ELIGIBILITY:
- postmenopausal (including women with chemically induced menopause with LHRH agonists)
- Initial stage II or III only (pT2-4 pN0-3; pT0-4pN1-3), or
- Post neo-adjuvant chemotherapy stage ypT2-4 ypN0-3; ypT0-4 ypN1-3
- Biomarkers: ER any PR any
- Adequate renal function (CrCl greater than or equal to 30 mL/min)
- Bisphosphonate therapy recommended to begin within 1 year of diagnosis and should start no later than 18 months of definitive breast cancer surgery

TESTS:
- Completion of necessary dental assessment and dental work is recommended prior to starting zoledronic acid
- Baseline and prior to each treatment: serum creatinine
- If clinically indicated: serum calcium* and albumin (or ionized calcium)
  *corrected calcium (mmol/L) = total calcium (mmol/L) + (0.02 x [40 – albumin in g/L])

PREMEDICATIONS:
- None

TREATMENT:

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>BCCA Administration Guideline</th>
</tr>
</thead>
<tbody>
<tr>
<td>zoledronic acid</td>
<td>4 mg</td>
<td>IV in 100 mL NS over 15 minutes</td>
</tr>
</tbody>
</table>

Repeat once every 6 months (24 weeks) for 5 years
DOSE MODIFICATIONS:
1. Renal dysfunction: Zoledronic acid

<table>
<thead>
<tr>
<th>Creatinine clearance (mL/min)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Greater than or equal to 60</td>
<td>4 mg</td>
</tr>
<tr>
<td>50 to less than 60</td>
<td>3.5 mg</td>
</tr>
<tr>
<td>40 to less than 50</td>
<td>3.3 mg</td>
</tr>
<tr>
<td>30 to less than 40</td>
<td>3 mg</td>
</tr>
<tr>
<td>less than 30</td>
<td>not recommended</td>
</tr>
</tbody>
</table>

- There is limited experience with zoledronic acid in patients with serum creatinine greater than 440 micromol/L; caution is required.

PRECAUTIONS:
1. Zoledronic acid should NEVER be given as a bolus since severe local reactions and thrombophlebitis may result from high concentrations.
2. Symptomatic hypocalcemia (e.g., muscle spasms, irritability) may occur and may require calcium supplement. Avoid concomitant use of other calcium lowering agents such as corticosteroids and loop diuretics.
3. After the use of bisphosphonates, there is a persistent risk of jaw osteonecrosis. Patients in whom bisphosphonates are planned should have prophylactic assessment and management by a dentist and all later dental work should be undertaken cautiously by dental specialists experienced in the recognition and management of jaw osteonecrosis.

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

References: