SACT PROTOCOL

The Clatterbridge Cancer Centre NHS Foundation Trust

Systemic Anti Cancer Therapy Protocol

ABVD
Hodgkin's Lymphoma

PROTOCOL REF: MPHAABVDHA
(Version No. 2.0)

Approved for use in:

- Hodgkin's Lymphoma

Dosage:

Drug	Dose	Route	Frequency
Doxorubicin	**25mg/m^2**	IV infusion	Day 1
Bleomycin*	**10,000units/m^2**	IV infusion	Day 1 *May be stopped after 4 cycles depending on results of interim PET CT scan. MDT will decide and document decision
Vinblastine	**6mg/m^2**	IV infusion	Day 1
Dacarbazine	**375mg/m^2**	IV infusion	Day 1

Each cycle is 14 days. Maximum of 12 cycles

NOTE ABVD is traditionally a 28 day cycle with treatment given on day 1 and day 15 for up to a maximum of 6 cycles. However, to enable a clinical check prior to day 15 prescription, Meditech requires that each day of treatment be referred to as a new cycle. Therefore in Meditech ABVD is given every 14 days for up to a maximum of 12 cycles.

PLEASE EXCERCISE CAUTION WHEN COUNSELLING PATIENTS AND BOOKING SCANS ETC

Administration:

- Doxorubicin may impart a red colour to the urine. Patients should be cautioned that this does not pose any health hazards.

Emetogenic risk:

Severely emetogenic.

Supportive treatments:

Pre-Medication

- Aprepitant 125mg oral stat
- Dexamethasone 8mg oral stat
- Ondansetron 8mg IV stat
- *Lorazepam 1mg BD prn may be added for anticipatory / anxiety related nausea*

Take Home Medication

- Allopurinol 300mg daily (dose dependant on renal function) for first two cycles
- Aprepitant 80mg once daily on day 2 and 3
- Dexamethasone 4mg daily for 2 days
- Ondansetron 8mg BD for 5 days
- Metoclopramide 10mg TDS prn
- Docusate PO 200mg BD prn
- Co-trimoxazole 480mg daily for duration of treatment and 3-6 months after

Extravasation risk:

Doxorubicin: vesicant

Bleomycin: non-vesicant

Vinblastine: vesicant

Dacarbazine: irritant

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

Dosing in renal and hepatic impairment:

Doxorubicin

Renal Function	
Haemodialysis	Consider 75% of dose
Liver Function	
Bilirubin (micromole/L)	Dose
20-50	50%
51-86	25%
>86 or Child Pugh C	Omit

Bleomycin

Renal Function	
CrCl (ml/min)	Dose
10-50	75%
<10	50%
Haemodialysis	Consider 50%

Vinblastine

Liver Function	
Bilirubin (micromole/L)	Dose
>51	50%

Dacarbazine

Renal Function	
CrCl (ml/min)	Dose
≥30 with no hepatic impairment (in patients with combined renal and hepatic dysfunction elimination is impaired)	No dose adjustment required
<30	Consider 70%
Haemodialysis	Consider 70%
Liver Function	
Mild and moderate impairment without renal dysfunction (in patients with combined renal and hepatic dysfunction elimination is impaired)	No dose adjustment required
Severe	Not recommended

Interactions:

Refer to the SPC for full list of interactions and more detail

Doxorubicin

- Care required with drugs that cause cardiotoxicity or that affect cardiac function (e.g. trastuzumab or felodipine). Also care required with drugs that cause hepatotoxicity.
- Doxorubicin undergoes metabolism via CYP450 so concomitant use of inhibitors may increase toxicity and inducers may reduce efficacy.
- Ciclosporin and cimetidine increase the AUC of doxorubicin; dose adjustments may be required.

- Barbiturates may lead to an accelerated plasma clearance of doxorubicin, while the concomitant administration of phenytoin may result in lower plasma phenytoin levels.
- Doxorubicin is a potent, radio sensitizing agent.

Bleomycin

- An increased risk of pulmonary toxicity has been reported with concomitant administration of other agents with pulmonary toxicity, e.g. carmustine, mitomycin, cyclophosphamide, methotrexate and gemcitabine.
- These are case reports of a reduced effect of digoxin as a result of a reduced oral bioavailability when combined with bleomycin.
- There are case reports of reduced levels of phenytoin when combined with bleomycin. Concomitant use is not recommended.
- The bacteriostatic efficacy of gentamicin and amikacin may be reduced

Vinblastine

- Macrolide antibiotics increases the exposure to vinca alkaloids. Manufacturer advises caution
- Azole antifungals increases the exposure to vinca alkaloids. Manufacturer advises caution
- Aprepitant / fosaprepitant increases the exposure to vinca alkaloids. Manufacturer advises caution
- Phenytoin / phenobarbital / carbemazepine decreases the exposure to vinca alkaloids.

