

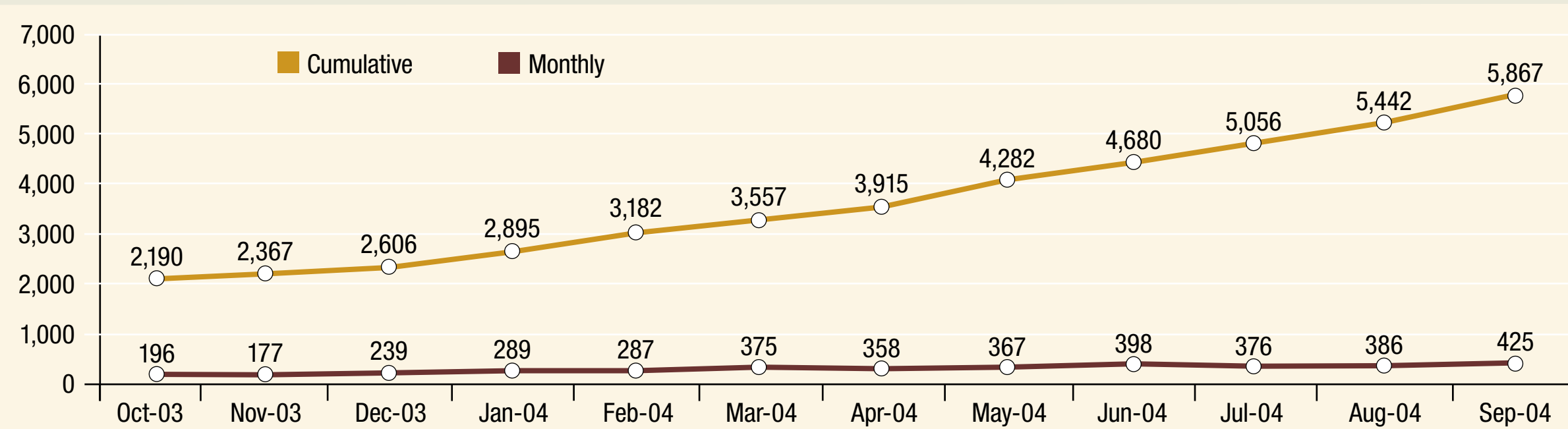
Cancer Trials Support Unit and Central Institutional Review Board

27TH ANNUAL
San Antonio
Breast Cancer
Symposium

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The primary goal of this system is to rapidly accelerate the pace of clinical cancer research by enabling oncologists in the United States to offer patients NCI-sponsored clinical trials and by simplifying and standardizing procedures related to participation. The Cancer Trials Support Unit (CTSUS) promotes cross-group accrual among Cooperative Group members. Features include standardization of data collection and online data reporting, simplified informed consent and a Central Institutional Review Board (CIRB) process. The CIRB model shares responsibility for protection of research participants between the local IRB and the CIRB, which conducts full board review, the results of which are distributed to participating local IRBs via a confidential website.

CTSUS ACCRUAL SUMMARY AS OF 09/30/04



SOURCE: CTSUS correspondence, October 2004.

PHASE III BREAST CANCER TRIALS OPEN THROUGH THE CTSUS

Study number	Study name	Accrual to date/goal as of date
ACOSOG-Z0011	Axillary node dissection in women with clinical T1 or T2, N0, M0 breast cancer who have a positive sentinel node	849/1900 (09/29/04)
CALGB-40101	Adjuvant CA (4 vs 6 cycles q2wk) versus paclitaxel (4 vs 6 cycles q2wk) for women with node-negative breast cancer	1221/4646 (09/27/04)
CALGB-49907	Adjuvant chemotherapy with standard regimens, CMF or AC, versus capecitabine in women 65 years and older with node-positive or high-risk node-negative breast cancer	239/720 (09/27/04)
IBCSG-24-02 (SOFT)	Adjuvant tamoxifen versus Ovarian Function Suppression (OFS) + tamoxifen versus OFS + exemestane in premenopausal women with endocrine-responsive breast cancer	75/3000 (09/30/04)
IBCSG-25-02 (TEXT)	Adjuvant triptorelin + exemestane versus triptorelin + tamoxifen in premenopausal women with endocrine-responsive breast cancer	147/1845 (09/30/04)
IBCSG-26-02 (PERCHE)	OFS + tamoxifen or exemestane ± adjuvant chemotherapy in premenopausal women with endocrine-responsive breast cancer	3/1750 (09/30/04)
NCIC-MA.20	Regional radiation therapy in early breast cancer	1051/1822 (10/04/04)
NCIC-MA.21	Adjuvant sequenced EC + filgrastim + epoetin alfa followed by paclitaxel versus sequenced AC followed by paclitaxel versus CEF for premenopausal women and early postmenopausal women with node-positive or high-risk node-negative breast cancer	1789/2100 (10/04/04)
NCIC-MA.27	Exemestane versus anastrozole ± celecoxib in postmenopausal women with receptor-positive primary breast cancer	1176/6830 (10/04/04)
NSABP-B-35	Anastrozole versus tamoxifen in postmenopausal patients with DCIS undergoing lumpectomy with radiation therapy	1157/3000 (10/04/04)
NSABP-B-36	Adjuvant FEC x six cycles versus AC x four cycles, ± celecoxib in women with node-negative breast cancer	175/2700 (10/04/04)
NSABP-B-38	Adjuvant TAC versus dose-dense (DD) AC followed by DD paclitaxel versus DD AC followed by DD paclitaxel + gemcitabine	0/4800 (10/07/04)
RTOG-98-04	Whole-breast radiotherapy versus observation ± tamoxifen in women with DCIS	468/1790 (10/04/04)
SWOG-S0012	Neoadjuvant standard AC followed by weekly paclitaxel versus weekly doxorubicin + daily oral cyclophosphamide + G-CSF followed by weekly paclitaxel for women with inflammatory and locally advanced breast cancer	247/350 (10/01/04)
SWOG-S0221	Adjuvant continuous-schedule AC + filgrastim versus every two-week AC + pegfilgrastim, followed by paclitaxel given every two weeks versus weekly for 12 weeks in women with node-positive or high-risk node-negative breast cancer	340/4500 (10/01/04)
SWOG-S0226	Anastrozole versus anastrozole + fulvestrant as first-line therapy for postmenopausal women with metastatic breast cancer	11/690 (10/01/04)

SOURCES: CTSUS website (CTSUS Active Protocol List & Accrual Report), October 2004; NCI Physician Data Query, October 2004.

