BC Cancer Protocol Summary for Palliative Therapy for Renal Cell Carcinoma Using SORAfenib

Protocol Code	*GUSORAF*
Tumour Group	*Genitourinary*
Contact Physician	*Dr. C. Kollmannsberger*

ELIGIBILITY:

- Advanced renal cell carcinoma after cytokine failure
- Any histology and IMDC risk group
- ECOG performance status less than or equal to 2
- Severe early toxicity from Sunitinib (in selected patients)
- Patients unsuitable for first-line Sunitinib (If patient exhibits poor prognosis criteria consider Temsirolimus (GUTEM)

EXCLUSIONS:

- Significant cardiovascular disease and/or known LVEF less than 50%
- Uncontrolled hypertension

TESTS:

- Baseline: CBC, differential, platelets, sodium, potassium, creatinine, total protein, albumin, bilirubin, alkaline phosphatase, urine analysis, thyroid stimulating hormone.
- Before each cycle: CBC, differential and platelets, creatinine, ALT, Bilirubin.
- MUGA scan or echocardiogram if clinically indicated or if history of cardiac problems

PREMEDICATIONS:

- Antiemetic not usually required

TREATMENT:

Drug	Dose	BC Cancer Administration Guideline
SORAfenib	400 mg BID continuously*	PO

*Each cycle consists of 4 weeks of SORAfenib.

Dose reduction:
Dose level -1: 400 mg **once** a day continuously
Dose level -2: 400 mg **every other day** continuously

DOSE MODIFICATIONS:

1. **Hematological**

ANC ($x10^9$/L)		Platelets ($x10^9$/L)	Dose (all drugs)
greater than or equal to 1.0	and	greater than or equal to 75	100%
less than 1.0	or	less than 75	Delay

2. Non-Hematological toxicity:

CTC-Grade	Dose
1-2	100%
3-4	Delay until less than or equal to grade 1 Dose reduce by 1 dose level

3. **Renal dysfunction:** Only a very small percentage of SORAfenib and its metabolites are excreted by the kidney. SORAfenib appears safe in patients with mild renal impairment (creatinine less than or equal to 2x upper limit of normal).

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

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

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

PRECAUTIONS:

1. **Neutropenia**: Fever or other evidence of infection must be assessed promptly and treated aggressively. Refer to BC Cancer Febrile Neutropenia Guidelines.
2. **Cardiac Toxicity:**

Asymptomatic Patients – SORAfenib continuation based on serial LVEFs, if performed for clinical indication

Relationship of LVEF to LLN	Absolute Decrease Of less than 10%	Absolute Decrease Of 10 -15%	Absolute Decrease Of greater than or equal to 16%
Within Normal Limits	Continue	Continue	Hold *
1-5% below LLN	Continue	Hold *	Hold *
greater than or equal to 6 % below LLN	Continue *	Hold *	Hold *

- *Repeat LVEF assessment after 4 weeks
- If criteria for continuation are met – resume SORAfenib
- If 2 consecutive holds or a total of 3 holds occur, discontinue SORAfenib

Symptomatic Patients

- Symptomatic patients with evidence of cardiac dysfunction should have SORAfenib discontinued.

Precautions:

- SORAfenib is predominantly metabolized and excreted through cytochrome P4503A4 in the liver. Potential drug interactions with cytochrome P4503A4 interacting agents must be considered.

- Patients with hypertension should exercise caution while on SORAfenib. Rigorous treatment of blood pressure is necessary, since SORAfenib can cause a rapid onset of high blood pressure. Temporary suspension of SORAfenib is recommended for patients with severe hypertension (greater than 200 mmHg systolic or greater than 110 mmHg diastolic). Treatment with SORAfenib may be resumed once hypertension is controlled.

- It is recommended that for at least the first 2 cycles of treatment patients monitor their blood pressure daily (home measurements, GP's office, etc. and keep a journal of their blood pressure measurements that can be submitted to the physician at the next appointment.

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:

1. Escudier B, Eisen T, Stadler WM, et al. Sorafenib in advanced clear-cell renal-cell carcinoma. N Engl J Med 2007;356(2):125-34.
2. Szczylik C, Demkow T, Staehler M, et al. Randomized phase II trial of first-line treatment with sorafenib versus interferon in patients with advanced renal cell carcinoma: Final results. J Clin Oncol ASCO Annual Meeting Proceedings Part I. Vol 25, No. 18S (June 20 Supplement): 5025, 2007