

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

Protocol Code

UGUAJPG

Tumour Group

Genitourinary

Contact Physician

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ELIGIBILITY:

- Urothelial bladder cancer, clinical M0
- Able to start treatment within 90 days of radical (total) cystectomy
- Pathologic stage pT3 or pT4, and/or node +ve (pN1-3), no gross residual disease
- ECOG performance status 0 or 1
- Patients eligible for the NCIC BL8 trial should be offered study participation
- 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 (creatinine clearance less than 60 ml/min by GFR measurement or Cockcroft formula)
- Major co-morbid illness

TESTS:

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

PREMEDICATIONS:

- Antiemetic protocol for highly emetogenic chemotherapy protocols (see protocol SCNAUSEA).

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

Repeat every 21 days for 4 cycles.

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 1.0	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 1.0	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 D1	100%
45 - 59	35 mg/m ² D1+2 (same prehydration as 70 mg/m ² dose)	100%
less than 45	Delay	See below *

***Delay if day 1; if day 8 or 15, omit if serum 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. Nevin Murray or tumour group delegate at (604) 877-2730 or 1-800-663-3333 with any problems or questions regarding this treatment program.

Date activated: 01 July 2002

Date revised: 1 Aug 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. Stockle M, Meyenburg W, Wellek S, et al. Advanced bladder cancer (stages pT3b, pT4a, pN1 and pN2): improved survival after radical cystectomy and 3 adjuvant cycles of chemotherapy. Results of a controlled prospective study. *Journal of Urology* 1992;148(2 Pt 1):302-6; discussion 6-7.
3. Adjuvant chemotherapy in invasive bladder cancer: a systematic review and meta-analysis of individual patient data Advanced Bladder Cancer (ABC) Meta-analysis Collaboration. *Eur Urol* 2005;48(2):189-99; discussion 99-201.