Systemic Anti Cancer Treatment Protocol

Gemcitabine Chemo-Radiation Regimen Urothelial Bladder Cancer

PROCTOCOL REF: MPHAGECRUR
(Version No: 1.2)

Approved for use in:

Muscle-invasive transitional cell urothelial bladder cancer in patients where radical therapy is suitable.

Eligibility

- Patients with histologically confirmed diagnosis of muscle invasive bladder cancer that has not metastasized (M0).
- Aged 18+, not pregnant or lactating.
- Patients deemed adequate performance status (≤2) by the referring clinician to receive radical treatment.
- Patients with adequate renal function (eGFR ≥45) however may be lower and acceptable as judged by the clinician (note this does not exclude patients with nephrostomies/stents).

Dosage:

With concurrent radiotherapy.

Drug	Dose	Route	Frequency
Gemcitabine	**100mg/m2**	IV	Weekly

For one 4 week cycle.

Extravasation risk:

- Refer to local guidelines for management extravasation

Administration:

Day	Drug	Dose	Route	Diluent and rate
1	**Gemcitabine**	**100mg/m^2**	**IV**	Sodium Chloride 0.9% 250mL over 30 minutes

Main toxicities

Thrombocytopenia, neutropenia, diarrhoea.

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
Gastrointestinal	stomatitis and ulceration of the mouth, constipation
Additional side effects	alopecia, peripheral oedema, rash, influenza-like symptoms, dizziness during infusion, peripheral neuropathy,

Radiation colitis when given in combination with radiotherapy. Patients presenting with constipation, abdominal pain and possible nausea and vomiting with reduced appetite need clinical review.

Please refer to the electronic medicines compendium for each drug for more information on side effects.

Investigations:

	Pre	Day 1	Day 28	Ongoing
Informed Consent	X			Repeat investigations when clinically indicated
Clinical Assessment	X			
SACT Assessment (to include PS and toxicities)	X	X	X	
FBC	X	X	X	
U&E & LFTs	X	X	X	
CT scan	X			
Blood pressure measurement	X	X	X	
Weight recorded	X	X	X	
Height recorded	X	X	X	
Blood glucose	X			

Dose Modifications and Toxicity Management:

Toxicities

≥ Grade 3 Bowel toxicity	Consider deferring or omitting. Consider radiation colitis, discuss with clinical team. Radiation may be withheld for several days and chemotherapy likely to be stopped.
Any grade 3/4 Toxicity	Discuss with clinical team, Omit chemotherapy.

Haematological toxicity

Proceed on day 1 if-

ANC ≥ 1.5 x 10^9/L	Plt ≥ 100 x 10^9/L

Discuss with consultant oncologist if blood results are below these recommended limits

No dose modifications performed if blood parameter out of range. The clinician reviewing the patient may choose to omit that week of chemotherapy or discontinue the rest of the course. **Please note that radiotherapy will continue as planned.**

These haematological guidelines assume that patients are well with good performance status, that other acute toxicities have resolved and the patient has not had a previous episode of neutropenic sepsis.

Hepatic impairment:

- AST elevations do not seem to cause dose limiting toxicities.

Renal Impairment:

CrCl <30	Review of chemotherapy- clinical decision

References:

Accord Healthcare Limited Middlesex. Gemcitabine 100 mg/ml Concentrate for Solution for Infusion, Summary of Product Characteristics. Available from: https://www.medicines.org.uk/emc/product/2839/smpc. Last updated 18/03/2019.

Dosage Adjustment for Cytotoxics in Hepatic 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.

Choudhury, A et al. (2011). A Phase II study of conformal hypofractionated radiotherapy with concurrent Gemcitabine in Muscle-invasive Bladder Cancer.

Caffo, O et al (2016) Concurrent gemcitabine and radiotherapy for the treatment of muscle-invasive bladder cancer: A pooled individual data analysis of eight phase I-II trials.

The Christie SACT management protocol: Clinical Oncology guidelines for Management of bladder cancer: Last updated Jan 2019.