PROTOCOL

The Clatterbridge Cancer Centre NHS Foundation Trust

Systemic Anti Cancer Therapy Protocol

BeGEV
R/R Hodgkin's Lymphoma

PROTOCOL REF: MPHABEGEV
(Version No. 1.0)

Approved for use in:

- Relapsed/refractory (R/R) Hodgkin's Lymphoma

Blueteq registration not required

Dosage:

Drug	Dose	Route	Frequency
Gemcitabine	**800 mg/m^2**	IV infusion	Day 1 and 4
Vinorelbine	**20 mg/m^2**	IV infusion	Days 1
Bendamustine	**90 mg/m^2**	IV infusion	Days 2 and 3
Prednisolone	**100mg**	Oral	Days 1 to 4

Cycle length: 21 days. Maximum four cycles.

Administration:

- Patients will require irradiated blood products (lifelong) –the patients receive information booklets about irradiated blood when counselled by the specialist nurses. It contains an alert card that the patient carries around with them. The specialist nurses will then contact the lab to inform them of the need for irradiated blood products

Emetogenic risk:

Severely emetogenic.

Supportive treatments:

- Allopurinol PO 300mg OD for the first cycle (100mg OD in severe renal dysfunction)
- Chlorhexidine 0.2% mouthwash 10mls QDS
- Co-trimoxazole PO 480mg OD
- Filgrastim s/c 30 or 48 million units OD (30million units if ≤ 70kgs; 48 million units if ≥ 70kgs) from day 5 for 5 days
- Metoclopramide PO 10mg TDS prn
- Ondansetron IV 8mg prior to chemo on day 1 and then 8mg PO BD for 5 days

Extravasation risk:

Gemcitabine: non-vesicant

Bendamustine: vesicant

Vinorelbine: vesicant

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

Interactions:

Gemcitabine

No known drug interactions but gemcitabine is a radiation sensitiser so care is needed if radiotherapy is to be given concurrently.

Vinorelbine

As vinca alkaloids are known substrates for P_glycoprotein, and in the absence of specific study, caution should be exercised when combining vinorelbine with strong modulators of this membrane transporter.

As CYP3A4 is mainly involved in the metabolism of vinorelbine, combination with strong inhibitors of this isoenzyme (e.g. azole antifungals such as ketoconazole and itraconazole) could increase blood concentrations of vinorelbine and combination with strong inducers of this isoenzyme (e.g. rifampicin, phenytoin) could decrease blood concentrations of vinorelbine

Bendamustine

Bendamustine metabolism involves cytochrome P450 (CYP) 1A2 isoenzyme. Therefore, the potential for interaction with CYP1A2 inhibitors such as fluvoxamine, ciprofloxacin, aciclovir and cimetidine exists

For more detailed interactions please refer to the SPC and add a link to the appropriate SPC

Treatment schedule:

Day	Drug	Dose	Route	Diluent and rate
1 to 4	**Prednisolone**	**100mg**	**PO**	
1	**Ondansetron**	**8mg**	**IV**	30 minutes before chemotherapy
	Vinorelbine	**20mg/m^2**	**IV**	In 50ml sodium chloride 0.9% over 10 minutes
	Gemcitabine	**800mg/m^2**	**IV**	In 250mls sodium chloride 0.9% over 30 minutes
2	**Bendamustine**	**90mg/m^2**	**IV**	In 500mls sodium chloride 0.9% over 60 minutes
3	**Bendamustine**	**90mg/m^2**	**IV**	In 500mls sodium chloride 0.9% over 60 minutes
4	**Gemcitabine**	**800mg/m^2**	**IV**	In 250mls sodium chloride 0.9% over 30 minutes

Main toxicities:

Thrombocytopenia, neutropenia, anaemia, nausea, vomiting, diarrhoea, peripheral neuropathy

Investigations and treatment plan:

	Pre	Cycle 1	Cycle 2	Cycle 3	Cycle 4	Ongoing
Informed Consent	X					
Clinical Assessment	X	X	X	X	X	
FBC	X	X	X	X	X	Every cycle
U&E & LFTs	X	X	X	X		Every Cycle
CrCl (Cockcroft and Gault)	X	X	X	X		Every cycle
PET-CT scan**	X					At the end of treatment and if clinically indicated
ECG						If clinically indicated
Blood pressure measurement	X					Repeat if clinically indicated
Respiratory Rate						If clinically indicated
Height	X					
Weight recorded	X	X	X	X		Every cycle
Blood glucose	X					Repeat if clinically indicated

Dose Modifications and Toxicity Management:

Haematological toxicity:

Proceed on day 1 if-

ANC ≥ 1.0 x 10^9/L	Platelets ≥ 100 x 10^9/L

In case of cytopenias delay chemotherapy and repeat FBC in one week.

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:

Dosing in renal and hepatic impairment:

Renal	Gemcitabine	No dose adjustment needed for renal dysfunction but if the patient is receiving dialysis then dialysis should start 6 to 12 hours after gemcitabine administration
	Vinorelbine	No dose adjustment needed for renal dysfunction
	Bendamustine	No dose adjustment needed for renal dysfunction

Hepatic	Gemcitabine	Total bilirubin ≥ 27 micromol/L: either start at 80% of the original dose and increase the dose if tolerated or start with full dose with active monitoring
	Vinorelbine	In severe hepatic dysfunction consider 66% of original dose
	Bendamustine	Moderate (bilirubin 20 -51 micromol/L): 70% of the original dose Severe (bilirubin > 51 micromol/L): not recommended

References:

1. https://www.medicines.org.uk/emc. Gemcitabine 10mg/ml solution for infusion. Accessed 17/04/2023. Date revised 13/10/2022.

2. https://www.medicines.org.uk/emc. Navelbine 10mg/ml concentration for solution for infusion. Accessed 17/04/2023. Date revised 14/07/2021
3. https://www.medicines.org.uk/emc. Bendamustine hydrochloric 2.5mg/ml powder for solution for infusion. Accessed 17/04/2023. Date revised 25/03/2021
4. Armando Santoro, Rita Mazza, Alessandro Pulsoni, Alessandro Re, Maurizio Bonfichi, Vittorio Ruggero Zilioli, Manuela Zanni, Francesco Merli, Antonella Anastasia, Stefano Luminari, Giorgia Annechini, Manuel Gotti, Annalisa Peli, Anna Marina Liberati, Nicola Di Renzo, Luca Castagna, Laura Giordano, Francesca Ricci, Carmelo Carlo-Stella; Five-year results of the BEGEV salvage regimen in relapsed/refractory classical Hodgkin lymphoma. *Blood Adv* 2020; 4 (1): 136–140. doi: https://doi.org/10.1182/bloodadvances.2019000984
5. 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.

Circulation/Dissemination

Date added into Q-Pulse	31st August 2023
Date document posted on the Intranet	N/A

Version History

Date	Version	Author name and designation	Summary of main changes
May 2023	1.0	**Aileen McCaughey Haematology Pharmacist**	**New protocol. Bendamustine is within block contract.**