

Chemotherapy Protocol

LYMPHOMA

BLEOMYCIN-DACARBAZINE-DOXORUBICIN-VINBLASTINE

(ABVD)

Regimen

- Lymphoma – ABVD-Bleomycin-Dacarbazine-Doxorubicin-Vinblastine

Indication

- Hodgkin's Lymphoma

Toxicity

Drug	Adverse Effect
Bleomycin	Pulmonary toxicity, rigors, skin pigmentation, nail changes
Dacarbazine	Fatigue, facial flushing, rash, flu-like syndrome, photosensitivity
Doxorubicin	Cardiotoxicity, urinary discolouration (red)
Vinblastine	Peripheral neuropathy, constipation, jaw pain, ileus

The adverse effects listed are not exhaustive. Please refer to the relevant Summary of Product Characteristics for full details.

Patients diagnosed with Hodgkin's Lymphoma carry a lifelong risk of transfusion associated graft versus host disease (TA-GVHD). Where blood products are required these patients must receive only irradiated blood products for life. Local blood transfusion departments must be notified as soon as a diagnosis is made and the patient must be issued with an alert card to carry with them at all times.

Monitoring

Drugs

- FBC, LFTs and U&Es prior to day one and fifteen of treatment
- Ensure adequate cardiac function before starting therapy. Baseline LVEF should be measured in patients with a history of cardiac problems, cardiac risk factors or in the elderly. Discontinue doxorubicin if cardiac failure develops.
- Consider performing pulmonary function tests before starting therapy. These should be repeated if respiratory symptoms develop during treatment, particularly a drop in oxygen saturation on exercise. Bleomycin should be stopped until the results of such investigations are known.

Dose Modifications

The dose modifications listed are for haematological, liver and renal function and some limited drug specific toxicities only. Dose adjustments may be necessary for other toxicities as well.

In principle all dose reductions due to adverse drug reactions should not be re-escalated in subsequent cycles without consultant approval. It is also a general rule for chemotherapy that if a third dose reduction is necessary treatment should be stopped.

Please discuss all dose reductions / delays with the relevant consultant before prescribing, if appropriate. The approach may be different depending on the clinical circumstances.

Haematological

Deliver on time and at full dose regardless of haematological counts unless there is an overriding clinical reason not to do so. Any dose modifications or delays must be discussed and approved by the responsible consultant.

Growth factors are not often necessary with this regimen and may increase the risk of the pulmonary complications associated with bleomycin. The decision to use growth factors should be consultant led.

Consider blood transfusion if patient symptomatic of anaemia or has a haemoglobin of less than 8g/dL. **Irradiated blood products must be used in Hodgkin's Lymphoma patients.**

Hepatic Impairment

If abnormal liver function tests are lymphoma related proceed with treatment at full dose unless there is an overriding clinical reason not to do so.

Drug	Bilirubin μmol/L		AST/ALT units/L	Dose (% of original dose)
Bleomycin				Clinical decision. Increased risk of lung dysfunction
Dacarbazine				Activated and metabolised in the liver. Can be hepatotoxic. Consider dose reduction
Doxorubicin	less than *30	and	2-3xULN	75%
	*30-50	and/or	more than 3xULN	50%
	51-85		N/A	25%
	more than 85		N/A	Omit
Vinblastine	*30-51	or	60-180	50%
	more than 51	and	normal	50%
	more than 51	and	more than 180	Omit

* Limits reflect local practice and may vary from published sources

Renal Impairment

Drug	Creatinine Clearance (ml/min)	Dose (% of original dose)
Bleomycin	more than 50	100%
	10-50	75%
	less than 10	50%
Dacarbazine	45-60	80%
	30-44	75%
	less than 30	70%
Doxorubicin	less than 10	Consider dose reduction in severe renal failure
Vinblastine	N/A	No dose adjustment needed

Other

Dose reductions or interruptions in therapy are not necessary for those toxicities that are considered unlikely to be serious or life threatening. For example, alopecia, altered taste or nail changes.

Bleomycin

The risk of bleomycin induced pneumonitis is greater in those individuals who are older than forty years of age, have a history of smoking, those with underlying lung disease, previous mediastinal radiotherapy, poor renal function or who require growth factors. If pulmonary symptoms develop stop the bleomycin until they can be investigated fully and a diagnosis made.

Doxorubicin

Discontinue doxorubicin if cardiac failure develops.

