

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

Protocol Code

BRAJLHRHAI

Tumour Group

Breast

Contact Physician

Dr. Vanessa Bernstein

ELIGIBILITY:

- Premenopausal women (defined as those who have menstruated in the last 12 months OR who are biochemically premenopausal pre/post neoadjuvant or adjuvant chemotherapy) aged 50 years or younger with hormone receptor positive stage I-III operable breast cancer who have received neoadjuvant or adjuvant chemotherapy
- Premenopausal patients 35 years of age or younger with hormone receptor positive stage I-III operable breast cancer who decline chemotherapy
- Premenopausal women (defined as those who have menstruated in the last 12 months or who are biochemically premenopausal) of any age with any stage I-III hormone receptor positive breast cancer who are unable to receive tamoxifen due to a contraindication (i.e. thromboembolic disease or tamoxifen intolerance)
- May be given preoperatively as neoadjuvant therapy in premenopausal women with hormone receptor positive breast cancer who are 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 older than 35 years of age who do not receive neoadjuvant or adjuvant chemotherapy and do not have a contraindication to tamoxifen.
- 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
buserelin long acting (SUPREFACT DEPOT)* or goserelin long acting (ZOLADEX)* or leuprolide long acting (LUPRON DEPOT)*	6.3 mg every 6 weeks x 2 treatments then every 8 weeks x 5 years 3.6 mg every 4 weeks x 5 years 7.5 mg every 4 weeks x 5 years	subcutaneous 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
buserelin long acting (SUPREFACT DEPOT) or goserelin long acting (ZOLADEX LA) or leuprolide long acting (LUPRON DEPOT)	9.45 mg every 12 weeks 10.8 mg every 12 weeks 22.5 mg every 12 weeks	subcutaneous subcutaneous IM

PRECAUTIONS:

1. **Hepatic dysfunction:** Aromatase inhibitors are considered safe in mild-to-moderate hepatic dysfunction but have not been studied 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. Vanessa Bernstein or tumour group delegate at (250) 519-5500 or 1-800-663-3333 with any problems or questions regarding this treatment program.

References:

1. Francis PA, Regan MM, Fleming GF, et al. Adjuvant ovarian suppression in premenopausal breast cancer. *N Engl J Med* 2015;372:436-46.
2. Pagani O, Regan MM, Walley WA, et al. Adjuvant exemestane with ovarian suppression in premenopausal breast cancer. *N Engl J Med* 2014;371:107-18.
3. Jakesz R, Hausmaninger H, Kubista E, et al. Randomized adjuvant trial of tamoxifen and goserelin versus cyclophosphamide, methotrexate and fluorouracil: Evidence for the superiority of treatment with endocrine blockade in pre-menopausal patients with hormone-responsive breast cancer – Austrian Breast and Colorectal Cancer Study Group Trial 5. *J Clin Oncol* 2002;20:4621-7.
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.
5. Jonat W, Kaufmann M, Sauerbrei W, et al. Goserelin versus cyclophosphamide, methotrexate and fluorouracil as adjuvant therapy in pre-menopausal patients with node positive breast cancer. The Zoladex Early Breast Cancer Research Association Study. *J Clin Oncol* 2002;20:4628-35.
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.
7. Masuda N, Iwata H, Rai Y, et al. Monthly versus 3-monthly goserelin acetate in premenopausal patients with estrogen receptor positive early breast cancer. *Breast Cancer Res Treat* 2011;126(2):443-51.
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.