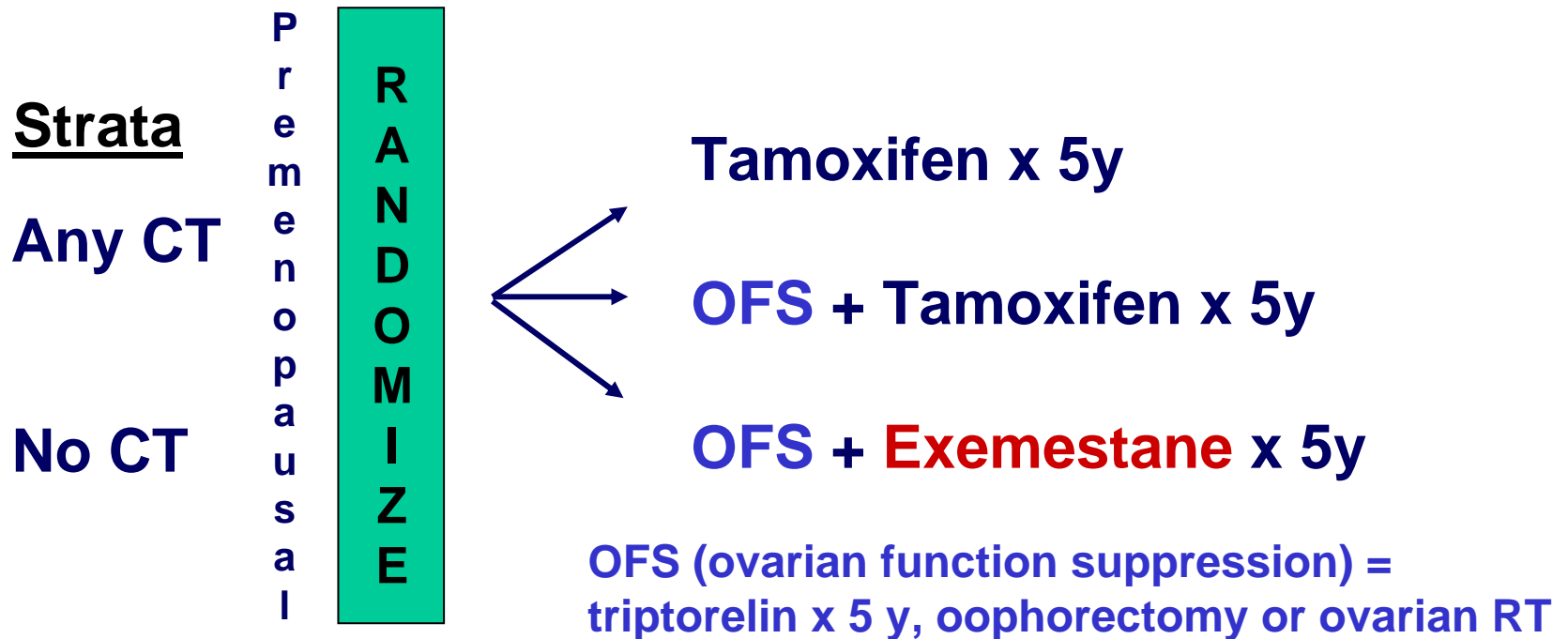


# SOFT [BIG 2-02, IBCSG 24-02]

Premenopausal, ER and/or PgR  $\geq$  10%

Patients who **remain premenopausal** within 8 months **after CT**, or receive tamoxifen alone as adequate treatment



Target sample size: 3000 patients

# SOFT (Suppression of Ovarian Function Trial)

- Study Chairs: P. Francis (BIG)  
G. Fleming (N. America)
- Target: 3000 patients
- 600 women/year for 5 years + 1.9 FU
- First patient entered: December 2003
- Entered through February 28, 2007: 1011



# SOFT Rationale

- Chemotherapy + Tamoxifen more effective than chemotherapy alone in pre-menopausal women
- Ovarian ablation an effective adjuvant therapy
- Uncertain if ovarian ablation adds efficacy if chemotherapy and/or 5 yrs tamoxifen are given
- Need to test this question in women who remain premenopausal (after chemotherapy if given)



# SOFT

Amendment # 1 (Oct 2005)



