LIPOSOMAL DOXORUBICIN CARBOPLATIN

INDICATION (ICD10) C54.1, C56

1. Second-line or third line treatment of advanced ovarian cancer.
2. Endometrial recurrence or metastatic 1st line if unable to have taxanes

REGIMEN

Day 1	**PEGYLATED LIPOSOMAL DOXORUBICIN**	30mg/m^2	IV infusion	#ml glucose 5% Cycle 1 infusion at a rate of 1mg/m^2 subsequent cycles over 60 minutes
	CARBOPLATIN	AUC* 5	IV infusion	#ml glucose 5% over 30 minutes

*Dose calculated by EDTA GFR or calculated (CrCl + 25) x AUC.
Maximum dose when using CrCl (125+25 x AUC)mg

diluent volume for dose prescribed as per national standardised product specification

CYCLE FREQUENCY AND NUMBER OF CYCLES

Every 28 days for up to 6-8 cycles

ANTI-EMETICS

High emetic risk day 1

CONCURRENT MEDICATION REQUIRED

Carboplatin	Anaphylaxis treatment should be prescribed if the patient has had an anaphylactic episode previously. Dexamethasone 20mg IV bolus Chlorphenamine 10mg IV bolus H_2 antagonist Carboplatin should be given at a slower rate e.g 2-4 hours.

EXTRAVASATION AND TYPE OF LINE / FILTERS

Carboplatin – irritant
Liposomal doxorubicin - exfoliant

Peripheral line

INVESTIGATIONS

Blood results required before SACT administration

FBC, U&E including Mg^{++} (>0.4) and LFTs Neutrophils x 10^9/L ≥1.5 provided patient is well (also see haematological dose modifications) Platelets ≥100x10^9/L (also see haematological dose modifications)	baseline and every cycle
GFR assessed using EDTA result (BMI <19 or >30 gynae patients) or calculated creatinine clearance at the Consultant's discretion.	baseline and every cycle
Serum creatinine	baseline and every cycle
CA125	baseline and every cycle or as required
ECG (possible ECHO)	required if patient has pre-existing cardiac disease
Virology	before cycle 1 if not previously checked
Weight	baseline and every cycle

MAIN TOXICITES AND ADVERSE REACTIONS

Carboplatin	Ototoxicity – monitor Neurotoxicity - monitor
Liposomal doxorubicin	Avoid where hypersensitivity to the active substance, peanut or soya. Cardiotoxicity – monitor cardiac function. Liposomal doxorubicin may be stopped in future cycles if signs of cardiotoxicity eg cardiac arrhythmias, pericardial effusion, tachycardia with fatigue. GI disturbances, mucositis, stomatitis. Paraesthesia. Infusion related reactions – allergic or anaphylactic like reactions discontinue infusion, treat, once fully recovered restart at reduced infusion rate. Palmar-plantar erythema - treat with steroids prednisolone 30mg od or dexamethasone 8mg od. Consider pyridoxine.

DOSE MODIFICATIONS

Liposomal doxorubicin maximum lifetime dose
= 400mg/m^2 (in patients with cardiac dysfunction or exposed to mediastinal irradiation)
= 450-550mg/m^2 (with normal cardiac function)

Haematological

Liposomal doxorubicin

Grade 1 ANC 1.5-1.9x10^9/l Platelets 75-150x10^9/l	Resume treatment with no dose reduction.
Grade 2 ANC 1.0-1.5x10^9/l Platelets 50-75x10^9/l	Wait until ANC ≥1.5 and platelets ≥75 redose with no dose reduction.
Grade 3 ANC 0.5-1.0x10^9/l Platelets 25-50x10^9/l	Wait until ANC ≥1.5 and platelets ≥75 redose with no dose reduction.
Grade 4 ANC <0.5x10^9/l Platelets <25x10^9/l	Wait until ANC ≥1.5 and platelets ≥75 give 75% dose or continue with GCSF.

