PACLITAXEL & GEMCITABINE

An option for second-line use in advanced or metastatic bladder cancer, ureteric cancer or renal pelvis carcinoma

Drugs/Dosage:	Paclitaxel	175 mg/m^2	IV	Day 1
	Gemcitabine	1000 mg/m^2	IV	Day 1 and Day 8

Administration: Paclitaxel in 500ml 0.9% sodium chloride over 3 hours via a PVC-free giving set with a 0.2 micron in-line filter
followed by:
Gemcitabine in 250ml 0.9% sodium chloride over 30 minutes

Pre-medication for paclitaxel:

Dexamethasone	16mg	IV 60 minutes prior to paclitaxel administration
Chlorphenamine	10mg	IV 30–60 minutes prior to paclitaxel administration
Ranitidine	50mg	IV 30–60 minutes prior to paclitaxel administration

Frequency: 3 weekly cycle for 6 cycles

Main Toxicities: paclitaxel infusion-related hypersensitivity reactions; myelosuppression; myalgia/arthralgia; alopecia; peripheral neuropathy; erythematous rash; flu-like syndrome; peripheral oedema (mild –moderate & reversible); ovarian failure/infertility

Anti-emetics: Day 1 and Day 8: mildly emetogenic

Extravasation: paclitaxel is a vesicant

Regular Investigations:	FBC	Day 1 and Day 8
	U&Es	Day 1
	LFTs	Day 1
	CA 15-3	On alternate cycles **only** if elevated prior to treatment

Dose Modifications

Haematological Toxicity:

Day 1: Neutrophils < 1.5 x 10^9/l or Platelets < 100 x 10^9/l — Delay for 1 week. Repeat FBC and, if within normal parameters, give full dose of both drugs*.

*Reduce the gemcitabine dose to 75% of the original cycle initiation dose (and do not increase this dose again) if any of the following have occurred:

- Neutrophils < 0.5 x 10^9/l for > 5 days
- Neutrophils < 0.1 x 10^9/l for > 3 days
- Febrile neutropenia
- Platelets < 25 x 10^9/l
- Cycle delay of more than one week due to toxicity

Reason for Update: N/A	Approved by Consultant: Dr J Money-Kyrle
Version: 1	Approved by Lead Chemotherapy Nurse: P Deery
Supersedes: none	Date: 14.11.14
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Day 8 Gemcitabine:

Neutrophils		Platelets	Gemcitabine Dose
≥ 1.2 x 10^9/l	**and**	> 75 x 10^9/l	Give 100% dose
1.0 – 1.19 x 10^9/l	**or**	50 – 75 x 10^9/l	Give 75% dose
0.7 – 0.99 x 10^9/l	**and**	≥ 50 x 10^9/l	Give 50% dose
< 0.7 x 10^9/l	**or**	< 50 x 10^9/l	Omit dose **(do not defer)**

If a dose reduction has been made, then the dose should be increased to 100% for subsequent doses, providing the FBC has returned to within normal limits as above.

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. If bilirubin > 27 µmol/L, consider initiating treatment with gemcitabine 800mg/m^2.

Neuropathy: If a Grade 2 or worse 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.

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:
Ikeda, M et al ; Japanese JCO 2011 ; 41 (10) : 1214 – 1210
Albers, P et al ; Ann Onc 2011 ; 22 (2) : 288 - 294