POLATUZUMAB-BENDAMUSTINE- RITUXIMAB

INDICATION: Relapsed/refractory diffuse large B-cell lymphoma

Prior to a course of treatment

- Check renal and liver function – *if abnormal discuss with consultant & see dose modification*
- Check FBC. Patient should have adequate bone marrow reserve, i.e neutrophils > 1.0, platelets >75 unless cytopaenia is due to disease, e.g marrow infiltration, splenomegaly - *if not discuss with consultant*
- Note tumour lysis syndrome has been reported with 1st cycle – assess risk, maintain hydration, consider Rasburicase or allopurinol prophylaxis (see below),
- Inform blood transfusion that all blood products must be irradiated
- If appropriate discuss possibility of pregnancy with female patients and need for contraception with both male and female patients. Discuss risk of infertility - offer semen cryopreservation to male patients.
- Written consent for course

Prior to each cycle

- Medical review of fitness for chemotherapy – exclude active infection, major changes in organ function
- Check FBC, U&Es, creat, LFTs - neutrophils should be >1.0 and platelets >75 *(see dose modification)*

Cycle 1			
Day 1	Rituximab	375mg/m^2	IV in 0.5L N saline *(see protocol for rituximab)*
Day 2	Polatuzumab*	1.8mg/kg	IV in 5% glucose 100ml over 90 mins
	Bendamustine	90mg/m^2	IV in N saline 0.5L over 30-60mins
Day 3	Bendamustine	90mg/m^2	IV in N saline 0.5L over 30-60mins
Day 5-10	GCSF		
Cycle 2-6			
Day 1	Rituximab	375mg/m^2	IV in 0.5L N saline
	Polatuzumab*	1.8mg/kg	IV in 5% glucose 100ml over 30mins **
	Bendamustine	90mg/m^2	IV in N saline 0.5L over 30-60mins
Day 2	Bendamustine	90mg/m^2	IV in N saline over 30-60mins
Day 5-10	GCSF		

*via 0.2micrometre filter **if previously well-tolerated

Premedication	Paracetamol 1g PO, chlorpheniramine 10mg IV, hydrocortisone 100mg IV on day 1 each cycle. Paracetamol 1g PO, chlorpheniramine 10mg IV day 2 of cycle 1
Prophylaxis for acute emesis	Ondansetron

Prophylaxis for delayed emesis	Metoclopramide
Other medications	Rasburicase or allopurinol with cycle 1 (excluding days 1 and 3 – severe skin reactions have been reported if given with bendamustine) Cotrimoxazole 480mg od, acyclovir 400mg bd

Dose modification for haematological toxicity (unless due to disease)

• Neuts > 1.0 and plats > 75	Proceed with 100% dose pola-BR
• Neuts <1.0 and/or platelets<75 when cycle due	Delay for up to 2 weeks and proceed if parameters met – if not met reconsider suitability for Pola-BR
• If treatment delayed due to neutropenia despite GCSF	Proceed with 75% dose Bendamustine for first delay, 50% for second delay
• If treatment delayed due to neutropenia despite GCSF and dose reduction	Proceed with 50% bendamustine
• If treatment delayed due to platelets <75 when treatment due	Proceed with 75% dose bendamustine for first delay, 50% for second delay
• Treatment delay due to thrombocytopenia despite bendamustine dose reduction to 50%	Reconsider suitability for pola-BR

Dose modification for renal dysfunction

• Creat. Clear <30ml/min	Limited data on polatuzumab – *discuss with consultant*
• Creat clearance <10/ml/min	Limited data on bendamustine - *discuss with consultant*

For liver dysfunction (unless due to disease)

• Moderate dysfunction – AST > 1.5 x ULN or bili >1.5 x ULN	Do not give polatuzumab, no data on bendamustine – d*iscuss with consultant*
• Mild dysfunction – AST 1 – 2.5 X ULN, bili 20-50	Reduce Bendamustine by 30%

Pola-BR toxicities

Neutropenic sepsis & thrombocytopenia	Nausea & vomiting
Amenorrhoea & infertility (offer semen cryopreservation)	Constipation
Diarrhoea	Fatigue
Infusion reactions – fever, rigors, hypotension, pruritus	Rash
Mucositis	Transient elevation of serum creatinine
Tumour lysis syndrome with 1st cycle	Infusion-related reactions (rituximab and polatuzumab)

Peripheral neuropathy (polatuzumab)

Author:	Dr MP Macheta
Date:	14.01.20
Review:	Jan 2022