Systemic Anti Cancer Treatment Protocol

Liposomal Doxorubicin (CAELYX) Gynaecological Cancer

PROCTOCOL REF: MPHAGYNCAE
(Version No: 1.1)

Approved for use in:

- Advanced ovarian cancer second/third line treatment option.
- Advanced endometrial carcinoma

Dosage

Drug	Dosage	Route	Frequency
Liposomal doxorubicin (caelyx)	40 mg/m^2	IV infusion	28 day cycle max 6 cycles

Supportive Treatments:

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

Interactions

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

Contraindications

Caelyx is contraindicated in patients with peanut or soya allergies.

Extravasation risk

Liposomal doxorubicin - vesicant.

Administration

Day	Drug	Dose	Route	Diluent and rate
1	Dexamethasone	8mg	Oral	30 minutes chemotherapy
	Liposomal Doxorubicin (Caelyx)	**40mg/m^2**	**IV Infusion**	***250 to 500mL glucose 5%. Initial infusion over 90 min. Subsequent infusions over 60 minutes**

* For doses < 90 mg: Caelyx is diluted in 250 ml 5% glucose solution for infusion.
For doses ≥ 90 mg: Caelyx is diluted in 500 ml 5% glucose solution for infusion.
Caelyx is incompatible with 0.9% sodium chloride.
In patients who experience an infusion reaction, the method of infusion should be modified as follows:
5% of the total dose should be infused slowly over the first 15 minutes. If tolerated without reaction, the infusion rate may then be doubled for the next 15 minutes. If tolerated, the infusion may then be completed over the next hour for a total infusion time of 90 minutes.

Diabetic patients: please note that each vial of Caelyx contains sucrose and the dose is administered in 5% (50 mg/ml) glucose solution for infusion.

Main Toxicities

Cardiac Disorders	Cardiomyopathy, ventricular arrhythmias
Eye Disorders	Lacrimation, blurred vision
Gastrointestinal and Nutritional Disorders	Constipation, diarrhoea, nausea, vomiting, stomatitis
General disorders and administration site conditions	Asthenia, fatigue, mucositis, weakness, fever, Paresthesia, somnolence, headache, dizziness, neuropathy, hypertonia. Back pain, myalgia
Haematological	Neutropenia, anaemia, thrombocytopenia
Hypersensitivity reactions	Flushing, urticarial rash, chest pain, fever, hypertension, tachycardia, pruritus, sweating, shortness of breath, facial oedema, chills, back pain, tightness in the chest and throat and/or hypotension
Skin and subcutaneous tissue disorders	Palmar-plantar erythrodysesthesia (Hand-foot syndrome), alopecia, rash. Dry skin, skin discolouration, pigmentation abnormal, erythema

	To minimise PPE for the first 4 to 7 days after caelyx infusion, keep hands and feet as cool as possible, avoid hot water, pat skin dry after washing, do not wear tight fitting gloves or socks.

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 *for 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:

Haematolgical Toxictiy

Proceed on day 1 if-

Plt ≥ 100 x 10^9/L	ANC ≥ 1.0 x 10^9/L

Delay 1 week on day 1 if-

Plt ≤ 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		

Hepatic Impairment

Bilirubin (µmol/L)	Dose
20-51	75%
>51	50%

Renal Impairment

No dose reductions required. Clinical decision in severe impairment.

Guidelines for liposomal doxorubicin dose modification

To manage adverse events such as palmar-plantar erythrodysesthesia (PPE), stomatitis or haematological toxicity, the dose may be reduced or delayed. Guidelines for dose modification of liposomal doxorubicin secondary to these adverse effects are provided in the tables below. The toxicity grading in these tables is based on the National Cancer Institute Common Toxicity Criteria (NCI-CTC).

Toxicity grade at current assessment	Week 4	Week 5	Week 6
Grade 1	**Redose unless** patient has experienced a previous grade 3 or 4 toxicity, in which case wait an additional week	**Redose unless** patient has experienced a previous grade 3 or 4 toxicity, in which case wait an additional week	**Decrease dose by 25%; return to 4 week interval** or withdraw patient per physician's assessment
Grade 2	**Wait an additional week**	**Wait an additional week**	**Decrease dose by 25%; return to 4 week interval** or withdraw patient per physician's assessment
Grade 3	**Wait an additional week**	**Wait an additional week**	**Withdraw patient**
Grade 4	**Wait an additional week**	**Wait an additional week**	**Withdraw patient**

References

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

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

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Phase II study of liposomal doxorubicin in platinum and paclitaxel refractory epithelial ovarian cancer
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