ABVD

INDICATION

Hodgkin lymphoma.

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)\textsuperscript{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 BsAg, 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.
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/m² IV bolus.

Day 1  **VINBLASTINE** 6 mg/m² IV infusion in 50 mL sodium chloride 0.9% over 10 minutes.

Day 1  **DACARBAZINE** 375 mg/m² IV infusion in 250-500 mL sodium chloride 0.9% over 1-2 hours.

Day 1  **BLEOMYCIN** 10,000 units/m² in 100 mL sodium chloride 0.9% IV infusion over >1 hour.

Day 15 **DOXORUBICIN** 25 mg/m² IV bolus.

Day 15 **VINBLASTINE** 6 mg/m² IV infusion in 50 mL sodium chloride 0.9% over 10 minutes.

Day 15 **DACARBAZINE** 375 mg/m² IV infusion in 250-500 mL sodium chloride 0.9% over 1-2 hours.

Day 15 **BLEOMYCIN** 10,000 units/m² in 100 mL sodium chloride 0.9% IV infusion over >1 hour.

**NB:**
- * Maximum of 6 courses (12 doses) of bleomycin may be given. 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 ABVD should not be delayed whilst waiting for the result.
- If interim PET-CT scan was Deauville 1 or 2 (or 3 in advanced stage disease) then a contrast-enhanced CT of the neck, chest, abdomen and pelvis should be performed at the end of treatment, a PET is not 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).
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:

<table>
<thead>
<tr>
<th>Renal impairment</th>
<th>Hepatic impairment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Discuss with consultant if renal impairment severe</td>
<td>Bilirubin micromol/L Dose</td>
</tr>
<tr>
<td></td>
<td>20-50 50%</td>
</tr>
<tr>
<td></td>
<td>51-85 25%</td>
</tr>
<tr>
<td></td>
<td>&gt;85 omit</td>
</tr>
<tr>
<td></td>
<td>If AST 2-3 x normal, give 75% dose</td>
</tr>
<tr>
<td></td>
<td>If AST &gt;3 x ULN, give 50% dose</td>
</tr>
</tbody>
</table>

Doxorubicin maximum cumulative dose (additive to other anthracyclines):
450-550 mg/m² (in normal cardiac function)
400 mg/m² (in patients with cardiac dysfunction or exposed to mediastinal irradiation).
Consider dose reduction in the event of cardiac impairment.

Bleomycin:

<table>
<thead>
<tr>
<th>Renal impairment</th>
<th>Hepatic impairment</th>
</tr>
</thead>
<tbody>
<tr>
<td>CrCl &gt;50 mL/min 100% dose</td>
<td>Clinical decision</td>
</tr>
<tr>
<td>CrCl 10-50 mL/min 75% dose</td>
<td></td>
</tr>
<tr>
<td>CrCl &lt;10 mL/min 50% dose</td>
<td></td>
</tr>
</tbody>
</table>

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)

Vinblastine:

<table>
<thead>
<tr>
<th>Renal impairment</th>
<th>Hepatic impairment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Bilirubin 26-51 micromol/L or ALT/AST 60-180 u/L -50% dose</td>
</tr>
<tr>
<td></td>
<td>Bilirubin &gt;51 micromol/L &amp; normal ALT/AST -50% dose</td>
</tr>
<tr>
<td></td>
<td>Bilirubin &gt;51 micromol/L &amp; ALT/AST &gt;180 u/L -omit</td>
</tr>
</tbody>
</table>

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

Dacarbazine:

<table>
<thead>
<tr>
<th>Renal impairment</th>
<th>Hepatic impairment</th>
</tr>
</thead>
<tbody>
<tr>
<td>CrCl &gt;60 mL/min give 100% dose</td>
<td>Activated and metabolised in the liver. Can be hepatotoxic. Discuss with consultant.</td>
</tr>
<tr>
<td>CrCl 46-60 mL/min give 80% dose</td>
<td></td>
</tr>
<tr>
<td>CrCl 30-45 mL/min give 75% dose</td>
<td></td>
</tr>
<tr>
<td>CrCl &lt;30 mL/min give 70% dose</td>
<td></td>
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</tbody>
</table>

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. However, no validated recommendations on dose reductions can be given currently (SPC).
INVESTIGATIONS
FBC, renal and liver profiles.

CONCURRENT MEDICATION

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dose/Instructions</th>
</tr>
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<tbody>
<tr>
<td>Allopurinol</td>
<td>300mg OD PO, to start 24 hours prior to chemotherapy and then continue for 7 days. (Cycle 1 only)</td>
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<tr>
<td>Aciclovir</td>
<td>200 mg TDS PO for the duration of chemotherapy and for 3 months after completion.</td>
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<tr>
<td>Co-trimoxazole</td>
<td>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)</td>
</tr>
<tr>
<td>Dexamethasone</td>
<td>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.</td>
</tr>
<tr>
<td>Nystatin</td>
<td>1mL QDS PO, rinse around mouth then swallow. Continue during treatment.</td>
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EMETIC RISK
Days 1-2, 15-16: High.

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS
For full exhaustive detailed descriptions, visit [https://www.medicines.org.uk/emc/](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.
- 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.
REFERENCES


