

BCCA Protocol Summary for Neo-Adjuvant Therapy for Urothelial Carcinoma Using Cisplatin and Gemcitabine

Protocol Code *UGUNAJPG*

Tumour Group *Genitourinary*

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GU Systemic Therapy Contacts

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ELIGIBILITY:

- Urothelial bladder cancer, clinical N0 M0
- Planned cystectomy
- Muscle invasive disease
- ECOG performance status 0 or 1
- An "Individual Use of Benefit Drug List Medication for a Undesignated Indication" form must be completed and approved before chemotherapy is booked

EXCLUSIONS:

- Pure squamous, adenocarcinoma or small-cell carcinoma
- Patients with poor renal function (initial creatinine clearance <60 ml/min by GFR measurement or Cockcroft formula)
- Major co-morbid illness; non-surgical candidate
- Significant hearing impairment

TESTS:

- Baseline: CBC & differential, platelets, creatinine, liver function tests, bilirubin
- Before each treatment:
 - Days 1: CBC & differential, platelets, creatinine, liver function tests, bilirubin
 - Day 8: CBC & differential, platelets, creatinine
- Baseline imaging of bladder and pelvis

PREMEDICATIONS:

- Antiemetic protocol for high [moderate](#) emetogenic chemotherapy protocols (see protocol SCNAUSEA).
- [May consider adding aprepitant 125 mg PO pre-chemo and 80 mg PO post-chemo daily for 2 days](#)

TREATMENT:

Drug	Dose	BCCA Administration Guideline
Gemcitabine	1250 mg/m ² /day on days 1 and 8 (total dose per cycle = 2500 mg/m ²)	IV in 250 mL NS over 30 min
Cisplatin	70 mg/m ² /day on day 1	Prehydrate with 1000 mL NS over 60 minutes, then Cisplatin IV in 1000 mL NS with 20 mEq/L KCl, 1 g/L MgSO ₄ , 30 g/L mannitol over 60 minutes

Repeat every 21 days for total of two cycles prior to restaging.

Plan for 4 cycles maximum prior to surgery, if tolerated and if no disease progression.

DOSE MODIFICATIONS:**1. Hematology****For gemcitabine day 1 of each cycle**

ANC (x 10 ⁹ /L)		Platelets (x 10 ⁹ /L)	Dose
≥ 1.0	and	> 100	100%
0.5-0.99	or	75-100	75%
< 0.5	or	< 75	Delay*
*Cisplatin also delayed			

For gemcitabine day 8 of each cycle

ANC (x 10 ⁹ /L)		Platelets (x 10 ⁹ /L)	Dose**
≥ 1.0	and	> 100	100%
0.5-0.99	or	75-100	75%
< 0.5	or	< 75	Omit
**Dose adjustment only for the day of treatment the CBC is drawn			

2. Renal Dysfunction

Creatinine Clearance (ml/min)	Cisplatin dose	Gemcitabine dose
≥ 60	70 mg/m ² on Day 1	100%
45 - 59	35 mg/m ² on Days 1 and 2 OR Days 1 and 8 (same prehydration as 70 mg/m ² dose)	100%
< 45	Delay	Delay/omit *

***Delay if day 1; if day 8, omit if serum creatinine > 3 x ULN where ULN = local upper limit of normal range.**

PRECAUTIONS:

1. **Neutropenia:** Fever or other evidence of infection must be assessed promptly and treated aggressively.
2. **Renal Toxicity:** Nephrotoxicity is common with cisplatin. Encourage oral hydration. Avoid nephrotoxic drugs such as aminoglycoside antibiotics. Irreversible renal failure associated with hemolytic uremic syndrome may occur (rare) with gemcitabine. Use caution with pre-existing renal dysfunction.
3. **Pulmonary Toxicity:** Acute shortness of breath may occur. Discontinue treatment if drug-induced pneumonitis is suspected.

Contact Dr. Susan Ellard or tumour group delegate @ (250) 712-3900 or 1-800-563-7773 with any problems or questions regarding this treatment program.

Date activated: 01 January 2005

Date revised: 1 Mar 2008 (antiemetics revised)

References:

1. von der Maase H, Hansen SW, Roberts JT, et al. Gemcitabine and cisplatin versus methotrexate, vinblastine, doxorubicin, and cisplatin in advanced or metastatic bladder cancer: results of a large, randomized, multinational, multicenter, phase III study. *J Clin Oncol* 2000;18(17):3068-77.
2. Neoadjuvant chemotherapy in invasive bladder cancer: a systematic review and meta-analysis. *Lancet* June 7, 2003,361:1927-34.
3. Neoadjuvant cisplatin, methotrexate, and vinblastine chemotherapy for muscle-invasive bladder cancer: a randomised controlled trial. *Lancet* 1999; 354: 533-40.
4. Neoadjuvant chemotherapy in invasive bladder cancer: update of a systematic review and meta-analysis of individual patient data advanced bladder cancer (ABC) meta-analysis collaboration. *Eur Urol* 2005;48(2):202-5; discussion 5-6.