ABVD

Any histologically proven Hodgkin's lymphoma
May be used in combination with rituximab for advanced CD20+ nodular lymphocyte predominant Hodgkin's lymphoma

Drugs / Dosage:	**Doxorubicin**	25mg/m^2	IV	Day 1 and 15
	Vinblastine*	6mg/m^2	IV	Day 1 and 15
		(*no cap in this regimen)		
	Dacarbazine	375mg/m^2	IV	Day 1 and 15
	Bleomycin	10,000iu/m^2	IV	Day 1 and 15 for 2 cycles, then see Frequency section
	plus, for advanced NLPHL only:			
	Rituximab	375mg/m^2	IV	Day 1 (i.e. every 4 weeks)

Other drugs: Allopurinol 300mg po daily - review at 4 weeks

Administration: Doxorubicin injection via fast running infusion of 0.9% sodium chloride
Vinblastine diluted in 50ml 0.9% sodium chloride and infused over 5-10 minutes
Dacarbazine diluted in 500ml sodium chloride 0.9% and infused over 1 hour
Dacarbazine bags and giving sets must be protected from exposure to UV light. Pain on administration may be minimised by slow infusion.
Bleomycin in 100 ml 0.9% sodium chloride over 15 - 30 minutes
For details on rituximab administration, infused according to standard instructions for the 375mg/m^2 dose (e.g. see R-CHOP)

Frequency: 4 weekly cycle, with chemotherapy on Days 1 and 15
Localised disease: 2 – 4 cycles with IF radiotherapy
Advanced disease: 2 cycles, then PET scan and review;
PET-ve patients: continue with 4 further cycles, but consider omitting the bleomycin[4]
PET+ve patients: urgent MDT review to consider escalation to more intensive regimen

Main Toxicities: myelosuppression; alopecia; mucositis; pulmonary toxicity; cardiomyopathy (see Comments); peripheral neuropathy; constipation; skin reactions to bleomycin; rigors during bleomycin infusion (ensure steroid given before bleomycin); vein pain during dacarbazine infusion (see Administration); ovarian failure; infertility

Anti-emetics: highly emetogenic

Extravasation: doxorubicin, vinblastine and dacarbazine are all vesicants

Regular Investigations:	FBC	Day 1 of every cycle, plus Day 15 of Cycle 1
	LFTs & U&Es	Day 1 of every cycle
	LDH	Day 1 of every cycle
	MUGA/echo	see Comments
	Lung function tests	according to local practice (see Comments)

Reason for Update: option to omit bleomycin after 2 cycles; routine CXRs removed	Approved by Chair of Alliance TSSG: Dr A Laurie
Version: 7	Date: 18.1.16
Supersedes: Version 6	Review Date: Feb 2018
Prepared by: S Taylor	Checked by: C Tucker

Comments: Maximum cumulative dose of doxorubicin = 450 - 550mg/m^2
A baseline MUGA scan/echocardiogram should be performed where the patient is considered at risk of having impaired cardiac function e.g. significant cardiac history, hypertension, obese, smoker, ≥ 70 years old, previous exposure to anthracyclines, previous thoracic radiotherapy. MUGA scan/echo should be repeated if there is suspicion of cardiac toxicity at any point during treatment.

Bleomycin pulmonary toxicity is age-dependent, with an increase in frequency and associated mortality as patient age rises above 40 years. Dose modifications for bleomycin should be made according to table below. Bleomycin should be used with caution if approaching max cumulative dose.
Lung function may be monitored throughout treatment, according to local practice.
If patient reports new respiratory symptoms, inform consultant for advice on required investigations prior to any further administration of bleomycin.
There should be a low threshold for omitting further bleomycin if clinical concerns develop.

Age (years)	Maximum Bleomycin dose/week (IU)	Max Cumulative Dose (IU)
< 60	30,000 – 60,000	500,000
60 – 69	30,000 – 60,000	200,000 – 300,000
70 – 79	30,000	150,000 – 200,000
80 and over	15,000	100,000

Dose Modifications

Haematological Toxicity: Chemotherapy may be given without delay or dose reduction, and without G-CSF support, in the presence of uncomplicated neutropenia with agreement of the responsible Consultant[1,2].

If platelets < 50 x 10^9/l, delay chemotherapy until recovered.

Secondary prophylaxis with G-CSF may be used according to the Alliance G-CSF guidelines, although there is a controversial link between G-CSF use and an increased risk of bleomycin-induced pulmonary toxicity - when reaching any decision, clinicians should take into account both case reports that have raised this concern and controlled studies which have not been able to demonstrate such an effect[3].

Renal Impairment: Cockcroft and Gault may be used to predict CrCl. If borderline, an EDTA may be requested.

CrCl (ml/min)	Dacarbazine Dose
45 - 60	Give 80%
30 - 45	Give 75%
< 30	Give 70%

CrCl (ml/min)	Bleomycin Dose
> 50	Give 100%
10 – 50	Give 75%
< 10	Give 50%

Hepatic Impairment:

Bilirubin (µmol/l)	Doxorubicin Dose
20 – 50	Give 50%
51 – 85	Give 25%
> 85	Omit

ALT/AST		Bilirubin (µmol/l)	Vinblastine Dose
60 – 180	**or**	26 –51	Give 50% dose
Normal	**and**	> 51	Give 50% dose
> 180	**and**	> 51	Discontinue

Consider a dose reduction of dacarbazine, but note that dacarbazine can rarely be hepatotoxic. If in doubt, contact the Consultant.

Neuropathy: If Grade 2 neuropathy develops, reduce dose of vinblastine to 3mg/m^2.

Lung Toxicity: Bleomycin must be discontinued permanently if any symptoms of lung toxicity.

Skin Toxicity: Severe skin lesions eg desquamation, may require discontinuation of bleomycin.

Patient Information: Macmillan leaflet for ABVD

References:

Follows, G et al; Br J Haem 2014; 166: 34 - 39
[1]Evens, AM et al; Br J Haematol 2007; 137 (6): 545 - 552
[2]Boleti, E & Mead, GM; Annals of Oncol 2007; 18 (2); 376 – 380
[3]Stockley's Drug Interactions 2008; Bleomycin + Colony-stimulating factors
Advani, R et al; Blood 2013; 122 (26): 4182 – 4188 (NLPHL)
[4]Johnson, P et al; abstract presented at ICML, 2015 (not yet published)