ABVD

INDICATION

Hodgkin lymphoma.
For patients > 60 year old or with additional risk factors for bleomycin lung toxicity consider:
- Omitting bleomycin entirely or
- Only giving 2 courses containing bleomycin and omitting from the remaining cycles (especially in a fit older patient)[11]

Bleomycin should also be omitted from cycle 3A onwards if planning to receive 6 cycles of chemotherapy and interim PET scan is negative (Deauville 1-3)[10]

TREATMENT INTENT

Curative.

PRE-ASSESSMENT

1. Ensure histology is confirmed prior to administration of chemotherapy and document in notes.
2. Record stage of disease - PET-CT (preferably with contrast) scan, presence or absence of B symptoms, clinical extent of disease.
3. Consider pulmonary function tests in those with a history of respiratory disease or heavy smoking before course one and as clinically indicated (see bleomycin supportive care document).
4. Blood tests - FBC, ESR, U&Es, LDH, urate, calcium, magnesium, creatinine, LFTs, glucose, Igs, hepatitis B core antibody and hepatitis B surface Ag, hepatitis C antibody, EBV, CMV, VZV, HIV 1+2 after consent.
5. **Send a "group and save" sample to transfusion and inform patient and transfusion laboratory that they will require irradiated blood products for all future transfusions**. Ensure card is attached to the patient's notes and copy given to the patient. See 'Guidelines for the use of blood components in adult haematology'.
6. Urine pregnancy test - before cycle 1 of each new chemotherapy course for women of child-bearing age unless they are postmenopausal, have been sterilised or undergone a hysterectomy.
7. ECG +/- Echo - *if clinically indicated*.
8. Record performance status (WHO/ECOG).
9. Record height and weight.
10. Consent - ensure patient has received adequate verbal and written information regarding their disease, treatment and potential side effects. Document in medical notes all information that has been given. Obtain written consent prior to treatment.
11. Fertility - it is very important the patient understands the potential risk of reduced fertility. All patients should be offered fertility advice by referring to the Oxford Fertility Unit.
12. Hydration - *in patients with bulky disease* pre-hydrate with sodium chloride 0.9% 1 litre over 4-6 hours. For patients at high risk of tumour lysis, refer to the tumour lysis protocol.by
13. Consider dental assessment / Advise dental check is carried out by patient's own dental

practitioner before treatment starts.

14. Treatment should be agreed in the relevant MDT.

For early stage disease, classify into favourable or unfavourable – see treatment pathway.

DRUG REGIMEN

Each 4 week cycle consists of:

Day 1	**DOXORUBICIN** 25 mg/m^2 IV bolus.
Day 1	**VINBLASTINE**** 6 mg/m^2 IV infusion in 50 mL sodium chloride 0.9% over 10 minutes.
Day 1	**DACARBAZINE** 375 mg/m^2 IV infusion in 1000 mL sodium chloride 0.9% over 1-2 hours.
Day 1	**BLEOMYCIN*** 10,000 units/m^2 in 100 mL sodium chloride 0.9% IV infusion over >1 hour.
Day 15	**DOXORUBICIN** 25 mg/m^2 IV bolus.
Day 15	**VINBLASTINE**** 6 mg/m^2 IV infusion in 50 mL sodium chloride 0.9% over 10 minutes.
Day 15	**DACARBAZINE** 375 mg/m^2 IV infusion in 1000 mL sodium chloride 0.9% over 1-2 hours.
Day 15	**BLEOMYCIN*** 10,000 units/m^2 in 100 mL sodium chloride 0.9% IV infusion over >1 hour.

NB: * Omit after 2 cycles for patients with a negative interim PET scan after 2 courses if progressing onto 6 cycles of chemotherapy.

** No 'ceiling' for vinblastine dosage in this protocol.

CYCLE FREQUENCY

- Each course is given every 28 days (ABVD is administered on Day 1 and Day 15).
- Treatment should be delivered on time irrespective of the neutrophil count.
- Patients should not be supported with G-CSF unless bleomycin has been discontinued
- Patients who are unwell should be deferred by one week.
- Patients normally receive a maximum of 6 courses.

