czuczman MS, Williams ME, Heyman MR, BenceBruckler I, White CA, Cabanillas F, Jain V, Ho AD, Lister J, Wey K, Shen D, Dallaire BK. Rituximab chimeric anti-CD20 monoclonal antibody therapy for relapsed indolent lymphoma: half of patients respond to a four-dose treatment program. J Clin Oncol. 1998 Aug;16(8):2825-33.
6. Trappe et al. Sequential treatment with rituximab followed by CHOP chemotherapy in adult B-cell posttransplant lymphoproliferative disorder (PTLD): the prospective international multicentre phase 2 PTLD-1 trial. Lancet oncol. 2012; 13 (2) 196-206

Circulation/Dissemination

Date added into Q-Pulse	For completion by DCM
Date document posted on the Intranet	For completion by DCM

Version History

		Author name and designation	Summary of main changes
April 2021	1.0	**Mark Nelson**	New protocol
Sept 2023	2.0	**Jennifer Gibson – Principal Pharmacist HO**	Transferred to new template. IO indication added. Indications reviewed.