TRIANGLE (maintenance) regimen

[R-CHOP (Rituximab, Cyclophosphamide, Doxorubicin, Prednisolone) alternating with R-DHAOx (Rituximab, Dexamethasone, Cytarabine, Oxaliplatin]

INDICATION

Mantle Cell Lymphoma (Blueteq) [ICD-10 code:C83.1]

TREATMENT INTENT

- Curative

TREATMENT CONTEXT

- First line treatment for Mantle Cell Lymphoma

DRUG REGIMEN

Day	Drug	Dose	Route	Administration
1	Rituximab	375mg/m^2	IV	Intravenous infusion in 500ml sodium chloride 0.9%
	Ibrutinib	560mg	PO	Once a day Oral

Cycle frequency

- 56 day cycle

Number of cycles

- 24 months of Rituximab 8 weekly maintenance and Ibrutinib

ADDITIONAL DOSE INFORMATION

- Rituximab dose will be rounded to the nearest 100mg (up if half way)

ADDITIONAL ADMINISTRATION INFORMATION

- The rate of administration of rituximab varies. Please refer to the rituximab administration guidelines
- Rituximab pre-medication 30 minutes prior to rituximab
  - Cetirizine 10mg oral
  - hydrocortisone 100mg intravenous bolus
  - paracetamol 1000mg oral
- Rituximab infusion reactions
  - hydrocortisone 100mg intravenous bolus when required for rituximab infusion related reactions
  - salbutamol 2.5mg nebule when required for rituximab related bronchospasm
  - consider pethidine 25-50mg intravenous bolus for rituximab related rigors that fail to respond to corticosteroids.

EXTRAVASATION RISK

Rituximab: neutral

SUPPORTIVE MEDICATIONSPre-medication	Rituximab pre meds
Anti-infective prophylaxis* (viral/fungal/bacterial)	Aciclovir 400mg TWICE a day
	Co-Trimoxazole 960mg ONCE a day on Monday, Wednesday and Friday
	Pentamidine 300mg nebuliser
Take home (outpatient setting)	
	Aciclovir 400mg twice a day for 21 days oral
	Co-trimoxazole 960mg once a day on Mondays, Wednesdays and Fridays only for 21 days oral

(*Only include where indicated – delete/add items as required)

CONTRAINDICATIONS

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INVESTIGATIONS before each cycle

Investigation	**Validity period**
FBC	7 days (or at consultant discretion)
U&E	7 days (or at consultant discretion)
LFTs	7 days (or at consultant discretion)
	7 days (or at consultant discretion)

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STANDARD LIMITS FOR TREATMENT TO GO AHEAD

If blood results not within range, authorisation to administer must be given by prescriber/ consultant

Neutrophils	1 x 10^9/L
Platelets	100 x 10^9/L
Creatinine Clearance (CrCl)	20mL/min
Bilirubin	Drug dependant – see individual drugs
AST/ALT	Drug dependant – see individual drugs

DOSE MODIFICATIONS

Please discuss all dose reductions / delays with the relevant consultant before prescribing, if appropriate. The approach may be different depending on the clinical circumstances. All dose reductions to be discussed with the Consultant.

In principle any dose reduction due to adverse drug reactions **should not** be re-escalated in subsequent cycles without consultant approval. It is also a general rule for chemotherapy that if a third dose reduction is necessary treatment should be stopped.

Dose modifications listed are for haematological, hepatic function, renal function and limited drug specific toxicities. Adjustments may be necessary for other toxicities as well.

Haematological toxicities on the day of treatment		
Neutrophils [x10^9/L]	1	Delay therapy until neutrophils are greater than or equal to 1x10^9/L Consider G-CSF as secondary prophylaxis. Reconsider treatment options if not recovered after 14 days.
Platelets [x10^9/L]	100	Delay therapy until platelets are greater or equal to 100x10^9 /L Reconsider treatment options if not recovered after 14 days

Renal toxicities	
CrCL (mL/min)	**Rituximab**
more than 20	100%
10-20	100%
less than 10	100%

No dose adjustment is needed for patients with mild or moderate renal impairment (greater than 30 mL/min creatinine clearance). Hydration should be maintained and serum creatinine levels monitored periodically. Administer ibruitinib to patients with severe renal impairment (<30 mL/min creatinine clearance) only if the benefit outweighs the risk and monitor patients closely for signs of toxicity. There are no data in patients with severe renal impairment or patients on dialysis

