Gemcitabine and radiotherapy (bladder)

Indication
First line therapy with concurrent radiotherapy for patients with muscle invasive bladder cancer.
WHO performance status 0-1 only.

Patients may have received 3 cycles of neo-adjuvant chemotherapy.

ICD-10 codes
Codes pre-fixed with C67

Regimen details

Day	Drug	Dose	Route
1 , 8, 15 and 22	Gemcitabine	100 mg/m²	IV infusion

Cycle frequency
Weekly for 4 weeks with concurrent radiotherapy.

Number of cycles
1 cycle
As above

Administration
Gemcitabine is administered in 250mL sodium chloride 0.9% over 30 minutes, 2-4 hours prior to radiotherapy.

Gemcitabine is a known radio-sensitizer. Patients should be carefully monitored for gastrointestinal toxicity.

Pre-medication
Nil

Emetogenicity
This regimen has low emetic potential.

Additional supportive medication
Antiemetics as per local guidelines.

Extravasation
Gemcitabine – neutral (Group 1)

Investigations – pre first cycle

Investigation	**Validity period** (or as per local practice)
FBC	7 days
U+E (including creatinine)	7 days
LFTs	7 days

Investigations - pre subsequent cycles

Investigation	**Validity period** (or as per local practice)
FBC	Weekly, valid for 24 hours
U+E (including creatinine)	Weekly, valid for 24 hours
LFTs	Weekly, valid for 24 hours

Standard limits for administration to go ahead

If blood results not within range, authorisation to administer **must** be given by prescriber/ consultant

Investigation	**Limit**
Neutrophils	≥1.0 x 10^9/L
Platelets	≥100 x 10^9/L
Creatinine Clearance (CrCl)	≥30 mL/min
Bilirubin	< 1.5 x ULN

Dose modifications

- **Haematological toxicity**

If neutrophils < 1.0 x 10^9/L or platelets <100 x 10^9/L, omit gemcitabine but consider giving dose when counts recovered.

- **Renal impairment**

If CrCl < 30mL/min omit gemcitabine.

- **Hepatic impairment**

There is limited information about use of gemcitabine in hepatic impairment, therefore use with caution. AST elevations do not appear to cause dose limiting toxicity.
If bilirubin > 1.5 x ULN consider omitting gemcitabine.

- **Other toxicities**

If any ≥ grade 3 toxicity (particularly bowel or bladder) gemcitabine should be stopped. There are no circumstances for gemcitabine dose modification. Radiotherapy should continue to a full course and only be discontinued at the clinician's discretion. If chemotherapy is withheld due to unacceptable toxicity, it should not be recommenced.

*Gemcitabine should be discontinued at the first sign of microangiopathic haemolytic anaemia (such as rapidly falling haemoglobin with concomitant thrombocytopenia, elevated bilirubin, creatinine, blood urea nitrogen or LDH. Renal failure may not be reversible with discontinuation of therapy, dialysis may be required.

Adverse effects - for full details consult product literature/ reference texts

- **Serious side effects**

Interstitial pneumonitis, ARDS
Cardiotoxicity
Hepatotoxicity
Myelosuppression
Infertility
Haemolytic uraemic anaemia/ microangiopathic haemolytic anaemia *

- **Frequently occurring side effects**

Nausea and vomiting
Myelosuppression
Mucositis, stomatitis
Diarrhoea, constipation

Oedema
Proteinuria
Haematuria
Flu-like symptoms

- **Other side effects**

Raised transaminases
Alopecia (mild)
Headache
Fatigue

Significant drug interactions – for full details consult product literature/ reference texts

Warfarin/coumarin anticoagulants: increased or fluctuating anticoagulant effects. Avoid if possible, consider switching patient to a low molecular weight heparin during treatment or if the patient continues taking warfarin monitor the INR at least once a week and adjust dose accordingly.

Gemcitabine is a radiosensitiser.

Additional comments

References

- Summary of Product Characteristics Gemcitabine (Lilly) accessed via www.medicines.org.uk (23 December 2015)
- Cowan RA, et al. Radiotherapy for muscle invasive carcinoma of the bladder: results of a randomised trial comparing whole bladder with dose-escalated partial bladder irradiation, Int J Radiat Oncol Biol Phys (2004) **59**:197–207
- Sangar VK, et al. Phase I study of conformal radiotherapy with concurrent gemcitabine in locally advanced bladder cancer. Int J Radiat Oncol Biol Phys. 2005 Feb 1;61(2):420-5.
- Choudhury A, et al. Phase II study of conformal hypofractionated radiotherapy with concurrent gemcitabine in muscle-invasive bladder cancer. J Clin Oncol. 2011 Feb 20;29(6):733-8.

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