Constellation

Winter–2001
Volume 1, Issue 1

Welcome!

You are all STARs in a Constellation of Hope & Research

Welcome to the first issue of *Constellation*, a publication brought to you by the National Surgical Adjuvant Breast and Bowel Project (NSABP), the research group conducting STAR, the Study of Tamoxifen And Raloxifene.

Are you asking, "why *Constellation*?" For some the answer may be obvious; we thought the title reflected our desire to make this a publication for all the "stars" that have enrolled in this trial. Together you form a constellation. It's a reminder that great advances are due to great efforts from all and not necessarily a single individual. Without each of the over 8,000 individual women enrolled in this study giving of themselves, this trial would not be possible and the potential to advance breast cancer prevention would falter.

The aims of this publication are modest. As researchers, we take seriously our role of keeping you informed of important study information. Thus, we will use this newsletter to meet this obligation. This is your trial and *Constellation* is your vehicle for communicating to other participants. We always welcome contributions from you, the participants. That said, we hope you enjoy this issue and those in the future. Lastly, on behalf of the NSABP and women from all generations, thank you for selflessly putting yourself forward in the battle against breast cancer.

D. Lawrence Wickerham
NSABP Associate Chairman
& STAR Protocol Officer

New inside this issue

STAR's First Birthday: A Year of Great Strides

The first year and a half of the Study of Tamoxifen and Raloxifene (STAR) saw over 8,000 postmenopausal women at increased risk of breast cancer enroll in this landmark prevention study– and more than 61,000 women went through an individualized, no-obligation risk assessment to determine their risk of breast cancer and weigh the pros and cons of joining the trial. Enrollment began July 1, 1999.

Many of these 61,000 women did not have an increased risk of breast cancer that would make them eligible for the trial; slightly over 37,000 women were eligible for the trial based on breast cancer risk alone, but had to make the choice to participate based on their overall health and personal reasons.

STAR is designed to determine whether the osteoporosis prevention and treatment drug, raloxifene (Evista®), is as effective as tamoxifen (Nolvadex®) in reducing breast cancer risk. In 1998, tamoxifen was shown to reduce the chance of developing breast cancer by about half in the Breast Cancer Prevention Trial (BCPT), a study of over 13,000 premenopausal and postmenopausal women at increased risk of breast cancer.

The U.S. Food and Drug Administration (FDA) approved the use of tamoxifen to reduce the incidence of breast cancer in women at increased risk of the disease in October 1998. Raloxifene was shown to reduce the incidence of breast cancer in a large osteoporosis trial, the Multiple Outcomes of Raloxifene Evaluation, or MORE, study.

More than 500 centers across the United States, Puerto Rico, and Canada are enrolling participants in STAR. STAR is a study of the National Surgical Adjuvant Breast and Bowel Project (NSABP) and is supported by the U.S. National Cancer Institute (NCI).

The NSABP chairman, Norman Wolmark, M.D., said, "We are pleased that so many women have joined this trial to help us answer this important medical question. We encourage women to go through the risk assessment process to learn more about their breast cancer risk and about STAR. In the end, each woman who joins does so for her own reasons, but every single woman plays a vital role."

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STAR Accrual Report

22,000
Overall Goal after 5 year accrual process

11,000
YOU ARE HERE...
Accrual is 8,456 STARs as of January 14, 2001

5,500
June 30, 2000 Happy 1st Birthday, STAR! 6,136 entered STAR and more than 47,000 women received risk assessments.

2,750
July 1, 1999 Randomization Began

What is the NSABP?

The NSABP is a nonprofit, clinical trials cooperative group. Research conduct-ed by the NSABP is supported primarily by grants from the National Cancer Institute (NCI). For more than 40 years, the NSABP has successfully conducted large-scale, randomized clinical trials in breast and colorectal cancer that have altered and improved the standard of care for women and men with these diseases.

The NSABP, which includes the Operations Center and Biostatistical Center, is head-quartered in Pittsburgh, PA. Current membership includes more than 500 medical centers in the United States, Canada, and Australia with over 6,000 physicians, nurses, and other medical professionals. NSABP member institutions and their satellites conduct NSABP treatment and prevention trials, including patient enrollment, protocol treatment, and data submission.

