NSABP
National Surgical Adjuvant Breast & Bowel Project

Winter 1999/2000

Fore Front

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Fore Front

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Potential Paradigm Shifting Protocol Underway: NSABP Explores the Efficacy of Sentinel Node Resection

The National Surgical Adjuvant Breast and Bowel Project (NSABP) announced the opening of protocol B-32, a Phase III clinical trial that will compare sentinel node resection to the conventional axillary dissection in women who are clinically node-negative for breast cancer, this past Spring with the support of the National Cancer Institute (NCI).

Previous research has suggested that the sentinel nodes, the first node(s) which receives lymphatic flow from a tumor, can be used to determine if cancer has spread. In the breast, there are a limited number of nodes to which this drainage is likely to occur. Currently, conventional treatment includes the removal of most underarm (axillary) lymph nodes to control the spread of breast cancer. Performing this regional lymphadenectomy helps to provide staging and prognosis, regional control, and the possibility of improving a patient's survival and disease-free survival. However, this procedure comes at a significant cost to the patient's physical, emotional, and economical well-being. In this trial, it is hoped that surgeons will be able to localize and remove only one or a few sentinel node(s) through a simple biopsy to determine if the node is positive or negative for cancer and whether it is necessary to remove additional nodes to prevent further spreading. After surgery, patients will be followed for three to five years to study both cancer recurrence and overall survival.

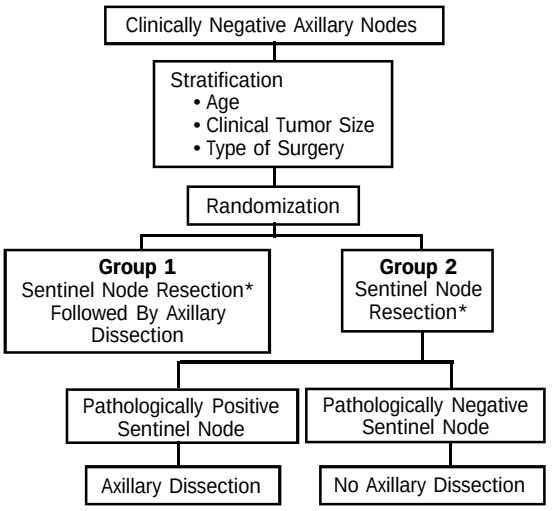
"Although research indicates that the sentinel node can be used to determine if cancer has spread, it is entirely unknown what the impact of only removing the sentinel nodes will have on cancer control and survival," said David Krag, M.D., who is the protocol chair for this study, and is a breast cancer surgeon at Fletcher Allen Health Care and the University of Vermont's Vermont Cancer Center.

B-32 is designed to determine if sentinel node resection will provide the same prognostic information, regional control, and survival as conventional axillary dissection while significantly reducing morbidity. The study will randomize 5,400 women who will be stratified into two groups according to age (#49, $50), clinical tumor size (#2.0 cm, 2.1-4.0 cm, $4.1 cm) and surgical treatment plan (lumpectomy, mastectomy). One group will undergo the current conventional surgery for breast cancer, which includes a lumpectomy or mastectomy, and a sentinel node biopsy with an axillary dissection. The second group will also undergo tumor removal and a sentinel node

Continued on Page 2...

biopsy that will be confirmed intraoperatively by a cytologic examination and postoperatively by a routine histologic examination (H + E). Women whose sentinel node is cytologically and histologically negative for cancer, will receive no axillary dissection. However, if the sentinel node is positive for cancer, then the women will undergo surgery to remove additional axillary nodes.

