ESCALATED BEACOPP

INDICATION: Advanced Hodgkin's lymphoma

Prior to a course of treatment

- Assess cardiac function by history & exam, ECG and CXR. If there is evidence of cardiac disease or risk factors, prior anthracyclines or patient > 70yrs perform a MUGA scan. *Inform consultant*.
- Check recent U&Es, creat, LFTs – *see dose modification and discus with consultant if abnormal*
- Check FBC. Patient should have adequate bone marrow reserve, i.e Neutrophils >1.5, platelets >80 unless cytopaenia is due to disease, e.g marrow infiltration, splenomegaly
- Consider PICC or Hickman line if venous access is poor.
- If appropriate discuss possibility of pregnancy with female patients and need for contraception with both male and female patients. Discuss risk of infertility - offer semen cryopreservation to male patients
- Written consent for course

Prior to each cycle

- Medical review of fitness for chemotherapy – exclude active infection, major changes in organ function
- Check FBC, U&Es, creat, LFTs – neutrophils must be > 1.5, platelets > 80 - *see dose modifications & algorithm below*

Cyclophosphamide	1250mg/m^2	IV *(see protocol for fluids & mesna)*	day 1
Doxorubicin	35mg/m^2	IV bolus	day 1
Etoposide	200mg/m^2	IV in 1.0L N saline over 1 hr	days 1-3
Procarbazine [#]	100mg/m^2 od	PO	days 1-7
Prednisolone	40mg/m^2	PO	days 1-14
Vincristine	1.4mg/m^2 *	IV in 50ml N saline over 5 minutes	day 8
Bleomycin	10000U/m^2	IV bolus	day 8
GCSF	5mcg/kg	SC od	from day 9 of each cycle

* maximum dose of vincristine is 2mg [#] 50mg capsules

GCSF PROPHYLAXIS IS MANDATORY WITH ESCALATED BEACOPP. Start on day 9 and continue until WBC has passed through the nadir and has been > 1.0 for 3 days. The nadir is expected at day 11-12. When neuts are < 1.0 FBC must be checked at least every second day.

Repeat cycle every 21 days for up to 6 cycles

NB: Patient must be advised to avoid alcohol while taking procarbazine

Prophylaxis for acute emesis	5HT antagonist
Prophylaxis for delayed emesis	5HT antagonist and metoclopramide
Other medications	Allopurinol 300mg od days 1-14 of cycle 1
	Fluconazole 50mg od days 1-14 of each cycle
	Nystatin 1ml qds & Corsodyl 10ml qds mouthwash
	Cotrimoxazole 480mg od throughout treatment plus 2 weeks

Administration of mesna & IV fluids is mandatory with BEACOPP when cyclophosphamide is >1.0g/m^2

Day 1	T - 1 hour	N Saline 0.5L over 1 hr
	T – 15mins	Mesna 1.0g/m^2 IV in 100ml N saline over 15mins
	T = 0	Ondansetron 8mg IV + dexamethasone 8mg IV
		CYCLOPHOSPHAMIDE 1250mg/m^2 in 1.0L N saline over 1hr
	T + 1 hours	N saline 1.0L over 3hrs
	T + 4 hours	Mesna 1.0g/m^2 IV in 100ml N saline over 15mins

- Check urinalysis for haematuria with each urine
- If not vomiting allow home with ondansetron 8mg bd for 3 days
- Instruct patient to drink at least 3L/day fluid over next 48hrs
- Instruct patient to return to ward if vomiting, frank haematuria, dysuria or fever
- If frank haematuria give additional mesna 1g, IV fluids and inform consultant

Dose modification for hepatotoxicity (unless due to lymphoma)

• Bilirubin <1.5 x upper limit of normal	100% dose doxorubicin
• Bilirubin 1.5 - 3 x upper limit of normal	75% dose doxorubicin
• Bilirubin > 3 x upper limit of normal	Reconsider whether further escalated BEACOPP is appropriate – *discuss with consultant*

Dose modification for renal dysfunction (unless due to lymphoma)