RESTAGING

- Clinical assessment at least prior to each course and document in notes.
- Interim PET-CT scan should be performed at least 11 days after course 2B. Course 3A AVD should not be delayed whilst waiting for the result
- If interim PET-CT scan was Deauville 1-3 then a contrast-enhanced CT of the neck, chest, abdomen and pelvis should be performed at the end of treatment, a PET is not usually required
- For patients receiving 6 courses of chemotherapy, omit the bleomycin for cycles 3-6 if the interim PET scan is negative (Deauville 1-3)[10]

DOSE MODIFICATIONS

All drugs will be given at full dose and on schedule with no dose delays or reduction for haematological toxicity. Discuss with consultant patients who are unwell / admission with neutropenic sepsis/platelets <50.

Doxorubicin:

Renal impairment	**Hepatic impairment**	
GFR>10mL/min: no dose adjustment is needed GFR<10mL/min: no need for dose adjustment is expected	**Bilirubin micromol/L** 20-50 51-86 >86 or Child-Pugh C	**Dose** 50% 25% omit

Doxorubicin maximum cumulative dose (additive to other anthracyclines):
450-550 mg/m^2 (in normal cardiac function)
400 mg/m^2 (in patients with cardiac dysfunction or exposed to mediastinal irradiation).
Consider dose reduction in the event of cardiac impairment.

Bleomycin:

Renal impairment	**Hepatic impairment**
GFR >50 mL/min: 100% dose GFR 10-50 mL/min: 75% dose GFR <10 mL/min: 50% dose	No need for dose adjustment is expected.

Consider omitting bleomycin for patients > 60 years old or with additional risk factors for bleomycin lung toxicity. Refer to the bleomycin supportive care document.
Consider omitting bleomycin from cycle 3A onwards if planning to receive 6 cycles of chemotherapy and interim PET scan is negative (Deauville 1-3)[10]

Vinblastine:

Renal impairment	**Hepatic impairment**
No dose adjustment is needed.	Bilirubin >51 micromol/L: 50% dose

Neuropathy - in the presence of motor weakness or severe sensory symptoms, discuss reducing or withholding vinblastine with a consultant.

Dacarbazine:

Renal impairment **- discuss with consultant**	**Hepatic impairment**
GRF ≥30 mL/min without hepatic impairment: 100% dose GFR <30 mL/min: 70% dose	Mild and Moderate without renal impairment: no dose adjustment is needed. Severe: not recommended

If there is mild to moderate renal or hepatic insufficiency alone, a dose reduction is not usually required. In patients with combined renal and hepatic impairment, elimination of dacarbazine is prolonged.

INVESTIGATIONS

FBC, renal and liver profiles.

CONCURRENT MEDICATION

Allopurinol	300mg OD PO, to start 24 hours prior to chemotherapy and then continue for 7 days. (Cycle 1 only)
Aciclovir	200 mg TDS PO for the duration of chemotherapy and for 3 months after completion.
Co-trimoxazole	480 mg OD PO on Mondays, Wednesdays and Fridays each week, during treatment and for 3 months after completion. (Consider reducing the dose to 480 mg twice weekly during neutropenic periods)
Dexamethasone	8 mg IV prior to chemotherapy, then Dexamethasone 4 mg BD PO starting lunchtime on day of chemo for 4 doses for prevention of toxicity from dacarbazine and bleomycin (include in TTO), starting on days 1 and 15.
Nystatin	1mL QDS PO, rinse around mouth then swallow. Continue during treatment.

EMETIC RISK

Days 1-2, 15-16: High.

EXTRAVASATION RISK

Bleomycin: neutral
Dacarbazine: vesicant
Doxorubicin: vesicant
Vinblastine: vesicant

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

For full exhaustive detailed descriptions, visit https://www.medicines.org.uk/emc/

- Reactions to bleomycin are common and may present with shortness of breath, cough or 'flu like' symptoms. The presentation may mimic the underlying lymphoma. If bleomycin lung is suspected, high resolution CT scanning of the chest, PFTs, measurement of arterial O2 saturation should be performed and the bleomycin discontinued. Alteration in liver function tests and a transient rise in the LDH may occur. Consider use of antibiotics and systemic steroids (see bleomycin supportive care policy).
- Anaphylaxis can occur very rarely following administration of Dacarbazine.
- Photosensitivity reactions may occur rarely.
- Cardiotoxicity - monitor cardiac function. Doxorubicin may be stopped in future cycles if signs of cardiotoxicity, e.g. cardiac arrhythmias, pericardial effusion, tachycardia with fatigue.