B-32 SCHEMA



**Patients in whom a sentinel lymph node is not identified will go on for axillary dissection*

To be eligible for this study, women must be diagnosed with invasive adenocarcinoma on cytologic or histologic examination, and the tumor must be operable. Patients must have clinically negative lymph nodes and a life expectancy of at least 10 years as determined by the investigator, excluding the diagnosis of cancer. The interval between the initial cytologic or histologic diagnosis of breast cancer and randomization must be no more than 63 days. Women who have been diagnosed with breast cancer utilizing fine needle aspiration cytology or core needle biopsy are preferred; however, patients who are diagnosed by open biopsy procedures are eligible. Those with prior excisional biopsy or lumpectomy will be eligible, and those with prior non-breast malignancies are eligible if they have been disease free for more than or equal to 5 years before randomization. Patients with squamous or basal cell carcinoma of the skin that has been effectively treated, carcinoma in situ of the cervix that has been treated by operation only, or LCIS of the ipsilateral or contralateral breast treated by surgery only are eligible, even if these conditions were diagnosed within 5 years before randomization. The enrollment of pregnant women is at the discretion of the individual investigator and must be in accordance with the policies of the local institution's nuclear medicine department.

"While this procedure shows promise in reducing complications with axillary dissection, it is important for patients to have clear and understandable data on the long-term outcome of this new procedure before making a decision," says Norman Wolmark, M.D., chairman of the NSABP.

This trial will attempt to determine three primary goals in regards to breast cancer patients who are clinically node negative and pathologically sentinel node negative: 1) whether sentinel node resection alone is equivalent to sentinel node resection followed by conventional axillary dissection in the long-term control of regional disease; 2) whether sentinel node resection alone is equivalent to sentinel node resection followed by conventional axillary dissection in regard to overall survival and disease-free survival; and 3) whether the morbidity associated with sentinel node resection alone is

B-32 Protocol Team

David Krag, M.D.

Dr. Krag, NSABP Protocol Chair for B-32, is a breast cancer surgeon at Fletcher Allen Health Care and the University of Vermont's Vermont Cancer Center.

Tom Julian, M.D.

Dr. Julian, NSABP Protocol Officer and Core Trainer for Protocol B-32, is a breast cancer surgeon at Allegheny General Hospital part of the West Penn Allegheny Health System in Pittsburgh, PA.

Ann Brown, Sc.D.

Dr. Brown, NSABP Coordinating Statistician for Protocol B-32, is a statistician for the NSABP Biostatistical Center at the University of Pittsburgh in Pittsburgh, PA.

Seth Harlow, M.D.

Dr. Harlow, NSABP Surgical Training Chair for Protocol B-32, is the Principal Investigator for B-32 at Fletcher Allen Health Care (FAHC) and a breast cancer surgeon at FAHC and the University of Vermont's Vermont Cancer.

significantly less than that associated with sentinel node resection followed by conventional axillary dissection.

The trial's secondary aims for patients who are clinically node negative and either sentinel node negative or positive by pathology will determine if the prognostic value of sentinel node resection alone is equivalent to that of sentinel node resection followed by conventional axillary dissection. And, for those who are pathologically sentinel node negative, if a more detailed pathology investigation of sentinel nodes can identify a group of patients with a potentially increased risk of systemic recurrence. In addition, the secondary aims of this study will include determining the proportion of patients for who at least one sentinel node is identified, or the technical success rate for sentinel node resection, and the variability of this rate in a broad population of participating surgeons who will determine the sensitivity of the sentinel node to detect nodal metastases. (This is the complement of the false-negative rate).

"The collection and submission of data throughout the B-32 trial will be critical for the success of this protocol," says Tom Julian, M.D., NSABP Core Trainer and Protocol Officer for Protocol B-32. For this trial, a node will be considered "sentinel" if any of the following three criteria are present during the surgical procedure: the node possesses a radioactive isotope as detected by the gamma detector; the lymph duct leading to the node is stained with blue dye; or if it is a clinically positive hard node. Surgeons wishing to participate in this study will be required to undergo an important program for procedural standardization of these criteria by a protocol Core Trainer from the NSABP surgical team.

