

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

Protocol Code UGUAJPG

Tumour Group Genitourinary

Contact Physician Dr. Nevin Murray (VCC)

Dr. Heidi Martins (VICC)

GU Systemic Therapy Contacts Dr. Susan Ellard (CCSI)

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 <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 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 4 cycles.

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

***Delay if day 1; if day 8 or 15, 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. Nevin Murray or tumour group delegate @ (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 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. 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.