PACLITAXEL & CISPLATIN

1. First-line treatment of advanced ovarian or endometrial cancer for carboplatin-allergic patients
2. A treatment option for carboplatin-allergic women with ovarian cancer whose disease responded to first-line platinum-based therapy, but relapsed > 6 months after completion of first-line treatment (NICE approved May 2005)
3. 2nd line option for cervical cancer, for carboplatin-allergic women

Drugs/Dosage:	Paclitaxel	175mg/m^2	IV	Day 1
	Cisplatin	75mg/m^2	IV	Day 2

Administration: Note that it is important that paclitaxel is administered prior to cisplatin.[1]

Day 1:	Dexamethasone	16mg	IV 60 mins prior to paclitaxel administration
	Chlorphenamine	10mg	IV 30–60 mins prior to paclitaxel administration
	Ranitidine	50mg	IV 30–60 mins prior to paclitaxel administration

Paclitaxel in 500ml 0.9% sodium chloride over 3 hours via non–PVC admin set with a 0.2 micron in-line filter

Day 2:
1 litre 0.9% sodium chloride + 20mmol KCl + 10mmol $MgS0_4$ IV over 2 hours
Mannitol 20% 100ml IV over 15 minutes
Cisplatin in 1 litre 0.9% sodium chloride IV over 3 hours
1 litre 0.9% sodium chloride + 20mmol KCl + 10mmol $MgS0_4$ IV over 2 hours
500ml sodium chloride 0.9% IV **or** 500ml water orally over 1 hour

Frequency: 3 weekly cycle for 6 cycles of both paclitaxel and cisplatin
Paclitaxel only to be extended to a maximum of 8 cycles if clinical benefit shown
Clinical review after Cycle 3

Main Toxicities: infusion-related hypersensitivity reactions; myelosuppression; alopecia; myalgia/arthralgia; nephrotoxicity; neuropathy / ototoxicity (cisplatin); peripheral neuropathy (paclitaxel)

Anti-emetics: highly emetogenic

Extravasation: paclitaxel is a vesicant

Regular investigations:	FBC	Day 1
	U&Es	Day 1
	LFTs	Day 1
	Mg^{2+} and Ca^{2+}	Day 1
	CA 125	Day 1
	EDTA	Prior to Cycle 1

Comments: For patients on Cycle 1 whose EDTA is not yet available, Cockcroft and Gault may be used to predict GFR. Cisplatin dose should be adjusted according to EDTA on subsequent cycles. EDTA should only be repeated if the result is borderline or if there is a 30% change in serum creatinine

Reason for Update: cervical indication added; haem toxicity updated in line with paclitaxel/carbo protocol	Approved by Consultant: Dr A Michael
Version: 2	Approved by Lead Chemotherapy Nurse: P Deery
Supersedes: Version 1	Date: 19.11.13
Prepared by: S Taylor	Checked by: C Tucker

Check electrolytes – additional supplementation of magnesium, calcium or potassium may be required.

Weight should be recorded prior to and at the end of cisplatin treatment, and a strict fluid balance chart should be maintained. An average urine output of at least 100ml/hr must be maintained throughout treatment, and cisplatin infusion should not be commenced unless this urine output is achieved. If the urine output is inadequate, the patient should be assessed and urine output increased by administering 500ml sodium chloride +/- furosemide 20 - 40mg. Furosemide 20 – 40mg po may also be given if there is a positive fluid balance of 1.5 litres, a weight gain of 1.5kg or symptoms of fluid overload. The patient should be asked to drink 2 litres of fluid in the 24hrs following treatment, and to contact the hospital if this is impossible because of problems e.g. nausea and vomiting.

Dose Modifications

Haematological Toxicity:

Neutrophils < 1.5** x 10^9/l or Platelets < 100 x 10^9/l	Delay treatment for 1 week. Repeat FBC and, if recovered, continue with treatment. Dose reductions may be required according to criteria below:

** If being given in the adjuvant setting and neutrophils 1.0 – 1.4 x 10^9/l, proceed with treatment, with G-CSF prophylaxis, without any delay. If in doubt, discuss with Consultant.

Neutrophils < 0.5 x 10^9/l or Grade 3 neutropenic sepsis	Delay treatment until recovered, then continue with paclitaxel 110mg/m^2 and full dose cisplatin.
Platelets < 75 x 10^9/l	Delay treatment until recovered, then continue with cisplatin 50% dose and paclitaxel 110mg/m^2.

Renal Impairment:

GFR (ml/min)	Cisplatin Dose
≥ 60	Give 100% dose
45 – 59	Give 75% dose
< 45	Cisplatin contra-indicated

Hepatic Impairment: For paclitaxel, if bilirubin < 1.25 x ULN and ALT < 10 x ULN, proceed with full dose. Otherwise, consider a dose reduction. Not recommended in severe hepatic impairment.

Neuropathy: If a Grade 2 or worse peripheral neuropathy develops, paclitaxel should be reduced to 135mg/m^2 in all subsequent cycles.
If progressive neuropathy is observed after this dose reduction, then treatment with paclitaxel should be discontinued. Also consider neurotoxicity may be due to cisplatin.
For any grade tinnitus, reduce to 50% dose of cisplatin. Inform and discuss with Consultant.

Myalgia / Arthralgia: Due to paclitaxel and often co-exist, usually Grade 1 or 2. Management consists of prescribing NSAIDs and reassuring patient that it is self-limiting.

References:

Muggia, F et al; JCO 2000; 18 (1): 106 - 115
McGuire, WP et al; N Engl J Med 1996; 334: 1 – 6
[1]Milcross, C et al; Int J Cancer 1995; 62 (5): 599 - 604

Reason for Update: cervical indication added; haem toxicity updated in line with paclitaxel/carbo protocol	Approved by Consultant: Dr A Michael
Version: 2	Approved by Lead Chemotherapy Nurse: P Deery
Supersedes: Version 1	Date: 19.11.13
Prepared by: S Taylor	Checked by: C Tucker