Results from NSABP clinical trials have been a major factor in altering breast cancer care. NSABP was the first to:

- demonstrate that the radical mastectomy was no more effective than less extensive procedures (lumpectomy). As a result of our studies, lumpectomy and breast irradiation is now considered the standard in breast cancer care;
- demonstrate that adjuvant chemo-therapy in node-positive breast cancer patients could alter the natural history of the disease and improve survival;
- evaluate the use of tamoxifen as an adjuvant therapy, either alone or in combination with chemotherapy, which reduced cancer recurrence rates and improved survival among estrogen-receptor positive breast cancer patients;
- evaluate the use of preoperative chemotherapy in patients with operable breast cancer, which set the stage for making surgery the adjuvant treatment in the clinical management of breast cancer;
- undertake a new direction in the battle against breast cancer, focusing on prevention. The Breast Cancer Prevention Trial (BCPT) showed that tamoxifen reduced the chance of developing breast cancer by about half in premenopausal and post-menopausal women at increased risk of the disease. As a result, tamoxifen was approved by the FDA to reduce breast cancer incidence in women at increased risk for the disease.

For more information on the NSABP or any of our clinical trials, please visit our Web site at **www.nsabp.pitt.edu**.

"We are pleased that so many women have joined this trial... ...every single woman plays a vital role."

–Norman Wolmark, MD, NSABP chairman

STAR Participant Advisory Board Appointed

All women who enroll in STAR are valued and important and we want to make sure that participants have a voice in how the study is conducted. This sentiment has given rise to formation of a STAR Participant Advisory Board (PAB). Fifteen women already enrolled in the trial have been appointed to the STAR PAB and will represent the voice of all women in the trial.

"The concept of a Participant Advisory Board is not new," said Lori Garvey, the director of public relations and communications, and NSABP liaison to the PAB. "In 1995, a PAB was established for the Breast Cancer Prevention Trial (BCPT). Working with women enrolled in that study was incredibly helpful. As participants, they were perfectly situated to provide the NSABP and National Cancer Institute (NCI) leadership with feedback and suggestions to improve the conduct of the trial." In STAR, the concept of a participant advisory board has once again been adopted. To provide continuity, two women, Lonnie Williams from Oklahoma City, OK and Jeannie Morice of Calgary, Alberta, Canada, who were part of the BCPT PAB have been asked to serve as co-chairs for the STAR PAB. Both Lonnie and Jeannie were participants in NSABP's first breast cancer prevention trial, the BCPT.

Background on the BCPT

The BCPT began in 1992 and was designed to determine if tamoxifen could prevent invasive breast cancer in women at increased risk for the disease. Women enrolled in the BCPT were assigned to take either tamoxifen or placebo (a pill with no active drug). In 1998, it became apparent that tamoxifen did reduce the incidence of invasive breast cancer—by almost 50%. The independent data monitoring committee who oversaw that trial recommended that the study be stopped and that women on placebo be offered the opportunity to take tamoxifen. Another alternative for postmenopausal women in the placebo group was to enroll in STAR. Lonnie and Jeannie chose that option.

The New STAR PAB

Joining Lonnie and Jeannie as STAR PAB members will be thirteen additional STAR participants. The new members were appointed after the NSABP made an announcement to its membership that they were seeking nominations to fill the vacancies. Each STAR clinical center was permitted to nominate only one participant. The NSABP received over 50 nominations making the selection process incredibly challenging. Senior staff from the NSABP poured over each application. Among the factors considered was appointing members who represented the various ages, races, ethnicities, and geographic locations of STAR participants. The initial selections made by the NSABP were shared with senior staff from the NCI for consensus.

New members are presently being informed by their study coordinator of their appointment and are being asked to sign a release so that the NSABP can be told their name (due to confidentiality policies, all women nominated for the PAB were identified by their study number only). Once identified, the new Board will meet in early 2001. Stay tuned for a future issue of *Constellation* when we will officially intro-duce the members of the new STAR PAB!

Reflections

From Inside a Clinical Trial

Reflections... was submitted by **Nancy Meneely**, a STAR participant from **Sibley Hospital in Washington, DC**. She has given permission for the NSABP to print this article in Constellation. The thoughts and words are her own and we thank her for sharing them with all of us. If you would like to share your experiences "from inside a clinical trial," please send them to the NSABP (address available on back page) and you too may see your story highlighted in an up-and-coming issue of Constellation.

Some people I've known wanted more than anything to be rich; others dreamed of beauty, influence, accomplishment. Myself, I've harbored the dream that I might be remembered as interesting, a character whose secrets, observations and habits were seen as noteworthy, even instructive.

But I couldn't have said until very recently that I might achieve this distinction. I'm a middle-aged woman of average height, weight and income, famous only within my nuclear family and that largely for mistakes. Though my days hold more than enough interest for me, my dramas have been small, my triumphs parochial.