"We feel that there will be only one opportunity to assess the impact of the sentinel node in the staging and prognosis in breast cancer," continues Dr. Julian. "The goals of this trial have been designed for just such an assessment. In order to achieve these goals, an ambitious attempt to review every participating surgeon and critique the surgical technique of sentinel node identification is being undertaken by a team of eight Core Trainers. A Core Trainer will visit each participating site before patients are permitted to be randomized for entry."

"The collection and submission of data throughout the B-32 trial will be critical for the success of this protocol."

The Core Trainer will conduct an on-site instructional visit that will include a review of the protocol with key personnel along with an operative observation. A subsequent review of 5 training cases will be performed before randomization of patients can begin. The Core Trainer will insure that the protocol is being followed in a standardized manner including both the procedure for sentinel node identification and for data entry. The first 20 randomized cases will also be reviewed by the Core Trainer, who will remain available to the participating surgeon to address any questions or concerns.

"There has been a tremendous response to the sentinel node trial," says Dr. Krag, "the Core Trainers have been very busy visiting sites across the United States and Canada to train surgeons. The trial has also been well received and valuable to cancer patients, who understand that surgery of lymph nodes is important for regional control as well as staging."

Surgeons who are interested in participating in the NSABP's B-32 trial, must have their institutions ensure that the following items are in place before patients can be randomized to the trial:

1- Surgeons must be a member of the NSABP to be eligible for this trial. Surgeons who are not currently members may contact Mary Ketner at the NSABP Operations Center by calling 412/330-4624 or via e-mail *(mary.ketner@nsabp.org)* for information regarding participation.

2- The surgeon must complete all training requirements necessary to obtain randomization privileges.

3- The Principal Investigator must have an up-to-date FDA Form 1572 on file with the National Cancer Institute.

4- The institution's IRB Assurance must be current with the Office for Protection from Research Risks (OPRR).

5- The institution must submit a document (chairperson's letter or Form 310) indicating full board review and IRB approval of the trial to the NSABP Biostatistical Center.

The B-32 sentinel node trial is on the *ForeFront* of breast cancer treatment. Due to the importance of this clinical trial, the NCI has committed the resources of the Office of Cancer Communications (OCC) to aid in recruitment activities. A referral network of open NSABP B-32 sites has been established in conjunction with the NCI's Cancer Information Service (CIS) at 1-800-4-CANCER. FF

Tamoxifen in Treatment of Intraductal Breast Cancer: NSABP B-24 Randomised Controlled Trial

NSABP Protocol B-17 determined that lumpectomy with radiation therapy was more effective than lumpectomy alone for the treatment of ductal carcinoma in situ (DCIS). Protocol B-24, a double-blind randomised controlled trial was conducted to find out whether lumpectomy, radiation therapy, and tamoxifen was of more benefit than lumpectomy and radiation therapy alone for DCIS.

One thousand, eight-hundred and four women with DCIS, including those whose resected sample margins were involved with tumor, were randomly assigned to lumpectomy, radiation therapy (50 Gy), and placebo (n = 902), or lumpectomy, radiation therapy, and tamoxifen (20 mg daily for 5 years)[n = 902]. Median follow-up was 74 months (range 57-93). The study compared annual event rates and cumulative probability of invasive or non-invasive ipsilateral and contralateral tumors over 5 years.

Findings for the B-24 trial showed that women in the tamoxifen group had fewer breast-cancer events at 5 years than did those on placebo (8.2 vs 13.4%, p = 0.0009). The cumulative incidence of all invasive breast-cancer events in the tamoxifen group was 4.1% at 5 years: 2.1% in the ipsilateral breast, 1.8% in the contralateral breast, and 0.2% at regional or distant sites. The risk of ipsilateral-breast cancer was lower in the tamoxifen group even when sample margins contained tumor and when DCIS was associated with comedonecrosis.

The study concluded that the combination of lumpectomy, radiation therapy, and tamoxifen was effective in the prevention of invasive cancer.