International Breast Cancer Study Group

IBCSG

# 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



# Amendments: Eligibility

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



# Amendments: Eligibility

- Reduce requirements for axilla:
  - allow dissection or radiation of positive axillary nodes
  - allow undissected axillary nodes if micro-metastasis in sentinel node (pN1mi, none >2.0 mm)



# Amendments: Eligibility

- Allow any prior non-breast *in situ* carcinoma without invasion
- Allow the following prior 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 chemo 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 E2 level to confirm menopausal status



# 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:
  - 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
- Exemestane – can start from 0-10 weeks after start OFS (suggest 6-8 weeks)

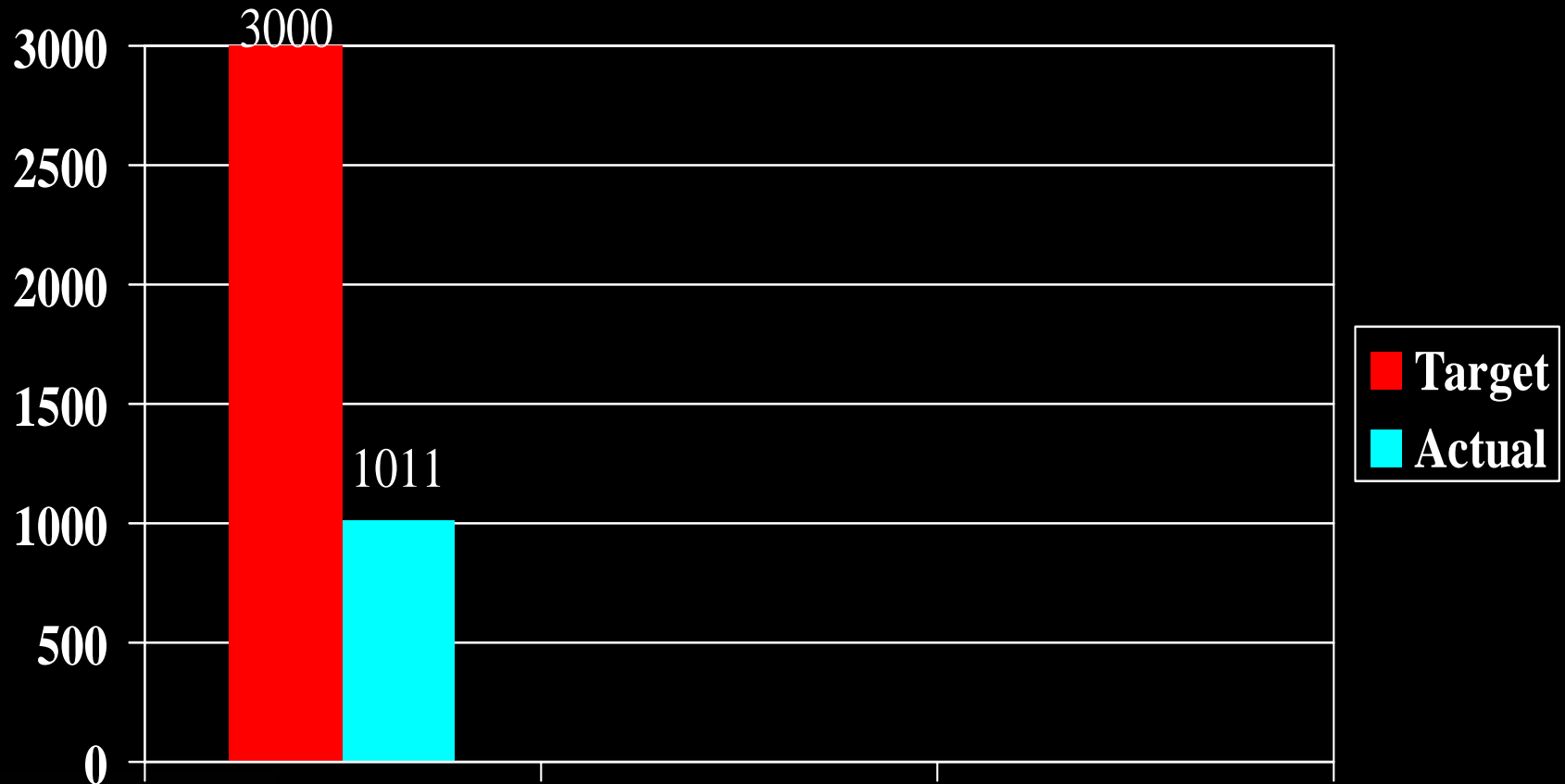


# Amendments

- 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

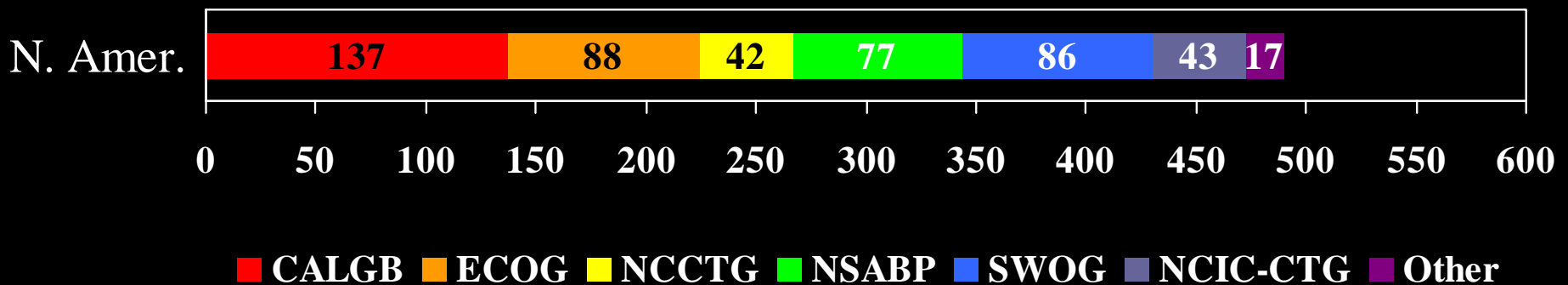
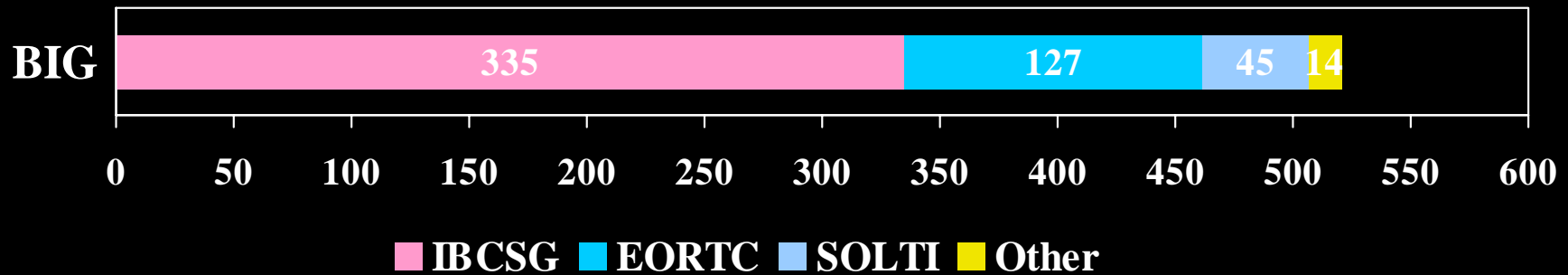


