GEMCITABINE AND CARBOPLATIN

An option for use in metastatic breast cancer
A particularly suitable option for patients with tumour types shown to be responsive to carboplatin e.g. triple negative disease, BRCA1 mutation

Drug / Dosage:	Gemcitabine 1000mg/m^2	IV	Day 1 and Day 8
	Carboplatin AUC 5	IV	Day 1

Administration: Gemcitabine in 250 ml 0.9% sodium chloride over 30 minutes
Carboplatin in 250 ml 5% glucose over 30 - 60 minutes

Frequency: 3 weekly cycle for 6 cycles

Main Toxicities: myelosuppression; erythematous rash; flu-like syndrome; peripheral oedema (mild-moderate & reversible); infertility/ovarian failure

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

Extravasation: non-vesicants

Regular Investigations:	FBC	Day 1 and Day 8
	U&Es	Day 1
	LFTs	Day 1
	EDTA	Prior to 1st cycle
	CA 15-3	Cycles 1, 3 & 5

Comments: 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 (C&G) 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.

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

Dose Modifications

Haematological Toxicity: **Day 1:**

Neutrophils < 1.5 x 10^9/l or Platelets < 100 x 10^9/l	Delay treatment for 1 week. Repeat FBC and, if normal, proceed with treatment*.

*Reduce the gemcitabine dose to 75% of the original cycle initiation dose if any of the following have occurred:

Reason for Update: added info on carboplatin hypersensitivity	Approved by Consultant: Dr T Crook
Version: 4	Approved by Lead Chemotherapy Nurse: S Wills-Percy
Supersedes: Version 3	Date: 2.11.17
Prepared by: S Taylor	Checked by: C Tucker

- 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

Day 8:

Neutrophils		Platelets	Gemcitabine
> 1.5 x 10^9/l	and	≥ 100 x 10^9/l	Give full dose
1.0 – 1.5 x 10^9/l	or	75 – 100 x 10^9/l	Give 50% dose
< 1.0 x 10^9/l	or	< 75 x 10^9/l	Omit **(do not defer)**

If a dose reduction to 50% has been made, the dose should be increased to 100% for subsequent doses, providing the FBC has returned to normal limits.

Renal Impairment: Carboplatin is contra-indicated if GFR < 20 ml/min.

If CrCl < 30ml/min, consider gemcitabine dose reduction – clinical decision

Hepatic Impairment: If bilirubin > 27 µmol/L, initiate treatment with gemcitabine 800mg/m^2

References:
Nagourney, RA et al; Clinical Breast Cancer 2008; 8 (5): 432 – 435
Laessig, D et al; ASCO Annual Meeting Proceedings; JCO 2007; 25 (18S): 1074
Leong, CO et al; J Clin Invest 2007; 117 (5): 1370 – 1380 (carboplatin)
Haematological dose modifications advice in line with Gemzar SPC advice for gem/carbo (ovary)