

BC Cancer Protocol Summary for Therapy for Advanced Renal Cancer Using Temsirolimus

Protocol Code

GUTEM

Tumour Group

Genitourinary

Contact Physician

C. Kollmannsberger

ELIGIBILITY:

- Advanced renal cell carcinoma with poor prognostic factors
- Any histology

EXCLUSIONS:

- Major surgery within the last 4 weeks
- Caution is advised for patients with significant lung compromise due to the risk for pneumonitis
- Concomitant Immunosuppressive therapies excluding corticosteroids as antiemetic or anaphylactic prophylaxis

TESTS:

- **Baseline:** CBC, differential, platelets, sodium, potassium, creatinine, BUN, glucose, calcium, phosphorus, ALT, LDH, total bilirubin, alkaline phosphatase, total cholesterol, triglycerides, appropriate radiographic evaluations including Chest X-ray, Oxygen saturation, if on anticoagulants: INR, PTT
- **Before each treatment:** CBC, differential, platelets, if on anticoagulants: INR, PTT
- **Prior to each cycle:**
 - CBC, differential, platelets
 - (required, but results do not have to be available to proceed with first treatment): sodium, potassium,, creatinine, BUN, glucose, calcium, phosphorus, ALT, LDH, total bilirubin, alkaline phosphatase, total cholesterol, triglycerides
- If clinically indicated: any abnormal baseline tests
- Response evaluation recommended every 8-10 weeks

PREMEDICATIONS:

- diphenhydramINE 25-50 mg IV given 30 minutes prior to start of each temsirolimus infusion.

TREATMENT:

Drug	Dose	BC Cancer Administration Guideline
temsirolimus	25 mg	IV in 250 mL NS (non-DEHP bag) over 30 min to 1 hour (non-DEHP tubing with 0.2 micron in-line filter)

repeat once weekly; 4 weeks of treatment comprise 1 cycle.

Subsequent doses may be given up to two days early or late because of holiday or scheduling reasons

Discontinue if tumor progression or if patient with Grade 3-4 toxicities fail to recover to Grade 0-2 within three weeks.

DOSE MODIFICATIONS:

Dose levels:

Standard	25 mg
Dose level – 1	20 mg
Dose level -2	15 mg

1. Hematological

ANC (x10 ⁹ /L)		Platelets (x10 ⁹ /L)	Dose
greater than or equal to 1.0	and	greater than or equal to 75	100%
less than 1.0	or	less than 75	Hold until ANC greater than or equal to 1.0 and/or PLT greater than or equal to 75 Reduce dose by 1 dose level

2. Temsirolimus Related Toxicity: Dose modification required for Temsirolimus.

Grade of Temsirolimus related adverse events	Dose Adjustments
Grade 0-2	100% Grade 2 adverse events that are persistent and intolerable can result in dose delays or dose reductions to the next lower dose level
Grade 3-4	Hold therapy until recovery to grade 0-2 If recovery within 3 weeks, reduce dose by one dose level for subsequent treatment.

PRECAUTIONS:

1. **Neutropenia:** Fever or other evidence of infection must be assessed promptly and treated aggressively. Refer to BC Cancer Febrile Neutropenia Guidelines.
2. **Hypersensitivity:** For reactions with Temsirolimus refer to BC Cancer Hypersensitivity Guidelines.
3. Temsirolimus is predominantly metabolized and excreted through cytochrome p4503A4 in the liver. Potential drug interactions with cytochrome P4503A4 interacting agents must be considered.
(see also: <http://medicine.iupui.edu/flockhart/table.htm>)
4. **Renal impairment:** Only a very small percentage of Temsirolimus and its metabolites is excreted by the kidney. Temsirolimus appears safe in patients with mild renal impairment (creatinine less than or equal to 2x upper limit of normal).

No data exist for temsirolimus in patients with moderate to severe kidney failure.

5. **Hepatic impairment:** Temsirolimus is mainly metabolized and excreted through the liver. Temsirolimus appears safe in patients with mild hepatic impairment (bilirubin less than or equal to 1.5x upper limit of normal).

No data exist for temsirolimus in patients with moderate to severe hepatic impairment.

6. **Lung dysfunction:** Caution is advised for patients with significant lung dysfunction due to the risk for pneumonitis (mTOR inhibitor class effect)

Call Dr. Kollmannsberger or tumour group delegate at (604) 877-6000 or 1-800-663-3333 with any problems or questions regarding this treatment program.

References:

Hudes G, Carducci M, Tomczak P et al. Temsirolimus, Interferon Alfa, or Both for Advanced Renal-Cell Carcinoma. NEJM 2007;356 (22): 2271-2281