BCCA Protocol Summary for Palliative Therapy for Renal Cell Carcinoma Using PAZOpabn

Protocol Code
UGUPAZO

Tumour Group
Genitourinary

Contact Physician
Dr. C. Kollmannsberger

ELIGIBILITY:
- Advanced renal cell carcinoma
- No prior systemic therapy (first-line therapy) or prior cytokines
- ECOG performance status less than or equal to 2
- Compassionate Access Program (CAP) approval granted by BCCA

EXCLUSIONS:
- Pregnancy
- Moderate or severe hepatic impairment (baseline plasma bilirubin greater than 1.5 x ULN and ALT elevations of greater than 2 x ULN)
- Significant cardiovascular disease and/or LVEF less than 45%
- Uncontrolled hypertension

TESTS:
- Baseline: CBC and differential, platelets, electrolytes, creatinine, total protein, albumin, bilirubin, alkaline phosphatase, ALT, AST, urine analysis, TSH
- Every 2 weeks for Cycle 1 and 2: CBC and differential, platelets, creatinine, ALT, AST, bilirubin
- Before Cycle 3 and each subsequent cycle: CBC and differential, platelets, creatinine, ALT, AST, bilirubin; TSH every other cycle or if clinically indicated
- MUGA scan or echocardiogram if clinically indicated or if history of cardiac problems

PREMEDICATIONS:
- Antiemetic protocol for low emetogenic chemotherapy protocols (see SCNAUSEA)

TREATMENT:

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>BCCA Administration Guideline</th>
</tr>
</thead>
<tbody>
<tr>
<td>PAZOpabn</td>
<td>800 mg once daily</td>
<td>PO on an empty stomach (at least one hour before or two hours after a meal). Do not break or crush tablet; swallow whole with a glass of water.</td>
</tr>
</tbody>
</table>

1 cycle = 4 weeks
**Dose reduction:**
Dose level – 1: 400 mg  
Dose level – 2: 200 mg

**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 and Greater than or equal to 75</td>
<td>100%</td>
<td></td>
</tr>
<tr>
<td>Less than 1 or Less than 75</td>
<td>Delay</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>
</tbody>
</table>
| 3-4 | Delay until less than or equal to grade 1  
Dose reduce by 1 dose level |

3. **Dosage in hepatic impairment:**

<table>
<thead>
<tr>
<th>Bilirubin total (µmol/L)</th>
<th>ALT (IU/L)</th>
<th>AST (IU/L)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than or equal to 1.5 X ULN and Less than or equal to 2 X ULN</td>
<td>Less than or equal to 2 X ULN and Less than or equal to 2 X ULN</td>
<td>100%</td>
<td></td>
</tr>
<tr>
<td>More than 1.5 X ULN and More than 2 -3 X ULN</td>
<td>More than 3 X ULN</td>
<td>Hold until ALT less or equal to 2.5 X ULN; If benefit outweighs risk, restart at reduced dose no more than 400 mg PO once daily and measure serum liver tests weekly x 8 weeks</td>
<td></td>
</tr>
<tr>
<td>More than 1.5 X ULN and More than 3 X ULN</td>
<td>-</td>
<td>Delay</td>
<td></td>
</tr>
</tbody>
</table>

**PRECAUTIONS:**

1. **Neutropenia:** Fever or other evidence of infection must be assessed promptly and treated aggressively. Refer to BCCA Febrile Neutropenia Guidelines.

2. **Hepatic dysfunction:** PAZOpanib is mainly metabolized and excreted through the liver. PAZOpanib appears safe in patients with mild hepatic impairment (bilirubin less than or equal to 1.5 x upper limit of normal). Therapy with PAZOpanib may result in hepatobiliary abnormalities (increase of serum transaminase levels and bilirubin). Severe and fatal hepatotoxicity has been reported. It is important to
monitor serum liver tests (ALT, AST, bilirubin) prior to initiation of PAZOpainb, increase frequency of monitoring during weeks 2, 4, 6, 8 and prior to each cycle or as clinically indicated.

3. **Renal dysfunction**: Only a very small percentage of PAZOpainb and its metabolites are excreted by the kidney. PAZOpainb appears safe in patients with mild renal impairment (creatinine clearance greater than or equal to 30 mL/min). No data exist for PAZOpainb in patients with severe renal impairment or in patients undergoing peritoneal dialysis or hemodialysis.

4. **PAZOpainb** is predominantly metabolized and excreted through cytochrome P450 3A4 in the liver. Potential drug interactions with cytochrome P450 3A4 interacting agents must be considered (see also: [http://medicine.iupui.edu/flockhart/table.htm](http://medicine.iupui.edu/flockhart/table.htm)).

5. **Hypertension**: Patients with hypertension should exercise caution while on PAZOpainb. Blood pressure should be well controlled prior to initiating treatment. Treatment with PAZOpainb should be discontinued if there is evidence of hypertensive crisis or if hypertension is severe and persists despite anti-hypertensive therapy and PAZOpainb dose reduction. 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.

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:**