ELIGIBILITY:
- Premenopausal women (defined as those who have menstruated in the last three months or who are biochemically premenopausal) with metastatic breast cancer whose tumour expresses either the estrogen or progesterone receptor (or whose ER/PR status is unknown but who have had a disease free interval of over two years from initial diagnosis).
- Patients may have had prior adjuvant chemotherapy or adjuvant tamoxifen if breast cancer recurred greater than 1 year since coming off adjuvant tamoxifen.

EXCLUSIONS:
- Prior endocrine treatment for advanced disease.
- Patients with a history of significant thromboembolic disease.

TESTS:
- Baseline: GGT, ALT, LDH, Alk Phos and bilirubin; calcium and albumin in those with known bone metastases.
- 3-7 days after starting treatment in patients known to have bone metastases: serum calcium* and albumin.
  *corrected calcium (mmol/L) = total calcium (mmol/L) + (0.02 x [40 – albumin in g/L])
- If clinically indicated: Bilirubin, GGT, ALT, LDH, Alk Phos, Creatinine, CA 15-3.
- Annually: gynecological exam (patients with an intact uterus).

TREATMENT:

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>BC Cancer Administration Guideline</th>
</tr>
</thead>
<tbody>
<tr>
<td>tamoxifen</td>
<td>20 mg daily</td>
<td>PO</td>
</tr>
</tbody>
</table>
| buserelin (base) depot      | 6.3 mg every 6 weeks x 2 treatments then every 8 weeks | SC 
(SUPREFACT DEPOT®)*           | SC                                |
| or goserelin (ZOLADEX®)*    | 3.6 mg every 4 weeks                      | IM                                |
| or leuprolide (LUPRON®)*    | 7.5 mg every 4 weeks                      |                                   |

Continue until disease progression. **Strongly consider surgical oopherectomy in responding patients.**
*Once response has been established, the following long-acting agents may be substituted at the physician’s discretion. Menstrual function, and if necessary, hormone levels can be monitored to ensure effective dosing.

<table>
<thead>
<tr>
<th>Long-Acting Agent</th>
<th>Dosage</th>
<th>Route</th>
</tr>
</thead>
<tbody>
<tr>
<td>buserelin (base) depot</td>
<td>9.45 mg every 12 weeks</td>
<td>SC</td>
</tr>
<tr>
<td>(SUPREFACT DEPOT®)</td>
<td>10.8 mg every 12 weeks</td>
<td>SC</td>
</tr>
<tr>
<td>or goserelin (ZOLADEX®)</td>
<td>22.5 mg every 12 weeks</td>
<td>IM</td>
</tr>
<tr>
<td>or leuprolide (LUPRON®)</td>
<td></td>
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</tr>
</tbody>
</table>

**PRECAUTIONS:**

1. **Flare Response:** A transient increase in bone pain, local disease flare (swelling and redness) and/or hypercalcemia may occur when treatment is initiated. Hypercalcemia is more likely with bone metastases and may require aggressive treatment (see supportive care protocol SCHYPCAL).

2. **Myelosuppression:** Mild myelosuppression with transient thrombocytopenia may occur rarely. The association with tamoxifen is uncertain.

3. **Endometrial Cancer:** Annual gynecologic examinations are recommended. Pelvic complaints, such as unusual vaginal bleeding, require prompt evaluation.

4. **Ocular Toxicity:** Ocular toxicity is rare and may occur after only a few weeks of therapy, although it is more common with prolonged treatment. Ophthalmologic examination is recommended if visual disturbances occur.

5. **Thromboembolism:** Tamoxifen is associated with an increased risk of thromboembolism that is comparable to estrogen replacement therapy.

6. **Hepatotoxicity:** While hepatotoxicity is rare and usually presents as elevated hepatic enzymes, more serious liver abnormalities have been reported.

7. **Hyperlipidemia:** Elevations in cholesterol and triglycerides may occur in patients with pre-existing hyperlipidemias.

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

**References:**