The full-length text of *Tamoxifen in Treatment of Intraductal Breast Cancer: National Surgical Adjuvant Breast and Bowel Project B-24 Randomised Controlled Trial* by Bernard Fisher, M.D., *et al*, is published in *The Lancet 353(9169):1993-2000, June 12,1999.* FF

Further Evaluation of Intensified & Increased Total Dose of Cyclophosphamide for the Treatment of Primary Breast Cancer: Findings from NSABP B-25

In 1989, the NSABP initiated the B-22 study to determine whether intensifying, or intensifying and increasing the total dose of cyclophosphamide in a doxorubicin-cyclophosphamide combination would benefit women with primary breast cancer and positive axillary nodes. The B-25 trial was initiated to determine whether further intensifying and increasing the cyclophosphamide dose would yield more favorable results.

Patients (n = 2,548) were randomly assigned to three groups. The dose and intensity of doxorubicin were similar in all groups. Group 1 received four courses, ie, double the dose and intensity of cyclophosphamide given in the B-22 standard therapy group; group 2 received the same dose of cyclophosphamide as in group 1, administered in two courses (intensified); group 3 received double the dose of cyclophosphamide (intensified and increased) given in group 1. All patients received recombinant human granulocyte colony-stimulating factor (GCSF). Life-table estimates were used to determine disease-free survival (DFS) and overall survival.

No significant difference was observed in DFS ($P = .20$), distant DFS ($P = .31$), or survival ($P = .76$) among the three groups. At 5 years, the DFS in groups 1 and 2 (61% *v* 64%, respectively; $P = .29$) was similar to but slightly lower than that in group 3 (61% *v* 66%, respectively; $P = 08$). Survival in group 1 was concordant with that in groups 2 (78% *v* 77%, respectively; $P = .71$) and 3 (78% *v* 79%, respectively; $P = .86$). Grade 4 toxicity was 20%, 34%, and 49% in groups 1, 2, and 3, respectively. Severe infection and septic episodes increased in group 3. The decrease in the amount and intensity of cyclophosphamide and delays in therapy were greatest in courses 3 and 4 in group 3. The incidence of acute myeloid leukemia increased in all groups.

Researchers concluded that because intensifying and increasing cyclophosphamide two or four times that given in standard clinical practice did not substantively improve outcome, such therapy should be reserved for the clinical trial setting.

The full-length text of *Further Evaluation of Intensified and Increased Total Dose of Cyclophosphamide for the Treatment of Primary Breast Cancer: Findings from National Surgical Adjuvant Breast and Bowel Project B-25* by Bernard Fisher, M.D., *et al*, was published in the *Journal of Clinical Oncology, Vol. 17, Issue 11, 3374-3388, November, 1999.* FF

Randomized Trial of 3-Hour Versus 24-Hour Infusion of High-Dose Paclitaxel in Patients With Metastatic or Locally Advanced Breast Cancer: NSABP Protocol B-26

Paclitaxel is an active drug for the treatment of breast cancer. The B-26 trial was designed to assess and compare the response rate, event-free survival, survival, and toxicity of paclitaxel 250 mg/m^2 delivered every 3 weeks as a 3-or 24-hour infusion. Results indicate that duration of administration is an important factor in the efficacy of the drug and the incidence of adverse events.

A total of 563 women with stage IV or IIIB breast cancer were randomized into one of two groups: 279 received 3-hour paclitaxel and 284 received 24-hour paclitaxel. Patients were stratified by age, stage of disease, and prior therapy.

