CAELYX (LIPOSOMAL DOXORUBICIN) & CARBOPLATIN

A treatment option for women with advanced ovarian cancer and whose disease relapses between 6 and 12 months from completion of platinum-based therapy

Drugs/Dosage:	Liposomal doxorubicin (Caelyx)	30mg/m^2	IV	Day 1
	followed by			
	Carboplatin	AUC 5	IV	Day 1

Carboplatin dose should be calculated using the Calvert Formula:
Dose = Target AUC x (25 + GFR)
Cycle 1 may be given using the Cockcroft and Gault formula to predict creatinine clearance if the EDTA is not yet available. When using C&G, a "cap" of 125 ml/min should be used for carboplatin dose calculations.

Carboplatin dose should be re-calculated using the EDTA result for subsequent cycles (do not "cap"). EDTA should only be repeated if there is a 30% change in serum creatinine.

Administration:
Prime the giving set with 5% glucose
Liposomal doxorubicin diluted in 5% glucose over 1 hour
Flush the line with 5% glucose
Carboplatin in 250ml 5% glucose over 30 – 60 minutes

For infusion-associated reactions to caelyx:
Stop the infusion – usually symptoms resolve without further intervention. However, emergency supportive treatment should be available. In most patients, treatment can be resumed at a slower rate after all symptoms have been resolved, without recurrence. Infusion reactions rarely recur after the first treatment cycle.

For patients who experience a hypersensitivity reaction to carboplatin, see the Alliance Carboplatin Hypersensitivity Guidelines.

Frequency: 4 weekly cycle for maximum of 9 cycles

Main Toxicities: myelosuppression; palmar/plantar erythema (PPE) (see Comments); stomatitis; infusion associated reactions (see Comments); cardiotoxicity (see Comments); alopecia (uncommon)

Anti-emetics: highly emetogenic (but omit ondansetron in patients at risk of obstruction)

Extravasation: non-vesicants

Regular Investigations:	FBC	Day 1
	U&Es	Day 1
	LFTs	Day 1
	CA 125	Day 1
	EDTA	Prior to 1st cycle
	MUGA	prior to starting, and during treatment (see Comments)

Comments:
Maximum cumulative dose of doxorubicin = 450 – 550mg/m^2
Consider previous anthracycline exposure.

Reason for Update: C&G capping added	Approved by Consultant: Dr A Michael
Version: 4	Approved by Lead Chemotherapy Nurse: P Deery
Supersedes: Version 3	Date: 15.6.16
Prepared by: S Taylor	Checked by: C Tucker

A baseline MUGA scan should be performed where the patient is considered at risk of having impaired cardiac function e.g. significant cardiac history, hypertension, obese, smoker, elderly, previous exposure to anthracyclines, previous thoracic radiotherapy. MUGA scan should be repeated if there is suspicion of cardiac toxicity at any point during treatment, or if cumulative anthracycline dose approaches maximum.

To minimise risk of PPE for the first 4 – 7 days after Caelyx infusion:
Keep hands & feet as cool as possible.
Do not wear tight fitting gloves or socks, and avoid wearing tight-fitting footwear and high heeled shoes.
Avoid exposing the skin to very hot water, such as the bath or washing up.
Do not rub the skin vigorously or use abrasive washcloths. Pat skin dry after washing
Avoid the use of topical anaesthetics as they can worsen skin reactions.

Dose Modifications

Haematological Toxicity:	Neutrophils < 1.5 x 10^9/l or Platelets < 100 x 10^9/l	Delay 1 week. Repeat FBC – if within normal parameters, proceed with dose reductions of carboplatin to AUC4 and caelyx to 25mg/m^2

Dose reduction to carboplatin AUC 4 and caelyx to 25mg/m^2 is also required in the following circumstances:

- neutrophils < 0.5 x 10^9/l for ≥ 7 days
- neutrophils < 0.1 x 10^9/l for 3 days
- an episode of febrile neutropenia (temp ≥38.5°C and neutrophils < 1.0 x 10^9/l)
- infection requiring intravenous antibiotics or hospitalisation
- platelets < 25 x 10^9/l, or bleeding that required a platelet transfusion

Renal Impairment: If EDTA or calculated CrCl < 20ml/min, carboplatin is contra-indicated.

Hepatic Impairment:

Bilirubin (µmol/l)	Caelyx Dose
< 20	Give 100%
20 – 51	Give 75%*
> 51	Give 50%*

*If the first dose is tolerated without an increase in bilirubin or LFTs, the second dose can be increased to the next dose level (from 50% to 75%; from 75% to 100%) and then titrated to full dose on subsequent cycles if again tolerated.

Cutaneous Toxicity (PPE & Stomatitis): Treat symptoms accordingly; pyridoxine can be used for Grade 1 or above PPE.
Wait until toxicity resolved, then follow dosing guidelines below for future cycles:

Toxicity Grade after prior Caelyx dose	Toxicity resolved before Day 28	Toxicity resolved by Week 5 – Week 6 (Day 35 – 42)	Toxicity not resolved by Week 6 (Day 42)
Grade 1	Continue with same dose caelyx	Reduce caelyx dose to 25mg/m^2	No further treatment
Grade 2	Reduce caelyx dose to 25mg/m^2	Reduce caelyx dose to 25mg/m^2	No further treatment
Grade 3 or 4	No further treatment		

Reference: Ferrero, JM et al; Ann Oncol 2007; 18 (2): 263 - 268

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