Non-haematological

Liposomal doxorubicin

Palmar-plantar erythrodysesthesia – week after prior pegylated liposomal doxorubicin dose

Current assessment	Week 4	Week 5	Week 6
Grade 1 (not interfering with daily activities)	Redose unless patient has experienced a previous grade 3 or 4 skin toxicity, in which case wait an additional week	Redose unless patient has experienced a previous grade 3 or 4 skin toxicity, in which case wait an additional week	Give 75% dose return to 4 week interval
Grade 2 (interfere with but not preclude normal physical activities. Blisters <2cm diameter)	Wait an additional week	Wait an additional week	Give 75% dose return to 4 week interval
Grade 3 (interfere with walking or normal daily activities. Can't wear regular clothes)	Wait an additional week	Wait an additional week	Withdraw patient
Grade 4 (diffuse or local infections, bedridden or hospitalised)	Wait an additional week	Wait an additional week	Withdraw patient

Stomatitis week after prior pegylated liposomal doxorubicin dose

Current assessment	Week 4	Week 5	Week 6
Grade 1 (painless ulcers, erythema, mild soreness)	Redose unless patient has experienced a previous grade 3 or 4 stomatitis toxicity, in which case wait an additional week	Redose unless patient has experienced a previous grade 3 or 4 stomatitis toxicity, in which case wait an additional week	Give 75% dose return to 4 week interval or withdraw patient per physician's assessment
Grade 2 (painful erythema, oedema, ulcers, but can eat)	Wait an additional week	Wait an additional week	Give 75% dose return to 4 week interval or withdraw patient per physician's assessment
Grade 3 (painful erythema, oedema, ulcers, but can't eat)	Wait an additional week	Wait an additional week	Withdraw patient
Grade 4 (requires parenteral or enteral support)	Wait an additional week	Wait an additional week	Withdraw patient

Hepatic impairment

Carboplatin

No need for dose adjustment is expected

Liposomal doxorubicin

Bilirubin 20-50micromol/L	give 75% dose
Bilirubin >51micromol/L	give 50% dose

Patients with impaired hepatic function should be reduced based as follows:
at initiation of therapy, if the bilirubin 1.2-3.0mg/dl, the first dose is reduced to 75%,
bilirubin >3.0mg/dl, the first dose is reduced to 50%.
If the patient tolerates the first dose without an increase in serum bilirubin or liver enzymes, the dose for cycle 2 can be increased to the next dose level, i.e., if reduced to 75% for the first dose, increase to full dose for cycle 2; if reduced to 50% for the first dose, increase to 75% of full dose for cycle 2.
Dosage can be increased to full dose for subsequent cycles if tolerated.
It can be administered to patients with liver metastases with concurrent elevation of bilirubin and liver enzymes up to 4xULN.
Prior to administration, evaluate hepatic function using conventional clinical laboratory tests such as ALT/AST, alkaline phosphatase, and bilirubin.

Renal impairment

Carboplatin

GFR / calculated CrCl ≤20ml/min or ≤30ml/min with pre-existing severe renal impairment	contraindicated

Liposomal doxorubicin

No need for dose adjustment is expected

REFERENCES

1. BMC cancer 2006, 6 page 202, Pignata et al.

Assessments

	Pre	Cycle 1	Cycle 2	Cycle 3	Cycle 4	Ongoing
Clinical assessment	X		Pre cycle		Pre cycle	Every cycle
SACT assessment (PS and toxicities)	X	X	X	X	X	Every cycle
FBC	X	X	X	X	X	Every cycle
U&E, calcium, magnesium & LFT	X	X	X	X	X	Every cycle
CrCl	X	X	X	X	X	Every cycle
CA125	X					Every cycle or as required
ECG or ECHO						Pre existing cardiac disease
CT scan	X					At cycle 6, Inform consultant team if not booked
Informed consent	X					Verbal each cycle
Height	X					
Weight recorded	X	X	X	X	X	Every cycle