Suddenly, however, busy people are calling me up to solicit information on my experience of life, to probe my moods, my spirit and my relationship to various parts of my body. I've been celebrated, fed, photographed, and quoted.

How has this happened? The answer is: Tamoxifen. Or maybe: Raloxifene. The mere act of taking one daily dose of one of these drugs has turned me into something of a fascination, even a hero of sorts.

How can this be, when hundreds of thousands of women take these medicines every day? And why can I not say whether it's tamoxifen or raloxifene to which I owe my celebrity? The answer to both questions is this: I swallow one (or the other) in connection with a "double blind" study of the two in which only a computer somewhere in Pittsburgh, PA knows which pill I'm taking. Because of the leap of faith required of us who participate, we are esteemed by the study staff. To them, we are pioneers who risk the consequences of taking a pill we can't name and whose effects are not entirely clear. They are grateful that we hope to further a science that may save many lives.

I think they know that at least some of us also hope we are taking the pill that will save our own lives.

That is certainly the hope that set me on the path toward this study. I have lived all my life under the shadow of breast cancer. My mother and her mother had the disease. Both caught it early; both lived many years after their mastectomies. But I was the one in my mother's hospital room when her surgeon arrived to tell her that her lymph nodes were clear. I remember her joy in that moment, how she came up off her pillows, face alight with relief. I also remember, though, how the air went out of the room when Dr. Carter first came in, how many lifetimes it took him to utter the news. I don't want to live through the beginning of that sentence again.

I thought a lot about what my sentence might be. Before last year, I lived with a faint but persistent anxiety about what my genes might be cooking up for me. No matter how much orange juice I drank and how much wine I didn't, no matter how much broccoli I piled on the part of my plate where red meat had sat, I felt pretty nearly helpless against the programming of my cells.

And then I read about tamoxifen and raloxifene. Studies were showing these "selective–estrogen receptor modulators (SERMs)" to be astonishingly effective in reducing the incidence of breast cancer. In early trials, tamoxifen proved to prevent the disease in 49% of the study population, and raloxifene looked even better. I began to think I could take a hand in steering my life instead of waiting for it to happen to me.

So I made an appointment with Dr. Frederick Barr, a well-respected local oncologist, for a mid-life reckoning. We agreed I'd reached what he called "a crossroads." I'd been on hormone replacement therapy (HRT) for a long (and blissful) time. I was approaching 55, the midpoint between my grandmother's age when she developed cancer and my mother's when she palpated her own lump. And, I said, there were these new drugs.

Dr. Barr's friendly smile deepened into one of pleasure. As Chair of the Sibley Hospital Cancer Committee, he had received first notification—within minutes of my arrival in his office—that Sibley had been approved as a site for the STAR trial, a comparative study of tamoxifen and raloxifene. The initial protocol sat face up in his FAX machine. And I sat before him. This was a match made in heaven: a healthy post-menopausal woman with an active interest in the drugs under study, and a group of medical people interested in serving up salvation and watching its effects like hawks.

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STAR's First Birthday...

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Lonnie Williams, co-chair of the Participant Advisory Board (PAB) of STAR, lost her 42-year-old daughter to breast cancer and was a part of the BCPT – the first woman in Oklahoma City, OK to join that study. When the trial was finished in April 1998, she found out she had been on a placebo. This made her eligible to either participate in STAR or to receive free tamoxifen from AstraZeneca Pharmaceuticals, the company that makes the drug and had promised to provide tamoxifen without charge to all the BCPT participants on placebo treatment. She chose STAR.

"I believe in clinical trials," said Williams. "And the trials being conducted by NSABP to prevent breast cancer are very important to all women. Having lost a daughter to breast cancer, which left a little boy to grow up without his mother, I feel that it is necessary that I do anything I can to help prevent this from happening to other women."

Postmenopausal women of all ethnicities and races are encouraged to participate in STAR, and about 5 percent of the first 8,000 women in STAR are minorities. In this first year of STAR, over 8,700 women from diverse racial and ethnic minority groups went through the risk assessment process, almost 2,500 had an increased risk of breast cancer that would qualify them for the study, and almost 400 have already decided to join.

In contrast, in the entire five years of enrollment for the BCPT, a total of 8,525 minority women went through the risk assessment process, 2,979 were risk-eligible, and 486 joined the trial.

"A goal of STAR is to make this trial accessible to women from all walks of life," said D. Lawrence Wickerham, MD, NSABP associate chairman and protocol officer for STAR. "We have programs underway to educate all women about the trial and a special program is geared to women from various racial and ethnic groups. Regardless of whether a woman chooses to enroll in the trial, simply knowing your risk for breast cancer is powerful information to have."

