ABVD

Indication
First line treatment of Hodgkin's Lymphoma.

ICD-10
Codes with a prefix C81

Regimen details

Day	Drug	Dose	Route
1 and 15	Doxorubicin	25mg/m^2 (max 50mg)	IV bolus
1 and 15	Bleomycin*	10,000 iu/m^2	IV infusion
1 and 15	Vinblastine	6mg/m^2 (max 10mg)	IV infusion
1 and 15	Dacarbazine	375mg/m^2	IV infusion

*consider omitting or reducing the dose of bleomycin if over 60 years of age/other risk factors for lung toxicity.

A baseline PET should be performed and an interim PET should be performed 11-14 days after cycle 2 day 15. Do not delay cycle 3 day 1 whilst awaiting the result. For patients in complete metabolic remission on this interim scan, consider stopping bleomycin in subsequent cycles.

Cycle frequency
28 days

Number of cycles
Usually up to 6 cycles.

Administration
Doxorubicin is administered by slow IV bolus into the arm of a fast running drip of sodium chloride 0.9%.

Prior to bleomycin, hydrocortisone 100mg IV stat should be administered. Bleomycin is administered in 250mL sodium chloride 0.9% over 60 minutes.

Vinblastine is administered in 50mL sodium chloride 0.9% over 10 minutes as per national guidance. Nurse to remain with patient throughout infusion.

Dacarbazine is administered in 500-1000mL sodium chloride 0.9% over 60 minutes.
Dacarbazine is sensitive to light exposure. All reconstituted solutions should be suitably protected from light including during administration, using a light-resistant infusion set.

Pre-medication
Antiemetics as per local policy.
Hydrocortisone 100mg IV stat is required prior to bleomycin.

Emetogenicity
This regimen has moderate-high emetic potential.

Additional supportive medication

Allopurinol 300mg OD (100mg OD if CrCl < 20mL/min) for the first 1-2 weeks.
Antiemetics as per local policy
Mouthwashes if required.
Aciclovir 400mg BD during treatment and for 3 months post treatment.
Co-trimoxazole 480mg BD Mon/Wed/Fri as PCP prophylaxis during treatment and to continue at least 3 months after treatment stopped.

Irradiated blood requirement

Patients with Hodgkin lymphoma are at risk of TA-GvHD. Inform patient and transfusion laboratory of irradiated "flag", which persists for life. Ensure card is attached to the notes and a copy given to the patient.

Extravasation

Vinblastine, doxorubicin and dacarbazine are vesicant
Bleomycin is neutral

Investigations – pre first cycle

Investigation	Validity period
FBC	7 days and pre day 15
LDH	7 days
U+Es (including creatinine)	7 days and pre day 15
LFTs	7 days and pre day 15
HbA1C	28 days
ESR if stage I or IIA	14 days
Hepatitis B core antibody and hepatitis BsAg, hepatitis C antibody, HIV 1+2 serology	Must have been sent, even if results pending

Baseline pulmonary function tests, including transfer factor, are recommended prior to commencing bleomycin.

Consider ECG and echocardiogram if patient has significant cardiac history.

Investigations – pre subsequent cycles

Investigation	Validity period
FBC	72 hours (prior to days 1 and 15)
U+Es (including creatinine)	72 hours (prior to days 1 and 15)
LFTs	72 hours (prior to days 1 and 15)

Standard limits for administration to go ahead and dose modifications

Investigation	Limit
CrCl	> 50mL/min
AST/ALT	≤ ULN
Bilirubin	≤ ULN

Dose modifications

- **Haematological toxicity**

Treatment delays/dose reductions are not required for haematological toxicity. Discuss with consultant if platelets < 50 $x10^9$/L or if patient has been admitted with previous neutropenic sepsis.

- **Renal impairment**

CrCl (mL/min)	**Bleomycin dose**	**Doxorubicin dose**
> 50	100%	100%
10 50	75%	100%
< 10	50%	Discuss with consultant

CrCl (mL/min)	**Dacarbazine dose**
>60	100%
45-60	80%
30-45	75%
<30	70% and use with caution (consultant decision)

Vinblastine: no dose reduction required.

