BCCA Protocol Summary for Treatment of Uterine Sarcoma Cancer Using DOCEtaxel and Gemcitabine

Protocol Code: GOSADG
Tumour Group: Gynecology
Contact Physician: Dr. Paul Hoskins

ELIGIBILITY:
- Uterine sarcoma, advanced (residual disease) or recurrent or failed other chemotherapy
  - Leiomyosarcoma*
  - Endometrial stromal sarcoma*
  - Sarcoma NOS*
  - Malignant mixed mullerian (GOENDCAT recommended as first choice chemotherapy)

*Alternative possible treatments are (1) SAAI and (2) SAAVA (see sarcoma tumour group protocols). It is not known which alternative is superior so is physician choice between GOSADG, SAAI, SAAVA as first line choice.

EXCLUSIONS (RELATIVE):
- Warfarin (increased anticoagulation – monitor INR)
- Pneumonitis
- Liver impairment (Alk Phos greater than or equal to 5 x ULN, AST & ALT greater than or equal to 5 x ULN)
- PACLItaxel hypersensitivity
- Age greater than or equal to 80 years

TESTS:
- Baseline: CBC & diff, platelets, AST and/or ALT, Alk Phos, Creatinine, Tumour markers (optional), electrolytes (optional), imaging (optional)
- Before each treatment:
  - Day 1: CBC & diff, platelets; if abnormal at baseline: AST, ALT, Alk Phos, Creatinine.
  - Day 8 in Cycle 1 and in any Cycle when a dose adjustment has been made: CBC & diff, platelets.
- If clinically indicated: Tumour markers, imaging.
PREMEDICATIONS:
- Dexamethasone 8mg PO bid x 6 doses, starting 24 hours prior to DOCEtaxel.
- Antiemetic protocol for low emetogenic chemotherapy protocols (see SCNAUSEA)
- DOCEtaxel-induced onycholysis and cutaneous toxicity of the hands may be prevented by wearing frozen gloves starting 15 minutes before DOCEtaxel infusion until 15 minutes after end of DOCEtaxel infusion; gloves should be changed after 45 minutes of wearing to ensure they remain cold during the entire DOCEtaxel infusion.

TREATMENT:

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>BCCA Administration Guideline</th>
</tr>
</thead>
<tbody>
<tr>
<td>DOCEtaxel</td>
<td>80* mg/m² on Day 1</td>
<td>IV in 250** mL NS (non-DEHP bag) over 1 hour</td>
</tr>
<tr>
<td>gemcitabine</td>
<td>800* mg/m² on Day 1 and Day 8</td>
<td>IV in 250 mL NS over 30 minutes</td>
</tr>
</tbody>
</table>

* if greater than 80 years old or prior pelvic radiotherapy, start with 80% dosing. Can escalate to 100% in subsequent cycle if feasible.
** If 75 to 185 mg, use 250 mL bag. If greater than 185 mg, use 500 mL bag.

Repeat every 21 days x 6 cycles.
Discontinue if no response after 3 cycles.

DOSE MODIFICATIONS:

1. Hematological (Day 1):

<table>
<thead>
<tr>
<th>ANC (x10⁹/L)</th>
<th>Platelets (x10⁹/L)</th>
<th>DOCEtaxel</th>
<th>Gemcitabine</th>
</tr>
</thead>
<tbody>
<tr>
<td>greater than or equal to 1 and greater than or equal to 100</td>
<td>100%</td>
<td>100%</td>
<td></td>
</tr>
<tr>
<td>less than 1 and/or less than 100</td>
<td>delay</td>
<td>delay</td>
<td></td>
</tr>
<tr>
<td>upon recovery</td>
<td>80%</td>
<td>80%</td>
<td></td>
</tr>
</tbody>
</table>

NB - Dose may be increased at physician’s discretion, 10% per cycle.
If monocytes greater than or equal to 20% of total WBC count and neutrophils greater than or equal to 0.8, then count recovery is likely imminent, and treatment can proceed at 100% dose, at physician’s discretion.

Hematological (Day 8 – if applicable): hold Gemcitabine if ANC less than 0.5 and/or Platelets less than 100. For next cycle dosing, call Contact Physician.
2. **Hepatic dysfunction**: Dose modification required:

<table>
<thead>
<tr>
<th>ALK PHOS</th>
<th>AST and/or ALT</th>
<th>DOCEtaxel</th>
<th>Gemcitabine</th>
</tr>
</thead>
<tbody>
<tr>
<td>less than 2.5 x ULN</td>
<td>less than 1.5 x ULN</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>2.6 to 5 x ULN</td>
<td>1.6 to 5 x ULN</td>
<td>75%</td>
<td>100%</td>
</tr>
<tr>
<td>greater than 5 x ULN</td>
<td>greater than 5 x ULN</td>
<td>Discuss with contact MD</td>
<td></td>
</tr>
</tbody>
</table>

3. **Hemolytic Uremic Syndrome**: discontinue Gemcitabine.

4. **Peripheral Neuropathy**: if greater than or equal to Grade 2, reduce DOCEtaxel to 80% of previous dose.

5. **Pneumonitis**: discontinue Gemcitabine.

**PRECAUTIONS:**

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

2. **Extravasation**: DOCEtaxel causes pain and tissue necrosis if extravasated. Refer to BCCA Extravasation Guidelines.

3. **Hypersensitivity**: Reactions to DOCEtaxel are common but it is not necessary to routinely initiate the infusion slowly. If slow initiation of infusion is needed, start infusion at 30 mL/h x 5 minutes, then 60 mL/h x 5 minutes, then 120 mL/h x 5 minutes, then complete infusion at 250 mL/h (for 500 mL bag, continue 250 mL/h for 5 minutes and then complete infusion at 500 mL/h). Refer to BCCA Hypersensitivity Guidelines.

4. **Renal Toxicity**: Irreversible renal failure associated with Gemcitabine-induced hemolytic uremic syndrome may occur (rare). Use caution with pre-existing renal dysfunction.

5. **Pulmonary Toxicity**: Acute shortness of breath may occur. Discontinue Gemcitabine if drug-induced pneumonitis is suspected.

6. **Fluid retention**: Dexamethasone premedication must be given to reduce incidence and severity of fluid retention caused by DOCEtaxel.

7. **Hepatic Dysfunction**: DOCEtaxel undergoes hepatic metabolism. Hepatic dysfunction (particularly elevated AST) may lead to increased toxicity and usually requires a dose reduction (see table, above).
Call Dr. Hoskins or tumour group delegate @ (604) 877-6000 or 1-800-663-3333 with any problems or questions regarding this treatment program.

Date activated: 01 Dec 2009
Date revised: 1 Aug 2014 (non-PVC changed to non-DEHP)

References: