

BCCA Protocol Summary for Therapy for Transitional Cell Cancers of the Urothelium using Methotrexate, vinBLASStine, DOXOrubicin and CISplatin

Protocol Code

GUMVAC

Tumour Group

Genitourinary

Contact Physicians

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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 ² on days 1, 15, 22	IV push
vinBLASStine	3 mg/m ² on days 2, 15, 22	IV in 50 mL NS over 15 minutes
DOXOrubicin	30 mg/m ² on day 2	IV push
CISplatin	70 mg/m ² 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 ⁹ /L	66%
less than 1 x 10 ⁹ /L	delay 1 week or until recovery for day 1, 2 omit for days 15, 22
Platelets	Dose
less than 90 x 10 ⁹ /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.

Contact [Dr. Bernie Eigl](#), [Dr. Christian Kollmannsberger](#) or tumour group delegate at (604) 877-2730 or 1-800-663-3333 with any problems or questions regarding this treatment program.

Date activated N/A
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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.