- **Hepatic impairment**

Bilirubin (x ULN)		**AST/ALT** (x ULN)	**Doxorubicin dose**
< ULN	and	< 2	100%
< ULN	and	2-3	75%
1 – 2.5	or	> 3	50%
2.5 – 4			25%
> 4			Omit

Bilirubin (x ULN)		**AST/ALT** (x ULN)	**Vinblastine dose**
< 1.5	and	< ULN	100%
1.5 - 3	and/or	1 – 3.5	50%
> 3	or	> 3.5	Omit

Dacarbazine:
No dose modifications required for mild to moderate hepatic impairment. In patients with combined renal and hepatic impairment elimination of dacarbazine is prolonged, however there are no current recommendations on dose reductions. Consider dose reduction if moderate to severe hepatic impairment (consultant decision).

Bleomycin:
Little information: consultant decision.

- **Other toxicities**

Toxicity	**Definition**	**Dose adjustment**
Neurological toxicity	Grade ≥ 2	Discontinue vinblastine – discuss with consultant.
Constipation	Grade ≥ 3	Discontinue vinblastine – discuss with consultant.
Cardiac toxicity	Signs or symptoms of cardiac disease LVEF < 50%	Discuss with consultant Consider dose reduction or discontinuation of treatment
Pulmonary toxicity	Signs and symptoms of pulmonary toxicity Diffusing capacity < 50% of predicted value	Discontinue bleomycin

If suspected bleomycin induced pneumonitis, seek respiratory opinion and consider antibiotics (as per local policy) and prednisolone (1mg/kg/day).

Adverse effects - for full details consult product literature/ reference texts

- **Serious side effects**

Myelosuppression
Cardiotoxicity
Pulmonary fibrosis
Neurotoxicity
Hepatotoxicity
Cardiotoxicity, arrhythmias
post-therapy MDS

- **Frequently occurring side effects**

Myelosuppression
Nausea and vomiting
Mucositis
Fatigue
Constipation
Dyspepsia
Hyperglycaemia
Alopecia

- **Other side effects**

Rash
Headache
Confusion

Significant drug interactions – for full details consult product literature/ reference texts

Warfarin/coumarin anticoagulants: increased or fluctuating anticoagulant effects. Avoid if possible, consider switching patient to a low molecular weight heparin during treatment or if the patient continues taking an oral anticoagulant monitor the INR at least once a week and adjust dose accordingly.

Vinblastine:
Erythromycin: may increase vinblastine toxicity.

Dacarbazine:
CYP1A2 and 2E1 inhibitors: may enhance toxicity of dacarbazine.

CYP1A2 inducers: may reduce effect of dacarbazine.

Additional comments

Doxorubicin has a life time maximum cumulative dose of 450mg/m^2

References

- Summary of Product Characteristics. Dacarbazine (Medac) accessed 24 May 2017 via www.medicines.org.uk
- Summary of Product Characteristics Vinblastine (Hospira) accessed 24 May 2017 via www.medicines.org.uk
- Summary of Product Characteristics Doxorubicin (Hospira) accessed 24 May 2017 via www.medicines.org.uk
- Summary of Product Characteristics Bleomycin (Hospira) accessed 24 May 2017 via www.medicines.org.uk
- AM Evens et al, BJH 2007 (137) 545-552 and E Boleti & GM Mead, Ann Oncol 2007 (18) 376-380
- Duggan, D et al Randomised Comparison of ABVD and MOPP/ABV Hybrid for the Treatment of Advanced Hodgkin's Disease: Report of an Intergroup Trial. (2003); JCO, Vol 21: pp607 – 614
- Boleti E, Mead GM. ABVD for Hodgkin's lymphoma: full-dose chemotherapy without dose reductions or growth factors. Ann Oncol. 2007 Feb; 18(2):376-80.
- Evens AM, et al. G-CSF is not necessary to maintain over 99% dose-intensity with ABVD in the treatment of Hodgkin lymphoma: low toxicity and excellent outcomes in a 10-year analysis. Br J Haematol. 2007 Jun; 137(6):545-52

Written/reviewed by: Dr L Lowry (Consultant Haematologist, UHBristol NHS Trust)

Checked by: Sarah Murdoch (Senior Oncology/Haematology Pharmacist, SW Clinical Network)

Authorised by: Dr J Braybrooke (Consultant Oncologist, UHBristol NHS Trust, SW Clinical Network)

Date: August 2017