

# BCCA Protocol Summary for Therapy for Transitional Cell Cancers of the Urothelium using Methotrexate, Vinblastine, Doxorubicin and Cisplatin

**Protocol Code** GUMVAC

**Tumour Group** Genitourinary

**Contact Physician** Dr. Nevin Murray

**GU Systemic Therapy Contacts** CCSI Drs. Susan Ellard, Judy Sutherland  
VCC Drs. Nevin Murray, Kim Chi  
VICC Drs Heidi Martins, Catherine Fitzgerald

## ELIGIBILITY/TESTS:

- Histologically documented transitional cell carcinoma of the urinary tract.
- Unresectable locally-advanced tumor or metastatic disease.
- Adjuvant therapy of high risk completely resected tumour (pT3B, pT4A or any pT) node positive.
- Not receiving concurrent radiotherapy.
- Performance status 0-2.
- Calculated creatinine clearance greater than or equal to 60 mL/min (Cockcroft).
- Bilirubin less than or equal to 1.5 x upper limit of normal.
- No evidence of pre-existing congestive heart failure.

## PREMEDICATIONS ON DAY 2:

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

## TREATMENT: OUTPATIENT ADMINISTRATION

| Drug         | Dose                                   | BCCA Administration Guideline   |
|--------------|--|---|
| Methotrexate | 30 mg/m <sup>2</sup> on days 1, 15, 22 | slow IV push  |
| Vinblastine  | 3 mg/m <sup>2</sup> on days 2, 15, 22  | slow IV push  |
| Doxorubicin  | 30 mg/m <sup>2</sup> on day 2          | slow IV push  |
| Cisplatin    | 70 mg/m <sup>2</sup> on day 2          | Prehydrate with 1000 mL NS over 60 minutes, then Cisplatin IV in 500 mL NS with 20 mEq potassium chloride, 1 g magnesium sulfate, 30 g mannitol over 1 hour |

Adjuvant: Repeat cycle every 28 days x 3 cycles.

Advanced: Repeat cycle every 28 days x 2-4 cycles then reassess.

## DOSE MODIFICATIONS:

### 1. Hematological: methotrexate, vinblastine and doxorubicin:

| Total Granulocytes               | Dose   |
|----------------------------------|--|
| 1-1.5 x 10 <sup>9</sup> /L       | 66%  |
| less than 1 x 10 <sup>9</sup> /L | delay 1 week or until recovery for day 1, 2 omit for days 15, 22 |

| Platelets                         | Dose  |
|-----------------------------------|---|
| less than 90 x 10 <sup>9</sup> /L | delay 1 week or until recovery for day 1,2 omit for days 15, 22 |

### 2. Renal Dysfunction: Cisplatin

- Calculated creatinine clearance greater than 45 mL/min but less than 60 mL/min, reduce cisplatin by 25%.
- Hold cisplatin if creatinine clearance less than or equal to 45 ml/min

### 3. Renal dysfunction: Dose modification of methotrexate may be required.

BC Cancer agency Cancer Drug Manual© suggested dose modifications:

| Creatinine clearance (mL/min) | Methotrexate dose |
|-------------------------------|-------------------|
| 61-80                         | 75%               |
| 51-60                         | 70%               |
| 10-50                         | 30-50%            |
| less than 10                  | avoid             |

$$\text{Calculated creatinine clearance} = \frac{1.04 \times (140 - \text{Age}) \times \text{weight (kg)}}{\text{Serum Creatinine in micromol/L}}$$

## PRECAUTIONS:

- Fatigue, nausea, vomiting, alopecia common. Cardiac toxicity from doxorubicin. Renal toxicity. Good hydration prior to and after treatment necessary.

## BENEFITS

In a Phase 3 trial, MVAC has been shown to be superior to cisplatin alone, with response rate 39% (vs 12%), median time to progression 10 months (vs 4.3

months) and median overall survival 12.5 months (vs 8.2 months,  $p=.0002$ ). However toxicity was substantial and greater than the single agent.

**Call Dr. Nevin Murray or Cancer Centre tumour group delegate listed above at (604) 877-6000 or 1-800-663-3333 with any problems or questions regarding this treatment program.**

Date activated      N/A

Date revised      01 June 2011 (Infusion section revised)

## **REFERENCE**

Loehrer PJ, Einhorn LH, Elson PJ, et al. A randomized comparison of cisplatin alone or in combination with methotrexate, vinblastine, and doxorubicin, in patients with metastatic urothelial carcinoma: a cooperative group study. *J Clin Oncol* 1992;10:1066-73.