USE OF FACILITATED REVIEW BY GROUP

Cooperative group	Number of studies on CIRB menu	Number of facilitated reviews accepted for group's studies
ECOG	15	285
CALGB	12	242
SWOG	13	185
NSABP	7	160
NCIC	2	73
RTOG	7	84
GOG	4	61
NCCTG	1	48

SOURCE: CTSUS correspondence, October 2004.

CIRB PROTOCOL REVIEW OUTCOMES

78 protocols reviewed (01/22/01 – 10/01/04)	
Approved	65 (100%)
Disapproved	0 (0%)
Results of first review	
Approved	1 (1%)
Approved pending modification	65 (84%)
Disapproved	0 (0%)
Tabled*	12 (15%)

* Tabled means the project cannot be approved without significant modification or there is insufficient information available to fairly judge the protocol.

SOURCE: CTSUS correspondence, October 2004.

SELECT PUBLICATIONS

Comis RL et al. Public attitudes toward participation in cancer clinical trials. *J Clin Oncol* 2003;21(5):830-5.

Kornblith AB et al. Survey of oncologists' perceptions of barriers to accrual of older patients with breast carcinoma to clinical trials. *Cancer* 2002;95(5):989-96.

Paskett ED et al. Clinical trial enrollment of rural patients with cancer. *Cancer Pract* 2002;10(1):28-35.

Sateren WB et al. How sociodemographics, presence of oncology specialists, and hospital cancer programs affect accrual to cancer treatment trials. *J Clin Oncol* 2002;20(8):2109-17.

Simon MS et al. Factors associated with breast cancer clinical trials participation and enrollment at a large academic medical center. *J Clin Oncol* 2004;22(11):2046-52.

CENTRAL INSTITUTIONAL REVIEW BOARD

"The Central Institutional Review Board (CIRB) initiative is a pilot project sponsored by the National Cancer Institute (NCI), in consultation with the DHHS Office of Human Research Protections. Created to develop an innovative approach to human subjects' protection, the unique feature of the CIRB is its 'facilitated review' process that can streamline local IRB review for national multi-center cancer treatment trials. Local IRBs enrolled in the pilot can download CIRB reviews from a confidential webpage and decide whether or not to utilize the CIRB's review for a particular protocol. This 'facilitated review' can take place rapidly. ...

"A major benefit for local IRBs participating in the pilot will be the reduction in review workload while still retaining its authority to accept or reject a 'facilitated review' on a protocol-by-protocol basis."

— CIRB Website
www.ncicirb.org

RECRUITMENT OF PARTICIPANTS IN CLINICAL TRIALS

"An effective national cancer program can never be implemented without patient-oriented research. This requires that individuals be willing, able, and available to participate in clinical trials. Participation in clinical trials is an opportunity not only for discovery, but also to experience the most promising and valuable new preventions, diagnoses, screening procedures, and therapies. Despite the potential therapeutic advantage of participating in clinical trials, the current number of eligible cancer patients entering clinical research studies is less than three percent. This is related primarily to the impediments to enrollment into cancer clinical trials as well as the limited funding of cooperative groups, which is the critical rate-limiting barrier to increased accrual. And even in studies where accrual is good, compliance and retention are not optimal. As a result, slow accrual and retention rates give way to delayed completion of clinical trials, resulting in cost inefficiencies, slowed translation of bench science, and potentially inequitable distribution of the risks and benefits of research."

— NCI Armitage Report
http://deainfo.nci.nih.gov/advisory/BSA/bsa_program/bsactprgmin.htm

BENEFITS OF THE CTSUS

The CTSUS has developed a single regulatory support system. Instead of oncologists having to register and file different applications every year with each cooperative group they belong to, they register once and each group utilizes that information. The centralization of that data and the centralization of all the IRB data on a per-study basis has been very helpful. This system should ease the burden of clinical trial participation on investigators in the community and academic institutions and increase the speed in which we complete important trials, as witnessed by the recent MA17 trial evaluating letrozole after adjuvant tamoxifen. More than 5,000 patients enrolled in that study, and although the NCI of Canada led that trial, 3,500 of the patients enrolled were from the United States cooperative groups. We completed accrual to that trial in less than four years and had results about one and a half years later. The system does work, and it can rapidly provide answers to important questions.

— Jeffrey Abrams, MD

The concept behind the CTSUS is that a fairly large number of physicians don't want to belong to a cooperative group, but would love to enroll their patients in clinical trials. The cooperative groups themselves were heavily involved in the development of the process. All of the major adjuvant breast cancer trials are going on the CTSUS menu. Advertising the trials and educating physicians about participation is going to be important. This is a real experiment that is still being de-bugged, but I hope it works because we need more patients enrolled in these clinical trials. I suspect there is a large reservoir of oncologists who have never filled out the CTSUS form — not because it's difficult, but just because no one suggested that they do it.

— George W Sledge Jr, MD