Gem-Carbo: Gemcitabine/Carboplatin in Bladder Cancer (Advanced or Metastatic)

Indication:	Alternative Palliative therapy to Gemcitabine/Cisplatin in patients with Advanced or Metastatic Bladder Cancer unsuitable for Cisplatin			
Regimen details:	Gemcitabine	1000mg/m^2	IV	D1, D8 (see Hepatic impairment)
	Carboplatin	AUC 5	IV	D1 (see Renal impairment)
Administration:	Gemcitabine in 500ml Sodium Chloride 0.9% IV infusion over 30 min (depending on contract for Dose banding product) Carboplatin in 500ml Glucose 5% IV over 30 – 60 minutes Any device containing aluminium that may come in contact with Carboplatin must be avoided			
Frequency:	Repeat every 21 days, for a maximum of 6 cycles			
Extravasation:	Gemcitabine and Cisplatin: Non- vesicants			
Anti- emetics:	Day 1 : Moderate emetogenic Day 8 : Low Emetogenic Follow Local Anti-emetic policy			

Regular investigations:	FBC	D1, D8
	LFTs & U&Es	D1
	EDTA	Prior to 1st cycle , only if indicated (see Renal impairment)
	Disease evaluation	Every 3 cycles

Comments: Haemolytic anaemia – Gemcitabine
Gemcitabine should be discontinued at the first signs of any evidence of micro-angiopathic haemolytic anaemia, such as rapidly falling haemoglobin with concomitant thrombocytopenia, elevation of serum bilirubin, serum creatinine, blood urea nitrogen, or LDH, which may indicate development of haemolytic uraemic syndrome. Renal failure may not be reversible, even with discontinuation of therapy, and dialysis may be required

DOSE MODIFICATIONS

Haematological Toxicity

Day1

WBC < 3.0 x 10^9/L or Neutrophils < 1.5 x 10^9/L or Platelets < 100 x 10^9/L	Delay for 1 week. Repeat FBC - If within normal parameters, resume treatment with 100% doses

Subsequent cycles

If Febrile neutropenia is diagnosed, G-CSF support should be given as secondary prophylaxis

If Platelets < 25 x 10^9/L, Gemcitabine should be given at 75% dose and Carboplatin dose should be reduced by 1 x AUC from previous dose (do not escalate for subsequent cycles)

Day 8

Neutrophils		Platelets	Gemcitabine Dose
≥ 1.0 x 10^9/L	and	≥ 100 x 10^9/L	Give 100%
0.5 – 0.99 x 10^9/L	and/or	50 – 99 x 10^9/L	Give 75%
< 0.5 x 10^9/L	and/or	< 50 x 10^9/L	Omit

Renal Impairment: GFR should be calculated using the Cockcroft & Gault equation in all patients; if the calculated GFR < 60 or > 120ml/min, measure EDTA clearance before prescribing. Monitor trends in serum creatinine between treatments: if 25% from baseline value, re-calculate GFR using the Cockcroft & Gault equation

Gemcitabine should be used with caution in patients with impaired renal function:

GFR (ml/min)	Gemcitabine Dose
> 30	Give 100%
< 30	Consider dose reduction. Discuss with Consultant

Carboplatin: Contraindicated if GFR < 20ml/min

Hepatic Impairment

Gemcitabine: Use with caution in the presence of hepatic dysfunction
Administration of Gemcitabine in patients with liver metastases or a pre-existing medical history of hepatitis, alcoholism, or liver cirrhosis may lead to exacerbation of the underlying hepatic insufficiency
If Bilirubin > 27µmol/L, initiate treatment with Gemcitabine 800mg/m^2
BUT
If Bilirubin > 30µmol/L or ALT/ALP > 3 X ULN (> 5 x ULN if liver metastatses are present), treatment should be deferred unless approved by Consultant. These patients are at high risk of potentially fatal sepsis

Carboplatin: No dose reduction necessary

DOSE MODIFICATIONS FOR OTHER TOXICITIES AS APPROPRIATE

NON – HAEMATOLOGICAL TOXICITY

For any Grade 3 – 4 toxicity, treatment should be deferred until recovery, and then continued with an appropriate dose reduction. Discuss with Consultant

Toxicities: Myelosuppression; anaemia; fatigue; nausea; vomiting; mucositis; flu-like syndrome; elevation of transaminases; proteinuria and haematuria; peripheral oedema; dyspnoea; hypersensitivity reactions; skin rash; alopecia (mild)

Drug interactions:

Carboplatin

-Aminoglycoside antibiotics : increased risk of nephrotoxicity and ototoxicity
-Clozapine : increased risk of agranulocytosis, avoid concomitant use
-Diuretics : increased risk of nephrotoxicity and ototoxicity
-Nephrotoxic drugs : increased nephrotoxicity ; not recommended
-Phenytoin : reduced absorption of the antiepileptic
-Warfarin : increased anticoagulant effect of warfarin

Gemcitabine

-Gemcitabine is a radiosensitizer
-Warfarin : increased anticoagulant effect of warfarin

References:

www.medicines.org.uk
Summary of Product Characteristics. Gemcitabine. Lilly. September 2007
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GSTT guidelines for treating nausea and vomiting in adult patients. September 2007
SELCN Cytotoxic Extravasation Guidelines (draft).July 2008
Stockley's Drug Interactions. Interactions search: Carboplatin&Gemcitabine.March'09
CTCAE v3.0. August 2006