# SOFT Target and Actual Accrual (through February 28, 2007)



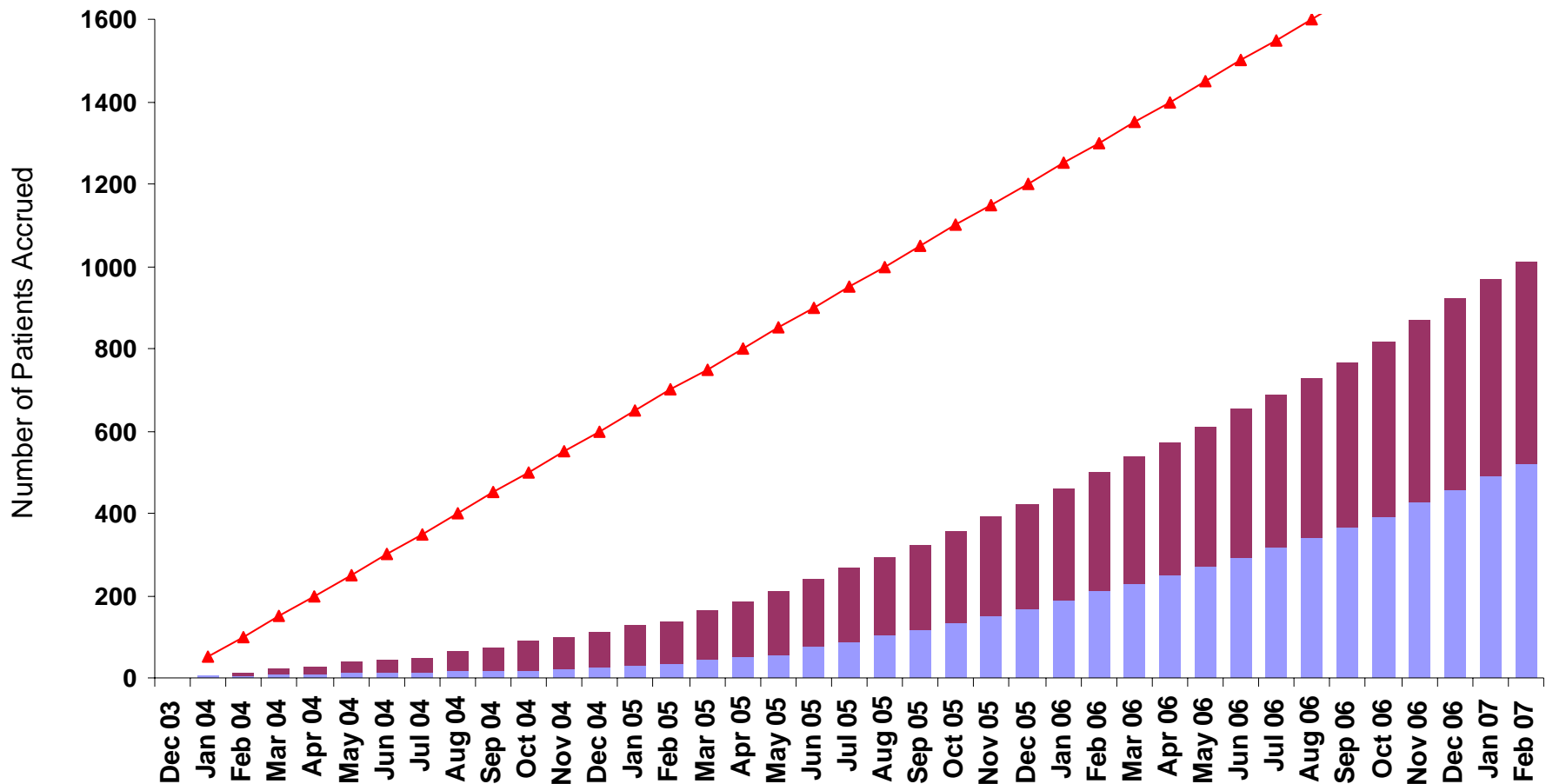
# SOFT Accrual

(through February 28, 2007)



