BC Cancer Protocol Summary for Neoadjuvant or Adjuvant Ovarian Suppression and Aromatase Inhibitor in Premenopausal Women or In Men with High Risk Early Stage Breast Cancer

Protocol Code	*BRAJLHRHAI*
Tumour Group	*Breast*
Contact Physician	*Dr. Nathalie LeVasseur*

ELIGIBILITY:

Patients must:

- Have hormone receptor positive stage I to III operable breast cancer, and
- Be either:
  - Premenopausal women (menstruated in the last 12 months OR biochemically premenopausal pre/post neoadjuvant or adjuvant chemotherapy), or
  - Male patients, and
- Meet one of the following criteria:
  - 50 years or younger who have received neoadjuvant or adjuvant chemotherapy,
  - 35 years or younger who decline chemotherapy, or
  - Any age who are unable to receive tamoxifen due to a contraindication (i.e. thromboembolic disease or tamoxifen intolerance), or
  - Patients under 50 years of age who did not receive chemotherapy but remain at high risk of relapse at the discretion of the treating physician

Notes:

- May be given preoperatively as neoadjuvant therapy in patients unsuitable for immediate surgery or preoperative chemotherapy and who are unable to receive tamoxifen due to a contraindication (i.e. thromboembolic disease or tamoxifen intolerance)
- For all other indications, a BC Cancer "Compassionate Access Program" request with appropriate clinical information for each patient must be approved prior to treatment (please refer to https://cap.phsa.ca/).

EXCLUSIONS:

Patients must not have:

- Hormone receptor negative breast cancer,
- Stage IV breast cancer (refer to BRAVLHRHAI)

TESTS:

- Bone density study before or after 2-3 months of therapy.
- Bone density every 2-3 years (refer to local osteoporosis guidelines).
- Consider intermittently testing LH, FSH, and serum estradiol levels in overweight women as ovarian suppression with LHRH agonists can be less effective in this population.
- If clinically indicated: serum cholesterol and triglycerides.

TREATMENT:

Drug	Dose	BC Cancer Administration Guideline
anastrozole or letrozole or exemestane	1 mg daily x 5 years 2.5 mg daily x 5 years 25 mg daily x 5 years	PO
goserelin long acting (ZOLADEX)** or leuprolide long acting (LUPRON DEPOT)**	3.6 mg every 4 weeks x 5 years 7.5 mg every 4 weeks x 5 years	subcutaneous IM

Surgical oophorectomy can be considered in older pre-menopausal women who do not want to preserve their fertility and who are tolerating the menopausal side effects of therapy.

**** Once response has been established, the following long-acting agents may be substituted at the physician's discretion for a total of 5 years of therapy. Menstrual function, and if necessary, hormone levels can be monitored to ensure effective dosing.**

Drug	Dose	BC Cancer Administration Guideline
goserelin long acting (ZOLADEX LA) or leuprolide long acting (LUPRON DEPOT)	10.8 mg every 12 weeks 22.5 mg every 12 weeks	subcutaneous IM

PRECAUTIONS:

1. **Hepatic dysfunction**: Aromatase inhibitors are considered safe in mild-to-moderate hepatic dysfunction but have not been studies in severe hepatic dysfunction.
2. **Bone density:** The long-term effects of aromatase inhibitors on bone density in adjuvant therapy patients are unknown. Supplementation with calcium, vitamin D and regular weight bearing exercise is recommended. A bisphosphonate or RANK

ligand inhibitor should be considered if clinically indicated. Caution in patients with an already established diagnosis of clinically significant osteoporosis.

3. **Hyperlipidemia**: An increase in cholesterol or triglyceride levels may occur when an aromatase inhibitor is initiated. Levels may need to be checked during the first few months of therapy, especially in those patients with prior significant lipid elevations.

Call Dr. Nathalie LeVasseur or tumour group delegate at (604) 930-2098 or 1-800-663-3333 with any problems or questions regarding this treatment program.

References:

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4. Boccardo F, Rubagotti A, Amoroso D, et al. Cyclophosphamide, methotrexate, and fluorouracil versus tamoxifen plus ovarian suppression as adjuvant treatment of estrogen receptor positive pre/perimenopausal breast cancer patients: results of the Italian Breast Cancer Adjuvant Study Group 02 Randomized Trial. J Clin Oncol 2000;18:2718-87.
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6. Cuzick J, Sestak I, Baum M, et. al. Effect of anastrozole and tamoxifen as adjuvant treatment for early-stage breast cancer: 10-year analysis of the ATAC trial. Lancet Oncol 2010;11(12):1135-41.
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8. Gnant M, Mlineritsch B, Schippinger W, et al. Endocrine Therapy plus zoledronic acid in premenopausal breast cancer. N Engl J Med 2009;360:679-91.