- Steroids side effects- Monitor BMs.
- ABVD is considered low risk for infertility.

TREATMENT RELATED MORTALITY

< 1% for young, fit patients; this rises in the over 60s and in smokers due to the risk of bleomycin long toxicity.

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Review

Name	Revision	Date	Version	Review date
NSSG Lymphoma Group	Annual protocol review	May 2017	3.8	
NSSG Lymphoma Group	Annual protocol review	May 2019	3.9	May 2021
Sara Castro (Advanced Haematology Pharmacist)	Annual Protocol Review	May 2021	4.1	May 2023

Nursing Care Plan ABVD

Frequency: Up to 6 cycles of 28 days. ABVD given days 1 and 15. Restaging PET CT scan post C2D15 (Bleomycin is omitted post C2 if there is adequate disease response)

Alopecia: Yes, may cause thinning or loss of hair.

Emetic Risk: High.

Send a group and save sample to blood transfusion and inform patient and laboratory that they will require irradiated blood products for all future transfusions. Give patient an irradiated blood product booklet and card

A = DOXORUBICIN (Adriamycin): Anthracycline antibiotic

Administrated as IV bolus on day 1 and 15

Classification of extravasation: vesicant

Emetic risk: moderate

Side effects: vein pain, red flush 'flare' reaction with higher doses/ sensitive veins, nausea/vomiting, red urine, mucositis, alopecia, Palmar Plantar Erythrodysaesthesia (PPE), bone morrow depression, fatigue, nail and skin pigmentation, life threatening cardiac toxicity/ cardiac symptoms.

V = VINBLASTINE: Vinca alkaloid

Administrated as 10 minute IV infusion on day 1 and 15.

Classification of extravasation: vesicant. Do not leave patient when drug running peripherally.

Emetic risk: minimal

Side effects: vein pain/cold sensation if given peripherally, nausea/vomiting, diarrhoea, abdo pain, mouth and skin vesiculation, constipation, peripheral neuropathy (tingling/loss of sensation in fingertips), alopecia, bone morrow depression, jaw pain

B = BLEOMYCIN: Cytotoxic antibiotic

Administrated as IV infusion over 1 hour on day 1 and 15. Use with caution in patient with impaired respiratory function, ask patient to report any changes including SOB, cough or chest pain for the duration of chemotherapy.

Classification of extravasation: neutral

Emetic risk: minimal

Side effects: fever, rigors, flu like symptoms, interstitial pneumonia, anorexia, nausea / vomiting, mucocitis, alopecia, nails deformation / discoloration, dizziness, diarrhoea, pulmonary fibrosis.

D = DACARBAZINE : Alkylating agent

Administrated as 1 to 2 hour IV infusion on day 1 and 15.

Classification of extravasation: vesicant

Emetic risk: high

Side effects: arm ache/ vein pain (can be severe and occur up to 3 days post administration) when given via cannula (run with fast flowing 0.9% saline, use heat pad and give over 2 hours if dacarbazine is given peripherally), nausea/vomiting, anorexia, diarrhoea, headache, facial flushing, bone morrow depression, alopecia.

Regime Specific Considerations :

- There are no dose reductions or delays due to neutropenia. Patients will often have a neutrophil count of less than 1.
- Anticipatory nausea and vomiting can be an issue. Consider use of lorazepam night before and day of chemotherapy and/or Aprepitant.
- Suggested order of administration: Doxorubicin, Vinblastine, Bleomycin, Dacarbazine.
- When given peripherally, Vinblastine must be administered via a gravity drip, never through a pump. The nurse must remain with the patient throughout the infusion in order to detect any signs of extravasation.
- Placement of central line/PICC is highly recommended due to vesicant nature of drugs and risk of arm pain which can be severe.