

BCCA Protocol Summary for Palliative Therapy for Breast Cancer Using a LHRH agonist and Tamoxifen

Protocol Code

BRAVLHRHT

Tumour Group

Breast

Contact Physician

Dr. Tamara Shenkier

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: liver enzymes 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 (or ionized calcium)
*corrected calcium (mmol/L) = total calcium (mmol/L) + (0.02 x [40 – albumin in g/L])
- Annually: gynecological exam (patients with an intact uterus)

TREATMENT:

Drug	Dose	BCCA Administration Guideline
Tamoxifen	20 mg daily	PO
Buserelin (base) depot (SUPREFACT DEPOT®)* or Goserelin (ZOLADEX®)* or Leuprolide (LUPRON®)*	6.3 mg every 6 weeks x 2 treatments then every 8 weeks 3.6 mg every 4 weeks 7.5 mg every 4 weeks	SC SC IM

Continue until disease progression. **Strongly consider surgical oophorectomy 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.

Buserelin (base) depot (SUPREFACT DEPOT®) or Goserelin (ZOLADEX®) or Leuprolide (LUPRON®)	9.45 mg every 12 weeks 10.8 mg every 12 weeks 22.5 mg every 12 weeks	SC SC IM
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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.

Date activated: 1 June 2006 (replacing BRAVBT)

Date revised: 1 May 2009 (unsafe abbreviations and symbols replaced)

References:

1. Klijn JG, Beex LV, Mauriac L, et al. Combined treatment with buserelin and tamoxifen in premenopausal metastatic breast cancer: a randomized study. *J Natl Cancer Inst* 2000;92(11):903-11.
2. Klijn JGM, Blamey RW, Boccardo F, et al. Combined Tamoxifen and Luteinizing Hormone-Releasing Hormone (LHRH) Agonist Versus LHRH Agonist Alone in Premenopausal Advanced Breast Cancer: A Meta-Analysis of Four Randomized Trials. *J Clin Oncol* 2001;19(2):343-53.