

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

Protocol Code

GUAVPG

Tumour Group

Genitourinary

Contact Physician

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ELIGIBILITY:

- Advanced urothelial carcinoma
- ECOG performance status 0, 1 or 2
- A BCCA “Class II Drug Registration Form” form for gemcitabine must be submitted

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:
 - Days 1: CBC & differential, platelets, creatinine, liver function tests, bilirubin
 - Day 8: CBC & 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 to two cycles beyond best response (maximum 6 cycles).
Discontinue if no response after 2 cycles.

Note: A growing international consensus is recommending that the 28 day cisplatin and gemcitabine cycle be replaced with a 21 day cycle that delivers the same dose of cisplatin on day 1 and gemcitabine 1250 mg/m² on days 1 and 8.

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 <u>serum</u> creatinine > 3 x ULN where ULN = local upper limit of normal range.		

**Alternatively, carboplatin may be used instead of cisplatin:
(See table below for modified Gemcitabine dosing)**

DRUG	DOSE	BCCA Administration Guidelines
Carboplatin	AUC 5 DAY 1 only Dose = AUC x (GFR* +25)	IV in 250mL D5W over 30 minutes.

* *Measured GFR* (e.g. nuclear renogram) is preferred whenever feasible, *particularly* in circumstances of co-morbidity that could affect renal function (third-space fluid accumulations, hypoproteinemia, potentially inadequate fluid intake, etc.). The lab reported GFR (MDRD formula) may be used as an alternative to the Cockcroft-Gault estimate of GFR.

Cockcroft-Gault Formula

$$\text{GFR} = \frac{N^* \times (140 - \text{age in years}) \times \text{wt (kg)}}{\text{serum creatinine (umol/L)}}$$

Note: The same method of estimation should be used throughout the treatment course (i.e. if lab reported GFR was used initially, this should be used for dosing in all subsequent cycles and not the Cockcroft-Gault estimate).

*For males N = 1.23; for females N = 1.04

When carboplatin is used, gemcitabine dose should be reduced:

DRUG	DOSE	BCCA Administration Guidelines
Gemcitabine	1000 mg/m ² /day on days 1 and 8 (total dose per cycle = 2000 mg/m ²)	IV in 250 mL NS over 30 min

PRECAUTIONS:

- Neutropenia:** Fever or other evidence of infection must be assessed promptly and treated aggressively.
- 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.
- 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 Aug 2001 (activated as UGUGEMCIS)

Date revised: 1 Mar 2008 (antiemetics revised)

References:

- 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.