

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

Protocol Code

GUNAJPG

Tumour Group

Genitourinary

Contact Physician

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GU Systemic Therapy Contacts

ELIGIBILITY:

- Urothelial bladder cancer, clinical N0 M0
- Planned cystectomy
- Muscle invasive disease
- ECOG performance status 0 or 1
- A BCCA "Class II Drug Registration Form" form must be submitted

EXCLUSIONS:

- Pure squamous, adenocarcinoma or small-cell carcinoma
- Patients with poor renal function (initial creatinine clearance less than 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-chemotherapy and 80 mg PO once daily in the morning on Days 2 and 3

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 1 hour, then CISplatin IV in 500 mL NS with 20 mEq KCl, 1 g MgSO ₄ , 30 g mannitol over 1 hour

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
greater than or equal to 1	and	greater than 100	100%
0.5-0.99	or	75-100	75%
less than 0.5	or	less than 75	Delay*
*CISplatin also delayed			

For gemcitabine day 8 of each cycle

ANC (x 10 ⁹ /L)		Platelets (x 10 ⁹ /L)	Dose**
greater than or equal to 1	and	greater than 100	100%
0.5-0.99	or	75-100	75%
less than 0.5	or	less than 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
greater than or equal to 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%
less than 45	Delay	Delay/omit *
*Delay if day 1; if day 8, omit if <u>serum</u> creatinine greater than 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 at (250) 712-3900 or 1-800-563-7773 with any problems or questions regarding this treatment program.

Date activated: 01 January 2005 (as UGUNAJPG)

Date revised: 1 June 2011 (Infusion section 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.