BC Cancer Protocol Summary for Combined Modality Therapy for Squamous Cell Cancer of the Genitourinary System using Fluorouracil and CISplatin with Radiation

Protocol Code	*GUFUPRT*
Tumour Group	*Genitourinary*
Contact Physician	*GU Systemic Therapy*

ELIGIBILITY:

- Locally advanced or metastatic squamous cell cancer of the genitourinary system.
- Any age. Patients over 69 years will be assessed individually.
- ECOG performance status 0-2.
- No hearing impairment.
- Adequate bone marrow function.
- Creatinine clearance greater than 50 mL/minute as calculated by Cockcroft/Gault formula.

TESTS:

- Baseline: CBC & Diff, platelets, creatinine, albumin, *DPYD* test (not required if previously tested, or tolerated fluorouracil or capecitabine)
- Before each treatment: CBC & Diff, platelets, creatinine
- If clinically indicated: total bilirubin, ALT, LDH, alkaline phosphatase

PREMEDICATIONS:

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

TREATMENT:

Chemotherapy:

Drug	Dose	BC Cancer Administration Guideline
CISplatin	25 mg/m^2 daily x 3 days* (total dose per cycle = 75 mg/m^2)	IV in 100 to 250 mL NS over 30 minutes
fluorouracil	1000 mg/m^2/day for 4 days (total dose = 4000 mg/m^2 over 96 h)	IV in D5W to a total volume of **480** mL by continuous infusion at **5** mL/h via appropriate infusor device**

*For patients with an excellent performance status who are being treated before radiation therapy has begun, the CISplatin total dose may be increased to 100 mg/m^2 given as 25 mg/m^2 daily for 4 days (cycles 1-4). In some circumstances the total dose of CISplatin may be given as a single dose with appropriate pre and post hydration.

**Inpatients: 1000 mg/m^2/day in 1000 mL D5W by continuous infusion daily over 24 h for 4 days

Repeat every 28 days x 4-6 cycles.
Discontinue if no response after 2 cycles.

Radiation Therapy: [policy awaiting input from GU Radiation Oncology Group].

DOSE MODIFICATIONS:

Fluorouracil Dosing Based on DPYD Activity Score (DPYD-AS)
Refer to "Fluorouracil and Capecitabine Dosing Based on DPYD Activity Score (DPYD-AS)" on www.bccancer.bc.ca/health-professionals/clinical-resources/cancer-drug-manual.

1. **Hematological:**

Day 1 counts:

ANC (x10^9/L)		Platelets (x10^9/L)	Dose - Fluorouracil only
greater than or equal to 1.5	and	greater than or equal to 100	100%
less than 1.5	or	less than 100	Delay x 1 week then reassess

2. **Renal dysfunction:**

Creatinine clearance based on day 1 serum creatinine. Recalculate using current weight.

Creatinine clearance (By Cockcroft/Gault formula)	**Dose - CISplatin only**
greater than 75 mL/minute	100%
50 to 75 mL/minute	50%
less than 50 mL/minute	Delay x 1 week then reassess

Cockcroft/Gault formula:

$$CrCl = \frac{N\ (140\text{-}age) \times weight\ (kg)}{serum\ creatinine\ (micromol/L)}$$

Where N = 1.04 for females, and 1.23 for males

3. **Neurotoxicity:** If clinically significant hearing loss or functionally significant peripheral neuropathy occurs, discontinue CISplatin. Replace with mitoMYcin 10 mg/m^2 on day 1 of every second cycle (maximum cumulative dose 20 mg/m^2). (See BCCA Cancer Drug Manual for administration guidelines).
4. **Gastrointestinal Toxicity:**
   (a) **Nausea and vomiting:** Grade 4 (greater than 10 episodes in 24 h or requires parenteral support, dehydration) - not helped by antiemetics. Decrease CISplatin dose to 80%, or QUIT.
   (b) **Stomatitis:** Grade 3-4 (painful erythema, edema or ulcers and cannot eat). If necessary, delay next cycle until recovery. Decrease duration of fluorouracil infusion to 3 days (1000 mg/m^2/24 hours x 72 hours; total dose per cycle = 3000 mg/m^2).
   (c) **Diarrhea:** Grade 4 (increase of greater than or equal to 10 stools/day or grossly bloody diarrhea; dehydration). Decrease duration of fluorouracil infusion to 3 days (1000 mg/m^2/24 hours x 72 hours; total dose per cycle = 3000 mg/m^2).

PRECAUTIONS:

1. **Nausea and vomiting** are common and patients should be treated with ondansetron and dexamethasone (at a minimum) before each dose of CISplatin (see premedication section)
2. **Renal toxicity** may occur with a salt and water losing nephropathy. Patients should be encouraged to maintain good oral hydration.
3. **Myocardial ischemia and angina occurs rarely in patients receiving fluorouracil or capecitabine.** Development of cardiac symptoms including signs suggestive of ischemia or of cardiac arrhythmia is an indication to discontinue treatment. If there is development of cardiac symptoms patients should have urgent cardiac assessment. Generally re-challenge with either fluorouracil or capecitabine is not recommended as symptoms potentially have a high likelihood of recurrence which can be severe or even fatal. Seeking opinion from cardiologists and oncologists with expert knowledge about fluorouracil / capecitabine toxicity is strongly advised under these circumstances. The toxicity should also be noted in the patient's allergy profile.
4. **CNS toxicity** such as tinnitus, mild high frequency hearing loss and delayed peripheral neuropathy may occur secondary to CISplatin.
5. **Nutrition**: It is important to maintain weight if possible and early consultation with a dietitian to advise about aggressive oral nutritional support and/or an enteral feeding tube is recommended.
6. **Possible drug interactions with fluorouracil and warfarin, phenytoin and fosphenytoin** have been reported and may occur at any time. Close monitoring is recommended (eg, for warfarin, monitor INR weekly during fluorouracil therapy and for 1 month after stopping fluorouracil).

Call GU Systemic Therapy physician at your regional cancer centre with any problems or questions regarding this treatment program.

References:

1. Shammas FV, Ous S, Fossa SD. Cisplatin and 5-fluorouracil in advanced cancer of the penis. J Urol 1992;147:630-2