**IBCSG Trial 24-02 (BIG 2-02) SOFT**  
**Cumulative Accrual through 28 Feb 2007**  
**Goal: 3000 patients (50/month)**

■ BIG (including IBCSG & GEAG)
 ■ North America
 ▲ Target

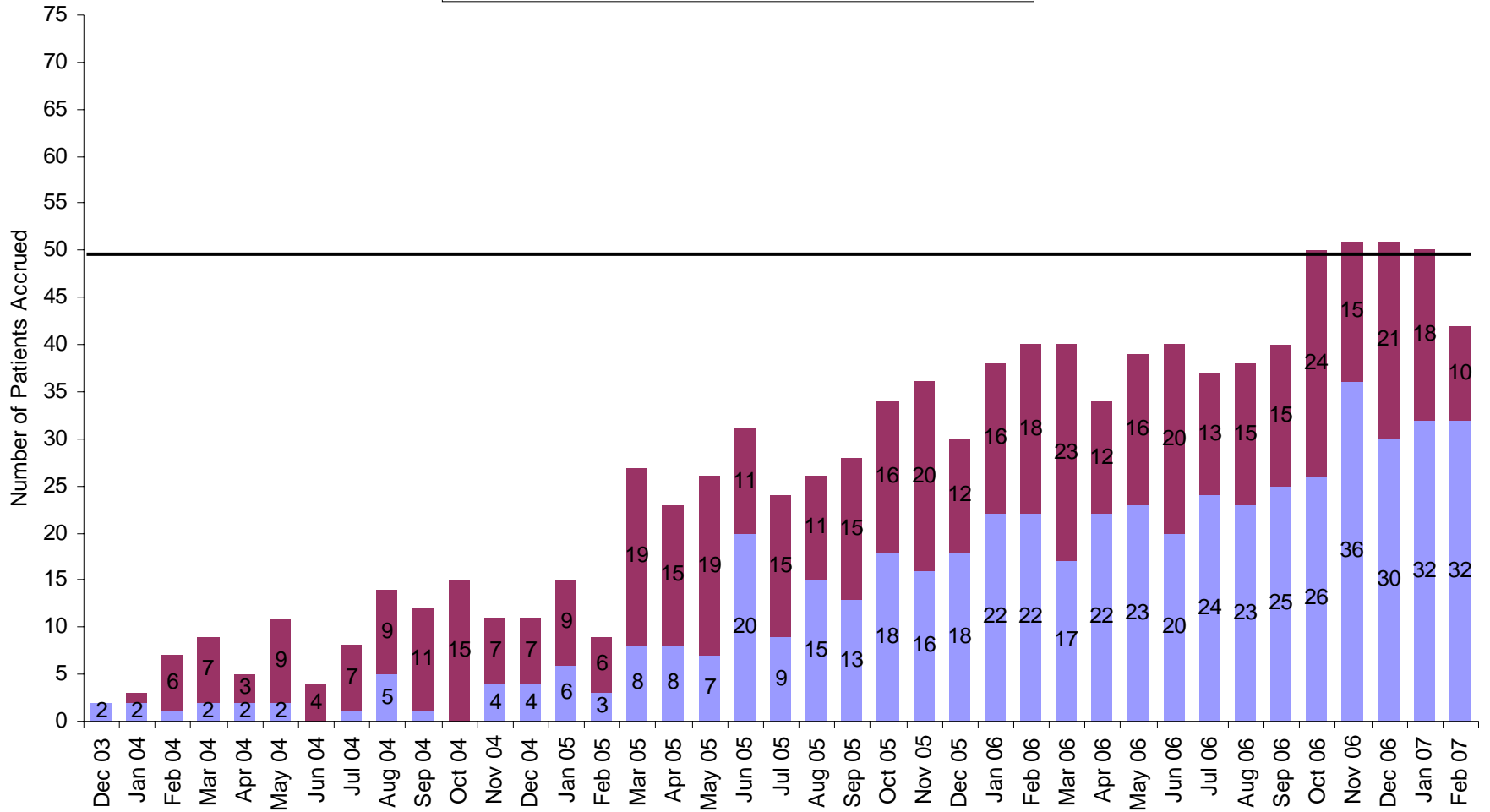


# IBCSG Trial 24-02 (BIG 2-02) SOFT

## Monthly Accrual through 28 Feb 2007

Goal: 50 patients/month

■ BIG (including IBCSG & GEAG) ■ North America



# SOFT Case Study

- 36 year old pre-menopausal woman
- **January 2006**: 20 mm grade 2 inf duct ca sentinel node positive but 11 negative nodes ER+ve PR+ve Her2 –ve
- Rx FEC 100 x 6 cycles, **last dose May 2006**



# SOFT Case Study

- **June 2006:** discuss adjuvant hormonal therapy. Last menses April 2006, hot flushes
- Interested in SOFT study
- E2, FSH and LH levels post-menopausal
- Commenced on tamoxifen (off study)
- **September 2006:** amenorrheic with frequent hot flushes



# SOFT Case Study

- **December 2006** reviewed in clinic (7 months since last chemotherapy). No menses, but hot flushes reduced. Continues tamoxifen.
- E2 re-tested and now pre-menopausal
- Randomized on SOFT



# SOFT Case study

- Chemotherapy induced “menopause” is often reversible in younger patients (eg < 40 yrs)
- Pre-menopausal E2 levels may return prior to menses, while on tamoxifen
- If interested in SOFT, check E2 again prior to 8 months after last chemotherapy
- To test menopausal status after chemotherapy: FSH, LH and E2 all helpful prior to tamoxifen but after starting tamoxifen only use E2



# SOFT Sub-Studies

- QOL
- Pathology
- Cognitive Function: Co-SOFT
- E2 Suppression (proposed by SOLTI)