Findings from Protocol B-26 showed that a significantly higher rate of tumor response occurred in the first four cycles of therapy in patients who received the 24-hour infusion of paclitaxel (51% v 41%, respectively; P = .025). Tumor response over all cycles was also significantly higher in the group that received 24-hour infusion (54% v 44%, respectively; P = .023). There were no significant differences in event-free survival or survival between the two arms of the study (P = .9 and .8, respectively). No treatment by stage or by age interactions were observed. During the first four cycles of therapy, at least one episode of greater than or equal to a grade 3 toxicity (excluding nadir hematologic values, alopecia, and weight change) occurred in 45% of patients who received the 3-hour paclitaxel infusion and in 50% of those who received the 24-hour paclitaxel infusion. Febrile neutropenia, greater than or equal to a grade 3 infection, and greater than or equal to a grade 3 stomatitis were less frequent, and severe neurosensory toxicity was more frequent in those who received the 3-hour paclitaxel infusion. Ten treatment-related deaths occurred in the first four cycles. Age, stage, and prior chemotherapy did not influence the effect of treatment.

The study concluded that when administered as a continuous 24-hour infusion, high-dose paclitaxel results in a higher tumor response rate than when administered as a 3-hour infusion but does not significantly improve event-free survival or survival. Paclitaxel as a 24-hour infusion results in increased hematologic toxicity and decreased neurosensory toxicity.

The full-length text of *Randomized Trial of 3-Hour Versus 24-Hour Infusion of High-Dose Paclitaxel in Patients With Metastatic or Locally Advanced Breast Cancer: National Surgical Adjuvant Breast and Bowel Project Protocol B-26* by Roy E. Smith, M.D., *et al,* is published in the *Journal of Clinical Oncology*, Vol. 17, Issue 11: 3403-3411, November 1999. FF

Protocol B-29 Closure

Accrual of patients to *Protocol B-29: A Clinical Trial to Evaluate the Benefit of Adding Octreotide (SMS 201-995 pa LAR) to Tamoxifen Alone or to Tamoxifen and Chemotherapy in Patients with Axillary Node-Negative, Estrogen-Receptor-Positive, Primary Invasive Breast Cancer,* has been terminated as of December 22, 1999. **Patients assigned to octreotide should receive no further injections**. Principal Investigators have been instructed to immediately notify all investigators and relevant IRBs. These actions have been taken on the recommendation of the NSABP's Independent Data Monitoring Committee (DMC), after review of biliary toxicity data collected as part of the ongoing adverse events monitoring program of the Protocol.

The DMC judged the rate of new gallstone formation and the incidence of cholecystectomies in patients receiving octreotide to be sufficiently high to recommend cessation of octreotide on Protocol B-29. Patients should continue to receive tamoxifen, and if applicable to continue with AC chemotherapy.

As of December 21, 1999, 893 patients had been accrued to this protocol, 446 of whom were assigned to receive octreotide. Seventy-eight octreotide patients who were free of gallstones at baseline have been reported to have developed gallstones following the initiation of treatment. The estimated one-year cumulative incidence of new gallstones in patients receiving octreotide is 47%. Two patients not receiving octreotide have reported new stones (cumulative incidence = 1.3%).

Twenty-five patients receiving octreotide have received cholecystectomies subsequent to the initiation of treatment, of whom 5 were diagnosed with gallstones prior to treatment. Three control patients have received cholecystectomies, all of whom had gallstones prior to treatment.

While an increased level of biliary toxicity was anticipated, these reported levels exceed expectations, and are considered to be greater than the level which may be justified in treatment of the relatively good prognosis cohort of patients who are eligible for B-29.

It is important to continue with follow-up and regularly scheduled tests for all B-29 patients. In spite of the necessity to terminate accrual to B-29, the NSABP remains indebted to each patient and investigator who contributed to clinical research by agreeing to participate in this effort. FF

NSABP Serum Bank has Moved...

As of February 1, 2000, the Breast Center at Baylor College of Medicine in Houston, Texas will serve as the central serum and lymphocyte bank for NSABP breast and colon cancer treatment trials.

The policies and procedures for collecting and processing blood and serum specimens for the NSABP Serum Bank have ***NOT*** changed. The Breast Center at Baylor College of Medicine will now provide all clinical sites with the supplies necessary to collect and send samples to the Serum Bank.

