

BENDAMUSTINE- RITUXIMAB

INDICATION: chronic lymphocytic leukaemia/ small lymphocytic 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 > 1.5, platelets >100 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 – maintain hydration, allopurinol prophylaxis (see below), monitor biochemistry
- Patients with CLL are at particularly high risk of severe reactions due to cytokine release syndrome. In patients with WBC > 25 x 10⁹/L the rituximab dose should be split (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 course

- Medical review of fitness for chemotherapy – exclude active infection, major changes in organ function
- Check FBC, U&Es, creat, LFTs - neutrophils should be >1.5 and platelets >100 (see *dose modification*)

CYCLE 1

DAY 1	Rituximab	375 mg/m ²	IV in 500ml sodium chloride 0.9% (see <i>protocol for rituximab</i>)
DAYS 1-2	Bendamustine	70 mg/m ²	IV in 500ml sodium chloride 0.9% over 30 minutes

Repeat cycle in 28 days

In patients with high risk of severe reactions, the dose of rituximab should be given as:

Day 1: Rituximab 50mg/m² IV in 50-100ml sodium chloride 0.9%

Day 2: Rituximab 325mg/m² IV in 500ml sodium chloride 0.9%

CYCLES 2-6

DAY 1	Rituximab	500 mg/m ²	IV in 500ml sodium chloride 0.9% (see <i>protocol for rituximab</i>)
DAYS 1-2	Bendamustine	70 mg/m ²	IV in 500ml sodium chloride 0.9% over 30 minutes

Repeat cycle every 28 days for max. 6 cycles

Prophylaxis for acute emesis Ondansetron+ Dexamethasone

Prophylaxis for delayed emesis Metoclopramide

Other medication Allopurinol with cycle 1 (excluding days 1 and 2- severe skin reaction have been reported if given with bendamustine)

Dose modification for haematological toxicity (unless due to disease)

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| • ANC > 1.5 and PLT > 100 | Proceed with Bendamustine 100% dose |
| • ANC < 1.5 and/or PLT < 100 when cycle due | Delay for up to 2 weeks and proceed if parameters met – if not met reconsider suitability for bendamustine |
| • If treatment delayed due to ANC < 1.5 | Proceed at 100% dose with GCSF support |
| • If treatment delayed due to ANC < 1.5 despite G-CSF | Proceed with 75% dose Bendamustine for first delay, 50% for second delay |
| • If treatment delayed due to ANC < 1.5 despite G-CSF and dose reduction | Proceed with 50% bendamustine at 100% dose with GCSF support |
| • If treatment delayed due to PLT < 100 when treatment due | Proceed with 75% dose bendamustine for first delay, 50% for second delay |
| • Treatment delay due to thrombocytopenia despite dose reduction to 50% | Reconsider suitability for bendamustine |

Dose modification for renal dysfunction

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| • Creat. Clear <40ml/min | Bendamustine has not been studied in this group – clinical decision. |
| • Creat. Clear 40-60 ml/min | Limited information – clinical decision. Use with caution |

Dose modification for liver dysfunction

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| • Moderate dysfunction – AST > 2.5 X ULN and bili >50 X ULN | Bendamustine has not been studied in this group of patients – clinical decision. Use with caution. |
| • Mild dysfunction – AST 1 – 2.5 X ULN, bili 20-50 | Reduce Bendamustine by 30% |

Bendamustine toxicity

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| • Neutropenic sepsis & thrombocytopenia | • Nausea & vomiting |
| • Amenorrhoea & infertility (offer semen cryopreservation) | • Constipation |
| • Diarrhoea | • Fatigue |
| • Mucositis | • Rash |
| | • Transient elevation of serum |

- Tumour lysis syndrome with 1st cycle

creatinine See also rituximab
toxicities

References:

1. Macheta MP. Bendamustine and Rituximab for Follicular lymphoma and mantle cell lymphoma.
2. Iannito E., Morabito F., Mancuso S., Gentile M., Montanini A. et al. Bendamustine with or without rituximab in the treatment of relapsed chronic lymphocytic leukaemia: an Italian retrospective study. *Br J Haematol.* 2011 Mar 4. doi: 10.1111/j.1365-2141.2011.08597.x.
3. Fischer K, Cramer P, Stilgenbauer S, et al. Bendamustine combined with rituximab (BR) in first-line therapy of advanced CLL: a multicenter phase II trial of the German CLL Study Group (GCLLSG). *Blood.* 2009;114:89. Abstract 205.

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