- Escalated BEACOPP may not be appropriate if serum creatinine > 150μmol/l or creatinine clearance < 40ml/min – *discuss with consultant*

Dose modifications for vincristine neurotoxicity

• Grade 2 motor (*mild objective weakness interfering with function but not with activities of daily living*) or grade 3 sensory (*sensory loss or paraesthesia interfering with activities of daily living*) toxicity	Reduce vincristine dose to 1mg
• Neurological toxicity increases despite dose reduction.	Stop vincristine. Consider vinblastine 4mg/m^2 – *discuss with consultant*

Modification for haemorrhagic cystitis

• If there is gross haematuria passing clots, requiring instrumentation or transfusion	Stop cyclophosphamide – further escalated BEACOPP inappropriate – *inform consultant*
• Significant microscopic or frank haematuria	Give additional mesna 1g IV

For bleomycin pulmonary toxicity

- If patient develops persistent unexplained dyspnoea or non-productive cough – stop bleomycin, perform chest X-ray and *discuss with consultant*. If there is clinical or radiological evidence of pulmonary fibrosis or transfer factor reduced <50% bleomycin should be permanently stopped.

For cardiotoxicity

- If symptoms or signs of cardiac failure develop, the LVEF should be measured by MUGA scan. Discontinue BEACOPP if LVEF <50%. *Inform consultant*.

For procarbazine intolerance or unavailability

- Replace with chlorambucil 6mg/m^2 (max.10mg) od PO for 7 days

Dose modification for haematological toxicity (unless due to disease)

- Depending on neutrophil and platelet count prior to each cycle dose reductions to steps 1, 2 or baseline BEACOPP may be indicated. Follow algorithm below – dose reduction steps are:

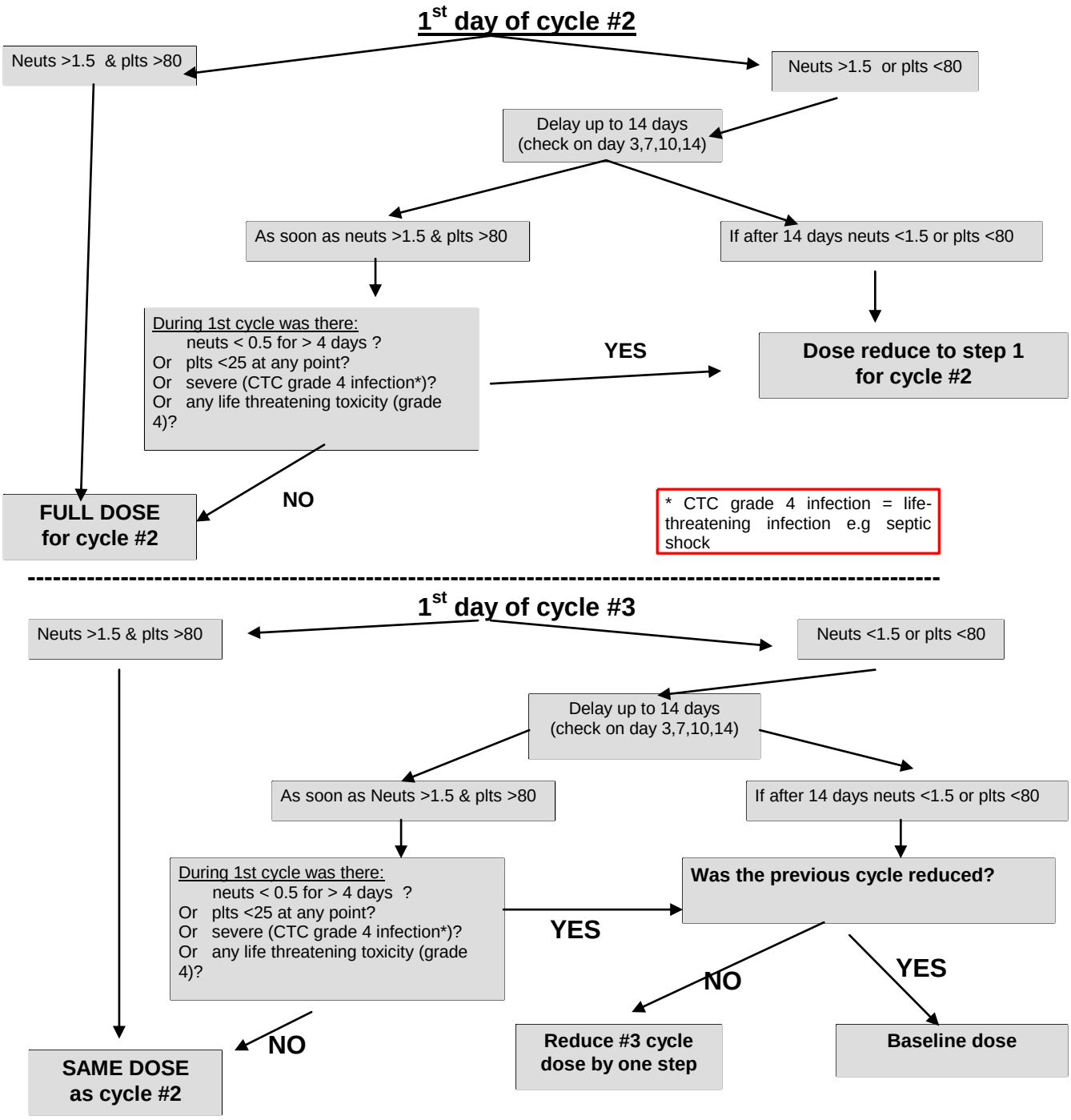
	Full dose	Step 1	Step 2	Baseline	
Cyclophosphamide	1250mg/m^2	1100mg/m^2	950mg/m^2	650mg/m^2	Day 1
Doxorubicin	35mg/m^2	35mg/m^2	35mg/m^2	25mg/m^2	Day 1
Etoposide	200mg/m^2	175mg/m^2	150mg/m^2	100mg/m^2	Days 1-3
Procarbazine	100mg/m^2	100mg/m^2	100mg/m^2	100mg/m^2	Days 1-7
Prednisolone	40mg/m^2	40mg/m^2	40mg/m^2	40mg/m^2	Days 1-14
Vincristine	1.4mg/m^2 *	1.4mg/m^2 *	1.4mg/m^2 *	1.4mg/m^2 *	Day 8
Bleomycin	10000U/m^2	10000U/m^2	10000U/m^2	10000U/m^2	day 8
GCSF	5mcg/kg	5mcg/kg	5mcg/kg	5mcg/kg	from day 9 of each cycle

* max. 2mg

BEACOPP Toxicities

Neutropenic sepsis & thrombocytopenia	Nausea (moderate) – but severe with alcohol & procarbazine
Mucositis	Amenorrhoea & infertility (offer semen cryopreservation)
Alopecia	Interstitial pneumonitis & (late) pulmonary fibrosis
Cardiac arrythmias & cardiomyopathy	Anaphylaxis (rarely) & febrile reactions with bleomycin (maybe several hours later)
Peripheral neuropathy	Mucocutaneous reactions & hyperpigmentation (bleomycin)
Second malignancies (late)	Photosensitivity (procarbazine)
Hyperglycaemia	Autonomic neuropathy – commonly constipation, ileus
Hypotension, chest pain, dyspnoea, flushing and bronchospasm (etoposide)	Haemorhagic cystitis

Escalated BEACOPP modifications for haematological toxicity



….etc for further cycles, i.e…….

- if a dose reduction is indicated during the present cycle & it was reduced in the previous cycle, reduce to baseline BEACOPP immediately
- if the dose was reduced by one step in an earlier cycle (but not the previous cycle) and a further dose reduction is indicated in the present cycle, reduce dose by one more step
- **once dose reduced never dose increase again**

Written by	Dr MP Macheta, Consultant Haematologist
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