Bryant McCue from the Breast Center at Baylor College of Medicine will be the NSABP Serum Bank contact person for ***ALL*** serum/ lymphocyte submissions and correspondence for both breast and colon cancer treatment trials.

Mr. McCue can be reached by phone at 713/ 798-1647, fax 713/ 798-1642, or via e-mail at *bmccue@bcm.tmc.edu*.

Ship ***ALL*** serum and lymphocyte submissions to:

Baylor College of Medicine
Breast Center
NSABP Serum Bank
Room 0059E
One Baylor Plaza
Houston, TX 77030

FF

NSABP Protocol Updates

ACTIVE TRIALS:	CURRENT STATUS:
B-27 Protocol: A Randomized Trial Comparing Preoperative Doxorubicin (Adriamycin) Cyclophosphamide (AC) to Preoperative AC Followed by Preoperative Docetaxel (Taxotere) and to Preoperative AC Followed by Postoperative Docetaxel in Patients with Operable Carcinoma of the Breast	**Current Status:** The protocol was activated December 20, 1995 with an original target accrual of 1,600 patients. In October 1998, the NSABP's independent Data Monitoring Committee agreed to increase the sample size to 2,400 patients; the expected date of completion is now May 2000. As of January 31, 2000, a total 2040 patients were accrued.
B-27.1 Protocol: A Trial to Evaluate the Worth of Serum ErbB-2 Extracellular Domain and Serum ErbB-2 Antibodies in Predicting Response to Preoperative Chemotherapy and Long-term Outcome in Patients with Operable Breast Cancer Who Are Participating in NSABP Protocol B-27	**Current Status:** This protocol was activated February 14, 1997 with a target accrual of 1,200 patients. As of January 31, 2000, a total of 472 patients were assigned to the trial.
B-27.2 Protocol: A Trial to Evaluate the Worth of Tumor Biomarkers Obtained by FNA or Core Biopsy in Predicting Response to Preoperative Chemotherapy and Long-term Outcome in Patients with Operable Breast Cancer Who Are Participating in NSABP Protocol B-27	**Current Status:** This protocol was activated February 14, 1997 with a target accrual of 720 patients. As of January 31, 2000, a total of 399 patients were assigned to the trial.
B-30 Protocol: A Three-Arm Randomized Trial to Compare Adjuvant Adriamycin and Cyclophosphamide Followed by Taxotere (AC → T); Adriamycin and Taxotere (AT); and Adriamycin, Taxotere, and Cyclophosphamide (ATC) in Breast Cancer Patients with Positive Axillary Lymph Nodes	**Current Status:** This study opened for accrual on March 15, 1999. It is designed to accrue 4,000 patients over 35 months. As of January 31, 2000, a total of 964 patients have been entered onto this trial.
B-32 Protocol: A Randomized, Phase III Clinical Trial to Compare Sentinel Node Resection to Conventional Axillary Dissection in Clinically Node-Negative Breast Cancer Patients	**Current Status:** This study opened for accrual on May 17, 1999. It is designed to accrue 5,400 patients over 45 months. As of January 31, 2000, a total of 192 patients were accrued.
***BI-65 (NCCTG N9431) Protocol :** Menstrual Cycle and Surgical Treatment of Breast Cancer	**Current Status:** This protocol was activated by the NCCTG on July 12, 1996, with subsequent entry by the NSABP effective May 1, 1997. The accrual goal for this trial is 884 patients. As of January 27, 2000, a total of 609 patients had been accrued to the trial; 144 by the NCCTG and 465 by the NSABP.
P-2 Protocol: Study of Tamoxifen and Raloxifene (STAR) for the Prevention of Breast Cancer	**Current Status:** This protocol was activated on July 1, 1999 with a target accrual of 22,000 participants. As of January 31, 2000, a total of 3,369 participants were accrued.

