BCCA Protocol Summary for Therapy for Advanced Hepatocellular Carcinoma Using SORAfenib (NEXAVAR®)

Protocol Code: UGISORAF

Tumour Group: Gastrointestinal

Contact Physician: Dr. Sharlene Gill

ELIGIBILITY:
- Patients with inoperable advanced hepatocellular carcinoma
- ECOG performance status less than or equal to 2 and Child-Pugh A status
- Platelets greater than 60, Bilirubin less than 2.5 X upper limit of normal, AST less than or equal to 5 times upper limit of normal, serum creatinine less than or equal to 1.5 X upper limit of normal
- BC Cancer Agency Compassionate Access Program (CAP) approval

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

TESTS:
- Baseline: CBC, differential, platelets, electrolytes, creatinine, total protein, albumin, bilirubin, alkaline phosphatase, INR.
- Prior to 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:

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>BCCA Administration Guideline</th>
</tr>
</thead>
<tbody>
<tr>
<td>SORAfenib</td>
<td>400 mg BID continuously</td>
<td>PO</td>
</tr>
</tbody>
</table>

One cycle is 28 days

Dose reduction:
- Dose level -1: 400 mg once a day continuously
- Dose level -2: 400 mg every other day continuously
- If dose level -2 not tolerated then discontinue.
DOSE MODIFICATIONS:

1. Hematological

<table>
<thead>
<tr>
<th>ANC (x10^9/L)</th>
<th>Platelets (x10^9/L)</th>
<th>Dose (all drugs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>greater than or equal to 1.0 and greater than or equal to 50</td>
<td>100%</td>
<td></td>
</tr>
<tr>
<td>greater than 0.5 – 1.0 and greater than or equal to 50</td>
<td>Decrease one dose level</td>
<td></td>
</tr>
<tr>
<td>less than or equal to 0.5 or less than 50</td>
<td>Delay until ANC greater than 0.5 and platelets greater than 50 then decrease one dose level. If no recovery after 4 weeks, treatment should be discontinued.</td>
<td></td>
</tr>
</tbody>
</table>

2. Non-Hematological toxicity:

<table>
<thead>
<tr>
<th>CTC-Grade</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-2</td>
<td>100%</td>
</tr>
<tr>
<td>3</td>
<td>Delay until less than or equal to Grade 2 then decrease one dose level</td>
</tr>
<tr>
<td>4</td>
<td>Discontinue therapy</td>
</tr>
</tbody>
</table>

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 BCCA Febrile Neutropenia Guidelines.

2. Cardiac Toxicity: Symptomatic patients with evidence of cardiac dysfunction should have SORAfenib discontinued.
3. **SORAfenib** 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. 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 (see also http://www.hypertension.ca).

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

**Date activated:** 1 Jan 2008

**Date revised:** 1 Feb 2017 (TALLman lettering formatted)

**References:**