GEMCITABINE AND CARBOPLATIN

First-line for advanced NSCLC - NICE 2001
Neo-adjuvant use in NSCLC

Drug / Dosage:	Gemcitabine 1200mg/m^2	IV	Day 1 and Day 8
	Carboplatin AUC 5	IV	Day 1

Administration: Gemcitabine diluted in 250 ml 0.9% sodium chloride and infused over 30 minutes
Carboplatin diluted in 250 ml 5% glucose and infused over 30 minutes

Frequency: 3 weekly cycle:

- 4 cycles in palliative context is adequate, but for patients with impressive objective responses and excellent tolerability, consideration could be given to consolidating to a maximum of 6 cycles.
- For patients receiving sequential radiotherapy, 3 cycles should be given, followed by radiotherapy starting 3 weeks after Day 1 of Cycle 3. However, if there is a delay in starting RT, a 4th cycle should be given.
- For resectable disease, 3 – 4 cycles before surgery

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

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

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 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.

Reason for Update: neo-adjuvant indication added	Approved by Consultant: Dr A Mehta
Version: 6	Approved by Lead Chemotherapy Nurse: S Wills-Percy
Supersedes: Version 5	Date: 13.9.17
Prepared by: S Taylor	Checked by: C Tucker

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:

- 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, consider initiating treatment with gemcitabine 800mg/m^2.

References:

Sederholm, C; Proc ASCO 2002, Abstract No: 1162
Rudd, RM et al; Proc ASCO 2002, Abstract No: 1164
Haematological dose modifications advice in line with Gemzar SPC advice for gem/carbo (ovary)