ACTIVE TRIALS:	CURRENT STATUS:
C-07 Protocol: A Clinical Trial Comparing 5-Fluorouracil (5-FU) plus Leucovorin (LV) and Oxaliplatin with 5-FU plus LV for the Treatment of Patients with Stages II and III Carcinoma of the Colon	**Current Status:** This trial opened in the US on February 1, 2000. Materials have been sent to all principal investigators and program coordinators for distribution to their participating satellites. The trial will also be conducted in Canada, Australia, and New Zealand; materials have been provided to investigators in these countries. When all the regulatory requirements have been met for each of these latter three countries, investigators will be notified to begin accrual.
***CI-63 (ECOG E1292) Protocol:** Phase III Intergroup Prospectively Randomized Trial of Perioperative 5-FU After Curative Resection, Followed by 5-FU/Levamisole for Patients with Colon Cancer	**Current Status:** This protocol was activated by the Intergroup with an accrual goal of 2,000 patients on August 19, 1993; NSABP joined the trial on August 7,1995. As of January 27, 2000, a total of 819 patients had been accrued; 18 by the NSABP.
***CI-64 (NCCTG 934653) Protocol:** A Phase III Prospective Randomized Trial Comparing Laparoscopic-Assisted Colectomy Versus Open Colectomy for Colon Cancer	**Current Status:** This protocol was activated by the Intergroup on August 2, 1994; NSABP joined the trial on April 25, 1997. The target accrual is 1,200 patients. As of January 28, 2000, a total of 686 patients were entered on trial; 15 by the NSABP.

PROPOSED TRIALS:	CURRENT STATUS:
B-31 Protocol: A Randomized Trial Comparing the Safety and Efficacy of Adriamycin and Cyclophosphamide Followed by Taxol (AC-T) to that of Adriamycin and Cyclophosphamide Followed by Taxol plus Herceptin (AC-T+H) in Node-Positive Breast Cancer Patients Who have Tumors that Overexpress HER2	**Current Status:** This protocol has been approved by the NCI and the proposed date of activation is February 21, 2000. A total of 2,700 patients are to be accrued over a 4 to 5 year period.
B-33 Protocol: A Randomized, Placebo-Controlled, Double-Blind Trial Evaluating the Effect of Exemestane in Clinical Stage Postmenopausal Breast Cancer Patients Completing at Least 5 Years of Tamoxifen Therapy	**Current Status:** This concept was approved by the NCI and the protocol is in development. The proposed sample size is 3,000 patients, to be accrued over a period of approx. 3-1/2 years. We anticipate opening the trial in late Spring 2000.
B-34 Protocol: A Trial Comparing Adjuvant Clodronate Therapy vs Placebo In Early Stage Breast Cancer Patients Receiving Systemic Chemotherapy and/or Tamoxifen, or No Therapy	**Current Status:** This concept was approved by the NCI and the protocol is in development. The proposed sample size is 2,400 patients, to be accrued during a period of up to 4 years. We anticipate opening the trial in late Spring 2000.
R-04 Protocol: ***As of this newsletter's print date, protocol R-04's title had not yet been determined.***	**Current Status:** A protocol design meeting is scheduled to take place in Pittsburgh on March 6, 2000 with NSABP staff, members of the Colorectal Committee Working Group, and outside consultants. Every effort will be made to have a trial in place within 7-9 months.

RECENTLY CLOSED TRIALS:	CURRENT STATUS:
B-29 Protocol: *(See Page 5 for more information.)* A Clinical Trial to Evaluate the Benefit of Adding Octreotide (SMS 201-995 pa LAR) to Tamoxifen Alone or to Tamoxifen and Chemotherapy in Patients with Axillary Node-Negative, Estrogen-Receptor-Positive, Primary Invasive Breast Cancer	**Current Status:** This trial was closed to further accrual on December 22, 1999, due to concerns raised by the NSABP's independent Data Monitoring Committee regarding biliary-related adverse events. Instructions regarding termination of dosing with octrecotide have been provided to participating principal investigators and program coordinators.
BP-58 Protocol: A Phase II Study in Patients with Metastatic or Locally Advanced Breast Cancer to Evaluate the Worth of the Combination of Adriamycin (doxorubicin), Taxotere (docetaxel), and Cyclophosphamide (ATC)	**Current Status:** This pilot study was closed after reaching its accrual goal of 89 patients on January 18, 2000.