Vinblastine

Reduce the vinblastine dose to 3mg/m^2 if a NCI-CTC grade 2 motor or a NCI-CTC grade 3 sensory neurological toxicity occurs. For higher toxicity grades or if toxicity increases despite dose reduction stop the vinblastine.

[Regimen](#)

28 day cycle

Localised disease give 3-4 cycles plus radiotherapy

Advanced disease give 6 cycles as standard but this may be increased to 8 cycles depending on response

6 cycles will be set in Aria

Drug	Dose	Days	Administration
Bleomycin*	10,000 international units/m ²	1 & 15	Intravenous bolus over 10 minutes
Dacarbazine	375mg/m ²	1 & 15	Intravenous infusion in 500ml sodium chloride 0.9% over 60 minutes
Doxorubicin	25mg/m ²	1 & 15	Intravenous bolus over 10 minutes
Vinblastine	6mg/m ²	1 & 15	Intravenous bolus in 50ml sodium chloride 0.9% over 10 minutes

*Administer bleomycin for the first six cycles only

[Dose Information](#)

- Bleomycin dose will be rounded to the nearest 1,000 international units (up if halfway)
- The maximum cumulative dose of bleomycin is 500,000 international units in people less than sixty years of age. Refer to SPC for further information in older patients.
- Dacarbazine will dose banded according to the CSCCN agreed bands
- Doxorubicin will dose banded according to the CSCCN agreed bands
- The maximum lifetime cumulative dose of doxorubicin is 450mg/m². However prior radiotherapy to mediastinal / pericardial area should receive a lifetime cumulative doxorubicin dose of no more than 400mg/m².
- Vinblastine dose will be rounded to the nearest 1mg (up if halfway)
- There is no maximum dose of vinblastine in this protocol

[Administration Information](#)

[Extravasation](#)

- Bleomycin - neutral
- Dacarbazine – vesicant

- Doxorubicin - vesicant
- Vinblastine - vesicant

Other

- Dacarbazine can cause considerable pain at the infusion site. This may be helped by adjusting the infusion time or infusion volume and protecting the infusion from light.

Additional Therapy

- Antiemetics

15-30 minutes prior to chemotherapy

- dexamethasone 8mg oral or equivalent intravenous dose
- ondansetron 8mg oral or intravenous

As take home medication

- domperidone 10mg three times a day when required oral
- ondansetron 8mg twice a day for three days oral
- Anti-infective prophylaxis as follows:
 - co-trimoxazole 960mg once a day on Monday, Wednesday and Friday only
- Allopurinol 300mg once a day oral for the first cycle only
- Mouthwashes according to local or national policy on the treatment of mucositis
- Gastric protection with a proton pump inhibitor or a H₂ antagonist may be considered in patients considered at high risk of GI ulceration or bleed.

Additional Information

- The National Patient Safety Agency report NPSA/2008/RRR04 must be followed in relation to intravenous administration of vinca alkaloids.

Coding (OPCS 4.6)

- Procurement – X70.2
- Delivery – X72.2 Day 1, X72.4 Day 15

References

1. Johnson PW, Radford JA, Cullen MH et al. Comparison of ABVD and alternating or hybrid multidrug regimens for the treatment of advanced Hodgkins lymphoma: results of the United Kingdom Lymphoma Group LY09 Trial (ISRCTN97144519). J Clin Oncol 2005; 23 (36): 9208-9218.
2. Evens A, Cilley J, Ortiz T 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. British Journal of Haematology. 2007;137: 545-552
3. Boleti E, Mead G. ABVD for Hodgkin's lymphoma: full-dose chemotherapy without dose reductions or growth factors. Annals of Oncology 2007; 18 (2): 376-380.

REGIMEN SUMMARY

ABVD – Bleomycin-Dacarbazine-Doxorubicin-Vinblastine

Cycle 1 Day 1

1. Warning –Check blood transfusion status
Administration Instructions
Patients with HODGKIN'S lymphoma carry a lifelong risk of transfusion associated graft versus host disease.
Where blood products are required these patients must receive ONLY IRRADIATED BLOOD PRODUCTS for life.
Ensure transfusion departments are notified and the patient has been issued with an alert card to carry with them at all times.
2. Dexamethasone 8mg oral or equivalent intravenous dose
3. Ondansetron 8mg oral or intravenous
4. Dacarbazine 375mg/m² intravenous infusion in 500ml sodium chloride 0.9% over 60 minutes
5. Doxorubicin 25mg/m² intravenous bolus over 10 minutes
6. Vinblastine 6mg/m² intravenous bolus in 50ml sodium chloride 0.9% over 10 minutes
7. Bleomycin 10,000 international units /m² intravenous bolus over 10 minutes

