BC Cancer Protocol Summary for Neoadjuvant or Adjuvant Therapy for Breast Cancer using a LHRH Agonist and Tamoxifen

Protocol Code	*BRAJLHRHT*
Tumour Group	*Breast*
Contact Physician	*Dr. Stephen Chia*

ELIGIBILITY:

- premenopausal women (defined as those who have menstruated in the last 12 months or who are biochemically premenopausal)
- hormone receptor positive
- May be given preoperatively in premenopausal women with hormone receptor positive breast cancer who are unsuitable for immediate surgery or preoperative chemotherapy
- node positive/high risk node negative patients who have turned down recommended adjuvant chemotherapy ***or***
- low risk node negative patients for whom goserelin and tamoxifen would be a reasonable alternative to chemotherapy

EXCLUSIONS:

- Patients with a history of significant thromboembolic disease

TESTS:

- Annually: gynecological exam

TREATMENT:

Drug	Dose	BC Cancer Administration Guideline
tamoxifen	20 mg daily x 5 years	PO
buserelin long acting (SUPREFACT DEPOT)**	6.3 mg every 8 weeks x 5 years*	subcutaneous
Or		
goserelin long acting (ZOLADEX)**	3.6 mg every 4 weeks x 5 years	subcutaneous
Or		
leuprolide long acting (LUPRON DEPOT)**	7.5 mg every 4 weeks x 5 years	IM

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

*** buserelin 6.3 mg every 8 weeks is an option for post cycle 1 if there is toxicity or break through on other LHRH agents.**

**** 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)	9.45 mg every 12 weeks	subcutaneous
Or		
goserelin long acting (ZOLADEX LA)	10.8 mg every 12 weeks	subcutaneous
or		
leuprolide long acting (LUPRON DEPOT)	22.5 mg every 12 weeks	IM

PRECAUTIONS:

1. **Myelosuppression**: Mild myelosuppression with transient thrombocytopenia may occur rarely. The association with tamoxifen is uncertain.
2. **Endometrial Cancer**: Annual gynecologic examinations are recommended. Pelvic complaints, such as unusual vaginal bleeding, require prompt evaluation.
3. **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.
4. **Thromboembolism**: Tamoxifen is associated with an increased risk of thromboembolism that is comparable to estrogen replacement therapy.
5. **Hepatotoxicity**: While hepatotoxicity is rare and usually presents as elevated hepatic enzymes, more serious liver abnormalities have been reported.
6. **Hyperlipidemia**: Elevations in cholesterol and triglycerides may occur in patients with pre-existing hyperlipidemias.

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:

1. 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 20:4621-27, 2002
2. 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 18:2718-87, 2000
3. 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 20:4628-35, 2002.
4. Regan M, Walley BA, Fleming GF, Francis PA, et al. Randomized comparison of adjuvant aromatase inhibitor exemestane (E) plus ovarian function suppression (OFS) vs tamoxifen (T) plus OFS in premenopausal women with hormone receptor-positive (HR+) early breast cancer (BC): update of the combined TEXT and SOFT trials. SABCS 2021. Cancer Res 2022;82 (4_Supplement):GS2–05.