* *Identifies Intergroup studies.*

99 Treatment Publications

C-01-C-04

Comparative Efficacy of Adjuvant Chemotherapy in Patients with Dukes' B Versus Dukes' C Colon Cancer: Results From Four National Surgical Adjuvant Breast and Bowel Project Adjuvant Studies (C-01, C-02, C-03, and C-04)

By.....Eleftherios P. Mamounas, M.D., M.P.H., *et al*
Published in.....*Journal of Clinical Oncology* 17(5):1349-1355, May 1999

B-13, B-14, B-17, B-18, B-19, B-20, & P-1

Highlights from Recent National Surgical Adjuvant Breast and Bowel Project Studies in the Treatment and Prevention of Breast Cancer

By.....Bernard Fisher, M.D., *et al*
Published in.....*CA - A Cancer Journal for Clinicians* 49(3):159-177, May-June 1999

B-24

Tamoxifen in Treatment of Intraductal Breast Cancer: National Surgical Adjuvant Breast and Bowel Project B-24 Randomised Controlled Trial

By.....Bernard Fisher, M.D., *et al*
Published in.....The *Lancet* 353(9169):1993-2000, June 12, 1999

B-17

Pathologic Findings from the National Surgical Adjuvant Breast Project (NSABP) Eight-Year Update of Protocol B-17: Intraductal Carcinoma

By.....Edwin R. Fisher, M.D., *et al*
Published in.....*Cancer* 86(3):429-38, August 1, 1999

C-04

Clinical Trial to Assess the Relative Efficacy of Fluorouracil and Leucovorin, Fluorouracil and Levamisole, and Fluorouracil, Leucovorin, and Levamisole in Patients With Dukes' B and C Carcinoma of the Colon: Results From National Surgical Adjuvant Breast and Bowel Project C-04

By.....Norman Wolmark, M.D., *et al*
Published in.....*Journal of Clinical Oncology* 17(11):3553-3559, November 1999

C-01-C-05

Outcomes Among African-Americans and Caucasians in Colon Cancer Adjuvant Therapy Trials: Findings From the National Surgical Adjuvant Breast and Bowel Project

By.....James J. Dignam, Ph.D., *et al*
Published in.....*Journal of the National Cancer Institute* 91(22):1933-40, November 17, 1999

B-25

Further Evaluation of Intensified and Increased Total Dose of Cyclophosphamide for the Treatment of Primary Breast Cancer: Findings From National Surgical Adjuvant Breast and Bowel Project B-25

By.....Bernard Fisher, M.D., *et al*
Published in.....*Journal of Clinical Oncology* 17(11):3374-3388, November 1999

B-26

Randomized Trial of 3-Hour Versus 24-Hour Infusion of High-Dose Paclitaxel in Patients with Metastatic or Locally Advanced Breast Cancer: National Surgical Adjuvant Breast and Bowel Project Protocol B-26

By.....Roy E. Smith, M.D., *et al*
Published in.....*Journal of Clinical Oncology* 17(11):3403-3411, November 1999

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Dept. of Public Relations & Communications
Four Allegheny Center
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Pittsburgh, PA 15212

Mark Your Calendars for Future NSABP Meetings...

June 10-13, 2000*
NSABP Annual Group Meeting
Hyatt Regency, New Orleans, Louisiana

November 3-6, 2000*
NSABP Fall Workshops
Westin William Penn Hotel, Pittsburgh, Pennsylvania

* NSABP's biannual meetings are for NSABP members only. Information regarding these meetings and travel arrangements are distributed to its members prior to each meeting. FF