			Hepatic toxicities	
Bilirubin (xULN)		**ALT/AST (xULN)**	**Dose (% of original)**	**Drug A**
No dose adjustment necessary				Rituximab

Ibrutinib is metabolised in the liver. In a hepatic impairment study, data showed an increase in ibrutinib exposure. For patients with mild liver impairment (Child-Pugh class A), the recommended dose is 280 mg daily. For patients with moderate liver impairment (Child-Pugh class B), the recommended dose is 140 mg daily. Monitor patients for signs of ibrutinib toxicity and follow dose modification guidance as needed. It is not recommended to administer ibrutinib to patients with severe hepatic impairment (Child-Pugh class C).

Ibrutinib Toxicity

Event	Toxicity Occurrence	Dose modification after recovery
Grade 2 cardiac failure	First	Restart at 420mg
	Second	Restart at 280mg
	Third	Discontinue Ibrutinib
Grade 3 cardiac arrythmias	First	Restart at 420mg
	Second	Discontinue Ibrutinib
Grade 3 or 4 cardiac failure Grade 4 cardiac arrythmias	First	Discontinue Ibrutinib

ADVERSE EFFECTS/REGIMEN SPECIFIC COMPLICATIONS

The adverse effects listed are not exhaustive. For full details consult product literature/ reference texts.

ADVERSE EFFECTS	
Drug	**Adverse Effects**
Rituximab	Severe cytokine release syndrome, increased incidence of infective complications, progressive multifocal leukoencephalopathy
Ibrutinib	Diarrhoea, musculoskeletal pain, upper respiratory tract infection, bruising, rash, nausea, pyrexia, neutropenia, thrombocytopenia, constipation, atrial fibrillation, ventricular tachycardia, hypertension, onycholclasis

SIGNIFICANT DRUG INTERACTIONS

- **There are many drug interactions associated with ibrutinib. Caution is advised when concurrently prescribing agents that affect coagulation or platelet function or that influence the hepatic enzyme system CYP3A4.**
- **Grapefruit and grapefruit juice, and Seville oranges, should be avoided while on ibrutinib**

REFERENCES

1. TRIANGLE (autologous transplantation after a Rituximab/Ibrutinib/Ara-c containing induction in generalized mantle cell lymphoma). Protocol version 1.6 November 2019

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1	11/06/2026		Nanda Basker/Alexandra Pritchard Pharmacist	Dr Rob Lown Consultant haemtologist

This SACT protocol has been developed by the Wessex Cancer Alliance SACT protocol development group. These documents have been approved on behalf of the following Trusts;

Hampshire Hospitals NHS Foundation Trust
NHS Isle of Wight
Portsmouth Hospitals NHS Trust
Salisbury NHS Foundation Trust
University Hospital Southampton NHS Foundation Trust
Western Sussex Hospitals NHS Foundation Trust
University Hospitals of Dorset

All actions have been taken to ensure these protocols are correct. However, no responsibility can be taken for errors which occur as a result of following these guidelines.

The regimen summary that follows is to facilitate building the protocols in the Aria prescribing system for those Trusts that utilise this system.

REGIMEN SUMMARY

56 day cycle

Cycle 1 Day 1

1. Cetirizine 10mg oral
2. Hydrocortisone 100mg intravenous
3. Paracetamol 1000mg oral
4. Rituximab 375mg/m2 intravenous infusion in 500ml sodium chloride 0.9% as per the rituximab administration guidelines
5. Hydrocortisone 100mg intravenous once only when required for the relief of rituximab infusion related reactions
6. Salbutamol 2.5mg nebule once only when required for the relief of rituximab related bronchospasm

Cycle 1 Day 1 TTOs

7. Ibruitnib 560mg once a day oral
   Administration instructions:
   Oral SACT

   Ibruitnib tablets should be swallowed whole with water at approximately the same time each day.

   Avoid grapefruit and grapefruit juice, and Seville oranges while on ibruitinib. Always check for drug interactions.

   Please dispense 56 days

8. Aciclovir 400mg twice a day oral
   Administration instructions: please dispense 56 days

9. Co-trimoxazole 960mg once a day on Monday, Wednesday and Friday oral
   Administration instructions
   Co-trimoxazole 960mg once a day on Mondays, Wednesdays and Fridays. This may be dispensed as 480mg twice a day on Mondays, Wednesdays and Fridays according to local practice. Please dispense 56 days.