STP
Tailored Treatment Investigations

Premenopausal patients with endocrine-responsive disease (ER ≥ 10% and/or PgR ≥ 10%)

AMENDMENT #1 (October 2005)

SOFT: Suppression of Ovarian Function Trial (IBCSG 24-02; BIG 2-02)

TEXT: Tamoxifen and Exemestane Trial (IBCSG 25-02; BIG 3-02)

PERCHE: Premenopausal Endocrine-Responsive Chemotherapy Trial (IBCSG 26-02; BIG 4-02)

North American Intergroup and Breast International Group (BIG) participation
Coordinating Group: International Breast Cancer Study Group (IBCSG)
Pharmaceutical Partner: Pfizer

International Breast Cancer Study Group
IBCSG

Breast International Group

CTSU

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Three protocols for two subpopulations:

A. Patients who should receive ovarian function suppression from the start:

TEXT: triptorelin (+/- CT) + tamoxifen vs.
triptorelin (+/- CT) + exemestane

PERCHE: OFS + (tam or exe) vs.
OFS + CT + (tam or exe)

Patients may enroll in both PERCHE (to select +/- CT) and TEXT (to select tam or exe).

CT = chemotherapy. OFS = ovarian function suppression using triptorelin x 5 years or surgical oophorectomy or ovarian irradiation. For TEXT, OFS = triptorelin x 5 years, but surgical oophorectomy or ovarian irradiation is allowed after 6 months.

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B. Patients who are premenopausal within 8* months after chemotherapy, or those for whom tamoxifen alone is considered adequate treatment:

SOFT: tamoxifen vs.
OFS + tamoxifen vs.
OFS + exemestane

OFS = ovarian function suppression using triptorelin x 5 years or surgical oophorectomy or ovarian irradiation.

**Changed from within 6 months to within 8 months in Amendment 1 (October 2005)*

International Breast Cancer Study Group
IBCSG

Rationale for Amendment

- Broaden and clarify eligibility criteria
- Clarify treatment details
- Update exemestane side effects data from trials in postmenopausal women

Amendments: Eligibility

- Allow patients with synchronous bilateral invasive breast cancers (diagnosed histologically within 2 months) if both fit the eligibility criteria
- Clarify that neoadjuvant/adjuvant Herceptin is allowed and is not considered to be chemotherapy for eligibility determination

Amendments: Eligibility

- Reduce requirements on management of axilla:
  - allow dissection or radiation of positive axillary nodes
  - allow undissected axillary nodes with micrometastatic involvement (pN1mi, none >2.0 mm) of sentinel nodes (previously these patients were allowed only if enrolled on a sentinel node clinical trial)

Amendments: Eligibility

- Allow any prior non-breast *in situ* carcinoma without invasion
- Allow the following malignancies:
  - Stage I papillary thyroid cancer
  - Stage IA carcinoma of the cervix
  - Stage Ia or b endometrioid endometrial cancer
  - Borderline or stage I ovarian cancer

  Diagnosed at least 5 yrs prior to randomization, adequately treated and without recurrence

Amendments: Eligibility

- Patients who have not received CT* and had regular menses over the 6 months prior to randomization (not using any hormonal contraception or other hormonal treatment during the 6 months prior to randomization) do not require estradiol level to confirm menopausal status

*CT: On the SOFT trial only, patients may have received chemotherapy prior to randomization

Amendments: Eligibility

- Following mastectomy:
  - DCIS at a margin is permitted if a complete mastectomy has been performed
- Following breast-conserving surgery:
  - If all other margins are clear, a positive posterior (deep) margin is permitted *provided the surgeon documents that the excision was performed down to the pectoral fascia and* all tumor has been removed
  - If all other margins are clear, a positive anterior margin (superficial; abutting skin) is permitted *provided the surgeon documents that all tumor has been removed*

Amendments: Eligibility

- SOFT only:
  - Increase timing for enrollment to within 8 months (formerly 6 months) of final dose of chemotherapy
  - Patients may have had neoadjuvant or adjuvant endocrine therapy for up to 8 months (formerly 6 mo) after diagnosis

  → In young women wishing to participate in the trial with postmenopausal estradiol levels after their chemotherapy, the patient should start tamoxifen and it is recommended to recheck an estradiol (i) if menses return or (ii) within 8 months of completing CT even in the absence of return of menses

Amendments: Eligibility

- SOFT only:
  - Clarify that patients may be randomized before, during or after RT to the breast; to meet timeframe for eligibility, a patient may be randomized prior to completion of RT and wait to start trial oral hormonal therapy until RT is completed if this is institutional practice

Amendments: Treatment Details

- Triptorelin should be given by IM injection every 28 +/- 3 days until 5 years from date of randomization
- The responsible investigator may authorize another qualified person to administer triptorelin

Amendments: Treatment Details

- TEXT/PERCHE trials:
  - Chemotherapy should start after randomization at the same time as GnRH analogue +/- 1 week
  - Tamoxifen or exemestane should start after adjuvant chemotherapy has been completed or approximately 6–8 weeks (+/- 2 weeks) after the initiation of GnRH analogue, whichever is later

Amendments

- Clarify a pregnancy test is recommended for women of child-bearing potential who are sexually active and not using reliable contraceptive methods
- Baseline CXR or chest CT is required

Amendments

- Update side effects of aromatase inhibitors with information from the ATAC, IES and BIG 1-98 trials in postmenopausal women