- When chemotherapy is being given in conjunction with radiation therapy through portals which include the liver, the use of vinblastine should be delayed until radiation therapy has been completed.
- Caution should be exercised in patients concurrently taking drugs known to inhibit drug metabolism by hepatic cytochrome P450 isoenzymes in the CYP 3A subfamily, or in patients with hepatic dysfunction.

Dacarbazine

- Dacarbazine is metabolised by cytochrome P450 (CYP1A1, CYP1A2, and CYP2E1). Review if used alongside other drugs that effect CYP enzymes.
- Phenytoin: absorption of phenytoin is reduced from the gastrointestinal tract and may predispose the patient to convulsions.

Treatment schedule:

Day	Drug	Dose	Route	Diluent and rate
1	**Aprepitant**	**125mg**	**PO**	30-60mins prior to chemotherapy (then 80mg daily on day 2 and 3)
	Dexamethasone	**8mg**	**PO**	30-60mins prior to chemotherapy (then 4mg daily on day 2 and 3). Take with food
	Ondansetron	**8mg**	**IV**	In 100ml sodium chloride 0.9% over 15 minutes 30-60mins prior to chemotherapy
	Vinblastine	**6mg/m^2**	**IV**	In 50ml sodium chloride 0.9% over 10 minutes
	Doxorubicin	**25mg/m^2**	**IV**	In 100mls sodium chloride 0.9% over 30 minutes
	Bleomycin*	**10,000units/m^2**	**IV**	In 100mls sodium chloride 0.9% over 30 minutes *NB if an interim PET-CT scan after cycle 4 is negative then bleomycin can be withheld for future cycles.
	Dacarbazine	**375mg/m^2**	**IV**	In 500mls sodium chloride 0.9% over 60 minutes

Main toxicities:

Thrombocytopenia, neutropenia, anaemia, nausea, vomiting, diarrhoea, pulmonary toxicity, autonomic (constipation) and peripheral neuropathy.

Investigations and treatment plan:

	Pre	Cycle 1	Cycle 2+	Ongoing
Informed consent	X			
Clinical Assessment	X	x	x	As clinically indicated or at the end of treatment
SACT Assessment (including performance status and toxicity assessment)		x	x	Every cycle
FBC	X	x	x	Every cycle (Bloods must be within 7 days of day 1 of treatment cycle)
U&E & LFTs & bone profile	X	x	x	Every Cycle (Bloods must be within 7 days of day 1 of treatment cycle)
CrCl (Cockcroft and Gault)	X	x	x	Every Cycle (Bloods must be within 7 days of day 1 of treatment cycle)
PET CT scan	X			Repeat after 4 cycles and again at the end of treatment
Pulmonary function tests	X			If clinically indicated
ECHO or MUGA scan	X			Before treatment in patients over 60 or with pre-existing cardiac disease
Height	X			
Weight recorded	X	x	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:

NB The first cycle should proceed regardless of blood counts

Proceed if-

Platelets > 75 x 10^9/L

If platelets are ≤ 75 x 10^9/L then delay chemotherapy and repeat FBC after one week. Patients should continue chemotherapy regardless of neutrophil count; G-CSF support can be considered but should be used cautiously given the increased risk of pulmonary toxicity when given in combination with bleomycin.

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 'Dosing in renal and hepatic impairment' section

References:

1. https://www.medicines.org.uk/emc Doxorubucin (accessed Feb 2020)
2. https://www.medicines.org.uk/emc bleomycin (accessed Feb 2020)
3. https://www.medicines.org.uk/emc vinblastine (accessed Feb 2020)
4. https://www.medicines.org.uk/emc dacarbazine (accessed Feb 2020)
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.
6. Johnson P, Federico M, Kirkwood A, et al: Adapted treatment guided by interim PET-CT scan in advanced Hodgkin's lymphoma. N Engl J Med 374:2419-2429, 2016.

Circulation/Dissemination

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Version History

		Author name and designation	Summary of main changes
			To be completed by author
	1.0	Aileen McCaughey	
	2.0	Jennifer Gibson	Dacarbazine infusion volume and duration updated. Streamline the interactions section.