Systemic Anti Cancer Treatment Handbook

DOXORUBICIN
Gynaecological Cancer

PROCTOCOL REF: MPHAGYNDOX
(Version No: 1.1)

Approved for use in:

- Treatment of advanced endometrial sarcoma

Dosage

Drug	Daily dosage	Route	Frequency
Doxorubicin	75mg/m²	IV bolus	21 day cycle max. 6 cycles

Supportive treatments:

Dexamethasone tablets, 4mg twice daily for 3 days

Domperidone 10mg tablets, to be taken three times a day when required

Interactions

Oral anticoagulants - in the event of simultaneous use of oral anticoagulants, it is advisable regularly to check the INR

Antiepileptics - barbiturates may lead to an accelerated plasma clearance of doxorubicin whilst plasma levels of phenytoin, carbamazepine and valproate may be reduced with concomitant administration with doxorubicin.

Enzyme Inducers (e.g. rifampicin, barbiturates) - plasma concentrations of doxorubicin might be decreased and reduce efficacy.

Calcium channel blockers - verapamil can increase doxorobucin levels

Ciclosporin - ciclosporin can increase the AUC of doxorubicin by 55%. The combination might require dose adjustment.

Cimetidine - the plasma clearance of doxorubicin can be reduced by cimetidine resulting in increased the AUC of doxorubicin.

Extravasation risk

Doxorubicin: VESICANT

Administration

Day	Drug	Dose	Route	Diluent and rate
1	Ondansetron	16mg	Oral	30 minutes before chemotherapy
1	Dexamethasone	8mg	Oral	30 minutes before chemotherapy
1	**Doxorubicin**	**75mg/m^2**	**IV Infusion**	IV bolus over 10 to 15 minutes Concurrent administration, doxorubicin at 400mL/hr and sodium chloride 0.9% at 100mL/hr

Main Toxicities

Cardiac Disorders	Cardiomyopathy (see below)
Gastrointestinal and Nutritional Disorders	Nausea, vomiting, diarrhoea, mucositis. Anorexia and dehydration
General disorders and administration site conditions	Shivering, fever, dizziness. Malaise/weakness, asthenia, chills
Haematological	Neutropenia, anaemia, thrombocytopenia
Hepatobiliary	Alterations in liver function tests (see below). Doxorubicin is contraindicated in patients with severe liver function disorder
Skin and subcutaneous tissue disorders	Alopecia, phlebitis Urticaria, exanthema, local erythematous reactions along the vein which was used for the injection, hyperpigmentation of skin and nails, onycholysis
Urinary disorders	Red coloration of urine. Patients should be cautioned that this does not pose any health hazards.

Investigations

	Pre	Cycle 1	Cycle 2	Cycle 3	Cycle 4	Cycle 5	Cycle 6	Ongoing
Medical Assessment	X				X			After cycles 3 and 6 then as per management plan
SACT Assessment	X	X	X	X	X	X	X	Every cycle
FBC	X	X	X	X	X	X	X	Every cycle
U&E & LFT	X	X	X	X	X	X	X	Every cycle
CrCl	X	X	X	X	X	X	X	Every cycle
CA125*	X	X	X	X	X	X	X	Every cycle *Ovarian patients only
CT scan	X				X			After cycles 3 and 6
Echo/MUGA/ECG								If clinically indicated based on cardiac fitness
Informed Consent	X							
PS recorded	X	X	X	X	X	X	X	Every cycle
Toxicities documented	X	X	X	X	X	X	X	Every cycle
Weight recorded	X	X	X	X	X	X	X	Every cycle

Dose Modifications and Toxicity Management

Haematological toxicity

Proceed on day 1 if:-

Platelets ≥ 100 x 10^9/L	ANC ≥ 1.0 x 10^9/L

Delay 1 week on day 1 if:-

Platelets ≤ 99 x 10^9/L	ANC ≤ 0.9 x 10^9/L

Non-haematological toxicities

Grading and Management of Toxicity

Toxicity should be grading according to the CTCAE v4.0 criteria. Following assessment treatment should be withheld for any toxicity until resolved to grade 0/1. For dose modification, follow the general guidance below and discuss with treating clinician.

	Grade 2	Grade 3	Grade 4
1st appearance	Interrupt treatment until resolved to grade 0/1, then continue at 100% of original dose with prophylaxis where possible	Interrupt treatment until resolved to grade 0/1, then continue at 75-80% of original dose with prophylaxis where possible	Discontinue treatment
2nd appearance	Interrupt treatment until resolved to grade 0/1, then continue at 75-80% of original dose	Interrupt treatment until resolved to grade0/1, then continue at 50% of original dose	
3rd appearance	Interrupt treatment until resolved to grade 0/1, then continue at 50% of original dose	Discontinue treatment	
4th appearance	Discontinue treatment		

Myocardial Toxicity

Cumulative total lifetime dose of Doxorubicin should not exceed 450-550mg/m^2 to avoid cardiomyopathy. Myocardial toxicity may occur at lower cumulative doses in patients with prior mediastinal irradiation or on concurrent cyclophosphamide therapy or with

pre-existing heart disease. Monitor cardiac function as necessary depending on patient's cardiac fitness.

Hepatic Impairment

Bilirubin (µmol/L)	Dose
20-51	50%
51-85	25%
>85	omit

If AST 2-3 x ULN, give 75% dose
If AST >3 x ULN, give 50% dose

Doxorubicin is contraindicated in patients with severe liver function disorder

Renal Impairment

No dose reductions required.

Clinical decision in severe impairment.

References

1. https://www.medicines.org.uk/emc

2. Dosage Adjustment for Cytotoxics in Hepatic Impairment. January 2009 UCLH - Dosage Adjustment for Cytotoxics in Hepatic Impairment (Version 3 - updated January 2009)

3. Dosage Adjustment for Cytotoxics in Renal Impairment. January 2009 UCLH - Dosage Adjustment for Cytotoxics in Renal Impairment (Version 3 - updated January 2009)

4. Stockley's drug interactions. Ninth edition. Edited K. Baxter. Pharmaceutical press. London. 2010