Take Home Medicines

8. Domperidone 10mg three times a day when required oral
Administration Instructions
Please supply sufficient for day 1 and 15 (30 tablets or nearest whole pack equivalent)
9. Ondansetron 8mg twice a day oral for 3 days to start on the evening of the day of chemotherapy administration (day 1 and 15)
Administration Instructions
Please supply sufficient for day 1 and 15 (12 tablets or nearest whole pack equivalent)
10. Allopurinol 300mg once a day oral for 28 days
11. Co-trimoxazole 960mg once a day on Monday, Wednesday and Friday oral for 28 days

Cycle 1 Day 15

1. Dexamethasone 8mg oral or equivalent intravenous dose
2. Ondansetron 8mg oral or intravenous
3. Dacarbazine 375mg/m² intravenous infusion in 500ml sodium chloride 0.9% over 60 minutes
4. Doxorubicin 25mg/m² intravenous bolus over 10 minutes
5. Vinblastine 6mg/m² intravenous bolus in 50ml sodium chloride 0.9% over 10 minutes
6. Bleomycin 10,000 international units /m² intravenous bolus over 10 minutes

Cycles 2, 3, 4, 5 and 6 - Day 1

1. Dexamethasone 8mg oral or equivalent intravenous dose
2. Ondansetron 8mg oral or intravenous
3. Dacarbazine 375mg/m² intravenous infusion in 500ml sodium chloride 0.9% over 60 minutes
4. Doxorubicin 25mg/m² intravenous bolus over 10 minutes
5. Vinblastine 6mg/m² intravenous bolus in 50ml sodium chloride 0.9% over 10 minutes
6. Bleomycin 10,000 international units /m² intravenous bolus over 10 minutes

Take Home Medicines

7. Domperidone 10mg three times a day when required oral
Administration Instructions
Please supply sufficient for day 1 and 15 (30 tablets or nearest whole pack equivalent)
8. Ondansetron 8mg twice a day oral for 3 days to start on the evening of the day of chemotherapy administration (day 1 and 15)
Administration Instructions
Please supply sufficient for day 1 and 15 (12 tablets or nearest whole pack equivalent)
9. Co-trimoxazole 960mg once a day on Monday, Wednesday and Friday oral for 28 days

Cycles 2, 3, 4, 5 and 6 - Day 15

1. Dexamethasone 8mg oral or equivalent intravenous dose
2. Ondansetron 8mg oral or intravenous
3. Dacarbazine 375mg/m² intravenous infusion in 500ml sodium chloride 0.9% over 60 minutes
4. Doxorubicin 25mg/m² intravenous bolus over 10 minutes
5. Vinblastine 6mg/m² intravenous bolus in 50ml sodium chloride 0.9% over 10 minutes
6. Bleomycin 10,000 international units /m² intravenous bolus over 10 minutes

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1.2	Jan 2015	Header changed Hepatic impairment updated Domperidone dose changed to 10mg Bolus removed from intravenous bolus throughout text "infusion" removed from bleomycin entry in regimen table Irradiated blood product statement updated in dose modification section. Mucositis recommendation changed "Warning – Check blood transfusion status" added to cycle 1. Domperidone TTO administration instructions updated Ondansetron administration clarified. Disclaimer added	Donna Kimber Pharmacy Technician	Rebecca Wills Pharmacist
1.1	Sept 2013	Toxicity advice removed. In the regimen summary the domperidone and ondansetron removed from day 15 and the administration instructions changed on day 1.	Dr Debbie Wright Pharmacist	Donna Kimber Pharmacy Technician
1	April 2012	None	Rebecca Wills Pharmacist Dr Debbie Wright Pharmacist	Dr Andrew Davies Consultant Medical Oncologist Dr Alison Milne Consultant Haematologist

This chemotherapy protocol has been developed as part of the chemotherapy electronic prescribing project. This was and remains a collaborative project that originated from the former CSCCN. These documents have been approved on behalf of the following Trusts;

Hampshire Hospitals NHS Foundation Trust
NHS Isle of Wight
Portsmouth Hospitals NHS Trust
Salisbury Hospitals NHS Foundation Trust
University Hospital Southampton NHS Foundation Trust
Western Sussex Hospitals NHS Foundation Trust

All actions have been taken to ensure these protocols are correct. However, no responsibility can be taken for errors which occur as a result of following these guidelines.