BC Cancer Protocol Summary for Palliative Therapy for Metastatic Castration Resistant Prostate Cancer Using Abiraterone and predniSONE

Protocol Code: UGUPABI

Tumour Group: Genitourinary

Contact Physician: Dr. Kim Chi

ELIGIBILITY:
- ECOG performance status 0-2
- Life expectancy greater than 3 months
- Patients with metastatic castration resistant prostate cancer who are either chemotherapy naïve or have received prior chemotherapy containing DOCEtaxel*
- Bilirubin less than ULN, AST/ALT less than 2.5 x ULN, Alkaline Phosphatase less than 6 x ULN
- Serum potassium more than 3.5 mmol/L
- A BC Cancer "Compassionate Access Program" (CAP) request must be approved prior to treatment
* Patients are eligible to receive abiraterone (UGUPABI) OR enzalutamide (UGUPENZ) OR cabazitaxel (UGUPCABA) but not sequential use of these agents.

EXCLUSIONS:
- Bilirubin greater than 1.5 x ULN, AST or ALT greater than 2.5 x ULN
- Uncontrolled hypertension (systolic blood pressure greater than 160 mmHg or diastolic greater than 95 mmHg)
- Active or symptomatic viral hepatitis or chronic liver disease
- History of adrenal dysfunction
- Clinically significant heart disease (LVEF less than 50% at baseline)

TESTS:
- Baseline: CBC and differential, platelets, bilirubin, liver enzymes, creatinine, glucose, electrolytes
- Before each treatment (every 4 weeks = 1 cycle): CBC & diff, platelets, liver enzymes, bilirubin, creatinine, glucose, electrolytes, blood pressure.
- For cycles 1 to 3: Monitor blood pressure, serum potassium, liver enzymes, bilirubin every 2 weeks
- PSA every 4 weeks
- MUGA scan or echocardiogram if clinically indicated or if history of cardiac problems

Warning: The information contained in these documents are a statement of consensus of BC Cancer professionals regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is at your own risk and is subject to BC Cancer's terms of use available at www.bccancer.bc.ca/legal.htm
TREATMENT:
Androgen ablative therapy (eg, LHRH agonist, LHRH antagonist) should be maintained.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>BCCA Administration Guideline</th>
</tr>
</thead>
<tbody>
<tr>
<td>abiraterone</td>
<td>1000 mg</td>
<td>PO daily on an empty stomach (one hour before or two hours after a meal)</td>
</tr>
<tr>
<td>predniSONE*</td>
<td>10 mg daily (or 5 mg bid)</td>
<td>PO daily</td>
</tr>
</tbody>
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* Dexamethasone may be substituted for patient or physician preference, based upon toxicity and patient tolerance. When substituting dexamethasone for predniSONE, the dose is 1.5 mg daily.

DOSE MODIFICATIONS:

1. Hepatic dysfunction:

<table>
<thead>
<tr>
<th>Bilirubin</th>
<th>AST and/or ALT</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than or equal to ULN–1.5 x ULN and Less than or equal to ULN to 2.5 x ULN</td>
<td>100%</td>
<td></td>
</tr>
<tr>
<td>1.5 – 3 x ULN and 2.5 – 5 x ULN</td>
<td>100%</td>
<td></td>
</tr>
<tr>
<td>greater than 3 x ULN or greater than 5 x ULN</td>
<td>Hold abiraterone. Monitor liver tests at least weekly until grade 1 (Bilirubin less than 1.5 x ULN, AST/ALT less than 2.5 x ULN) Reduce dose of abiraterone by 250 mg and resume only after liver tests less than or equal to grade 1</td>
<td></td>
</tr>
</tbody>
</table>

ULN = upper limit of normal

2. Hypokalemia Management:

Hypokalemia has been observed and should be aggressively managed. Serum potassium should be monitored closely in patients who develop hypokalemia.

<table>
<thead>
<tr>
<th>Serum potassium (mmol/L)</th>
<th>Grade of Hypokalemia</th>
<th>Action</th>
<th>Further Action or Maintenance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low potassium or History of hypokalemia</td>
<td>Weekly (or more frequent) laboratory electrolyte evaluations.</td>
<td>Titrate dose to maintain potassium greater than 3.5 mmol/L and less than 5.0 mmol/L (greater than 4.0 mmol/L recommended)</td>
<td></td>
</tr>
<tr>
<td>less than 3.5 – 3.0</td>
<td>Grade 1</td>
<td>Initiate oral or IV potassium supplementation. Consider monitoring magnesium and replacement if needed.</td>
<td>Titrate dose to maintain potassium greater than 3.5 mmol/L and less than 5.0 mmol/L (greater than 4.0 mmol/L recommended)</td>
</tr>
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<td>Serum potassium (mmol/L)</td>
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</tr>
<tr>
<td>less than 3.5 – 3.0</td>
<td>Grade 2</td>
<td>Withhold abiraterone until potassium corrected. Initiate oral or IV potassium supplementation. Consider monitoring magnesium and replacement if needed.</td>
<td>Titrate dose to maintain potassium greater than 3.5 mmol/L and less than 5.0 mmol/L (greater than 4.0 mmol/L recommended)</td>
</tr>
<tr>
<td>less than 3.0 – 2.5</td>
<td>Grade 3</td>
<td>Withhold abiraterone until potassium corrected. Initiate oral or IV potassium and cardiac monitoring. Consider monitoring magnesium and replacement if needed.</td>
<td></td>
</tr>
<tr>
<td>less than 2.5</td>
<td>Grade 4</td>
<td>Withhold abiraterone until potassium corrected. Initiate oral or IV potassium and cardiac monitoring. Consider monitoring magnesium and replacement if needed</td>
<td></td>
</tr>
</tbody>
</table>

**PRECAUTIONS:**

1. **Fluid retention:** Fluid retention can occur due to mineralocorticoid excess caused by compensatory adrenocorticotrophic hormone (ACTH) drive. The administration of prednisone will help reduce incidence and severity of fluid retention.

2. **Hypertension:** Patients with hypertension should exercise caution while on abiraterone. Rigorous treatment of blood pressure is necessary, since abiraterone can cause a rapid onset of high blood pressure. Blood pressure will need to be monitored once every 2 weeks for the first three months of abiraterone therapy. Temporary suspension of abiraterone is recommended for patients with severe hypertension (greater than 200 mmHg systolic or greater than 110 mmHg diastolic). Treatment with abiraterone may be resumed once hypertension is controlled (see also [http://www.hypertension.ca](http://www.hypertension.ca)).

3. **Renal impairment:** No dosage adjustment is necessary for patients with renal impairment.

4. **Hepatic Dysfunction:** Abiraterone undergoes hepatic metabolism. Hepatic dysfunction (particularly elevated AST and ALT) may occur during the first 3 months after starting treatment so a more frequent monitoring of liver function tests is required (every 2 weeks in the first three months and monthly thereafter).

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

**References:**

