Systemic Anti Cancer Treatment Protocol

Carboplatin and Gemcitabine Bladder Cancer

PROCTOCOL REF: MPHAUROCAG
(Version No: 1.1)

Approved for use in:

First-line locally advanced or metastatic bladder cancer

For patients with a performance status 0- 2 or if a cisplatin-based chemotherapy regimen is unsuitable, for example, because of performance status, inadequate renal function (typically defined as a GFR of less than 60 ml/min/1.73 m 2) or a comorbidity.

Dosage:

Drug	Dosage	Day	Route	Frequency
Gemcitabine	1000mg/m² day 1 and day 8	Day 1 & Day 8	IV infusion	21 day cycle max 6 cycles
Carboplatin	AUC 5 x (GFR +25)	Day 1		

Calvert formula for Carboplatin dosage-

Carboplatin dose in mg = AUC x (creatinine clearance + 25)

If estimated GFR is used the Wright formula must be used for creatinine clearance. **Avoid** the use of Cockcroft and Gault formulae as it is less accurate.

Supportive Treatments:

- Dexamethasone 4mg BD for three day
- Domperidone 10mg TDS when required

Extravasation risk:

Gemcitabine: refer to local guidelines for management extravasation

Carboplatin: refer to local guidelines for management extravasation

Administration:

Day	Drug	Dose	Route	Diluent and rate
1	**Dexamethasone** 30mins before chemotherapy	**8mg**	PO	
	Ondansetron 30mins before chemotherapy	**16mg**	PO	
	Gemcitabine	**1000mg/m²**	IV	Sodium Chloride 0.9% 250mL over 30 minutes
	Carboplatin	**AUC 5**	IV	Glucose 5% 500mL over 60 minutes
8	**Dexamethasone** 30mins before chemotherapy	**8mg**	PO	
	Ondansetron 30mins before chemotherapy	**16mg**	PO	
	Gemcitabine	**1000mg/m²**	IV	Sodium Chloride 0.9% 250mL over 30 minutes

<u>Hypersensitivity reactions</u>

- Patients should be observed closely for hypersensitivity reactions, particularly during the first and second infusions.
- Hypersensitivity reactions may occur within a few minutes following the initiation of the infusion of carboplatin.

- Facilities for the treatment of hypotension and bronchospasm must be available.
- If hypersensitivity reactions occur, minor symptoms such as flushing or localised cutaneous reactions do not require discontinuation of therapy. The infusion may be temporarily interrupted and when symptoms improve restarted at a slower infusion rate. Chlorphenamine 10mg IV may be administered.
- Severe reactions, such as hypotension, bronchospasm or generalised rash/erythema require immediate discontinuation of carboplatin and appropriate therapy.

Main Toxicities:

Neutropenia, thrombocytopenia and anaemia. Nausea and vomiting, diarrhoea and mucositis

Carboplatin	
Hepatobiliary	Hepatic enzymes increased, blood bilirubin increased
Cardiac disorders	Arrhythmia, bradycardia, tachycardia
Hypersensitivity	Anaphylaxis, anaphylactic shock. Urticaria, erythematous rash
Additional side effects	Loss of fertility
Gemcitabine	
Hepatobiliary	Elevation of liver transaminases (AST and ALT) and alkaline phosphatase, Increased bilirubin, uncommon reports (≥ l/1000 to <1/100), hepatotoxicity, including liver failure.
Urinary symptoms	Haematuria, Mild proteinuria
Additional side effects	alopecia, peripheral oedema, rash, influenza-like symptoms, dizziness during infusion, peripheral neuropathy,

Please refer to SPC for more information on toxicities.

Investigations:

	Pre	Cycle 1 Day 1	Cycle 1 Day 8	Ongoing
Medical Assessment	X	X		Alternate cycles
Nursing Assessment		X	X	Every cycle
SACT assessment	X	X	X	Every cycle
FBC	X		X	Every cycle
U&E & LFT	X	X	X	Every cycle
Calculate CrCl	X	X		Every cycle
CT scan	X			As clinically indicated
Informed Consent	X			
PS recorded	X	X	X	Every cycle
Toxicities documented	X	X	X	Every cycle
Weight recorded	X	X	X	Every cycle

Dose Modifications and Toxicity Management:

	Carboplatin	Gemcitabine
First dose reduction	AUC 4	800mg/m^2
Second dose reduction	AUC 4 x 20% dose reduction	600mg/m^2

Haematological Toxicity:

Delay 1 week on day 1 if-

ANC ≤ 0.9 x 10^9/L	Plt ≤ 100 x 10^9/L

Omit on day 8 if-

ANC ≤ 0.9 x 10^9/L	Plt ≤ 75 x 10^9/L

Hepatic impairment:

Carboplatin
Excretion is primarily by glomerular filtration in urine, hepatic impairment unlikely to affect elimination of carboplatin.

Gemcitabine
AST elevations do not seem to cause dose limiting toxicities. If bilirubin > 27 µmol/L, initiate treatment with dose of 800mg/m^2.

Renal impairment:

Carboplatin
Excretion is primarily by glomerular filtration in urine, with most of the drug excreted in the first 6hrs. ~32% dose is excreted unchanged. In case of a glomerular filtration rate of ≤ 20 mL/min, carboplatin should not be administered.

Gemcitabine: CrCl (mL/min)	**Dose**
Above 30	1000mg/m^2 (100% dose)
Below 30	Consider dose reduction – clinical decision.

References:

Gemcitabine 100 mg/ml Concentrate for Solution for Infusion, Summary of Product Characteristics. Accord Healthcare Limited Middlesex. 06/06/2012. Available from www.medicines.org.uk Last updated 23/08/12.

Carboplatin 10mg/ml concentrate for solution for infusion, Summary of Product Characteristics. Sun Pharmaceutical company.11/03/2010. Available from www.medicines.org.uk Last updated 11/07/2014.

Dosage Adjustment for Cytotoxics in Hepatic Impairment. January 2009 UCLH (Version 3 - updated January 2009)

Dosage Adjustment for Cytotoxics in Renal Impairment. January 2009 UCLH (Version 3 - updated January 2009)

Managing locally advanced or metastatic bladder cancer. NICE guideline NG2. Feb 2015. Available from pathways.nice.org.uk/pathways/bladder-cancer.