Actual study participants are expected to help guide the NSABP in the conduct of STAR. Recently the Participant Advisory Board (PAB), established during NSABP's first breast cancer prevention trial, was reconstituted to include women who have enrolled in STAR (*see page 2 for more details)*. "The women who were involved in the original PAB were a tremendous resource to us," said Lori Garvey, the director of public relations and communications and NSABP liaison for the PAB. "Feedback from the PAB was instrumental in helping us modify programs to enroll women, and to determine how we could keep those women who did enroll satisfied with the choice they made. We are looking forward to working closely with the new board members."

Reflections...

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He told me about the study, emphasizing both its value and its potential downsides. It might take a while for the study to get going. I would have to submit to a rigorous schedule of examinations. For the next few years, I wouldn't know what drug I was taking. And, oh yes, I would probably experience some side effects.

I felt exhilaration lightly tinged with the panic I'd experienced once running downhill when gravity got more of a hold on me than I liked. Then, as now, I wanted to get where I was going but not quite as fast as I was going to get there. Shouldn't I take some time to consider these questions: Did I have the courage to wait a while to start on what I saw as a lifesaving regimen? Should I risk the 50% possibility that I wouldn't be on Raloxifene, the drug I preferred? Should I commit myself to something I wouldn't find it easy to back away from if I hated the side effects?

But it seemed that Fate had shone her light directly on Dr. Barr's office. The omens were all good. This was an invitation to do something in my own interest that would also fulfill a scientific need and give me a shot at saving lives in the future, among them those of my beloved daughter and niece, swimmers in my own gene pool.

I couldn't see any reasonable way even to consider saying no. I said yes.

I needn't have worried about speed. It took a year for the trial to get underway. I called several times to be sure I hadn't missed the start, somehow, but that was definitely not the case. I understood the delay when Joyce Holley, the Sibley study coordinator, called me to schedule my initial interview and to describe the sequence of steps to be taken, the forms to be filled in and the schedule of clinical visits. This was a complex undertaking. We're talking here not only about national bureaucracies but also about science. Every "i" would be dotted and every "t" crossed as I progressed through the trial.

But first I had to qualify, via a process that put me in the complicated position of hoping to be found at such risk of developing what I dreaded that I could take a drug to reduce the risk. During my first visit to Sibley, Joyce gave me the risk graph that showed my hope was fulfilled: my family history of breast cancer combined with my late-life production of a first child to give me an estimated 13% probability of developing breast cancer before I was 80. This was risk enough for all of us.

I set that graph quickly to one side and studied the other piece of paper Joyce gave me, a chart entitled "Possible Benefits and Risks Associated with Treatment in the STAR (Study of Tamoxifen and Raloxifene) Trial." The hopeful news was that, of the 249 cases of invasive breast cancer expected in five years in 10,000 non-study women, 121 cases might be prevented by STAR participation. Of the 77 predictable cases of in situ breast cancer, 39 might be prevented. The scary part was the possibility of greater than normal incidence of uterine cancer, stroke, blood clot in a lung or large vein and cataract.

> *"I love this study. I love being part of it. [And] ...I know absolutely that something good will come out of this for all women."*
>
> –Nancy Meneely, STAR participant

But I only hesitated a moment. My worry had been cancer alone, none of these other things. And, anyway, I already felt connected to Joyce and her colleague, Mary Reiman, who sat with me, radiating eagerness for their project and affection for me, their first enrollee. In the months to come, they would cement our relationship by the genuineness of their commitment, their joy in my willingness to answer questionnaires and submit to examinations (though I told them these were more interesting than burdensome), their gentle remonstrances regarding my reluctance to examine my own breasts, and the many ways they found to celebrate my participation—with photo sessions and interviews and food. By the time I finished my first session with them, I knew these were people I couldn't disappoint.

I have to confess there were moments when I wished I didn't feel that way. There are side effects and though they bother me much less now, I wasn't quite ready for them at first. Suddenly I couldn't count on my good humor quite so much, nor on the guarantee of a good night's sleep. I sympathized with the television news program interviewee who said she went back on HRT after bursting into tears one day while leaning over to tie her shoe. My joints hurt and, sure enough, my optometrist announced the beginning of a cataract. But who knows: I was probably working on all of these before the study started. I do have some distinctly new sensations, though—phantom itches I can't find a place to scratch; a feeling late at night that my legs want to party when the rest of me wants to pack it in; and a weird and momentary ache across my midsection that foretells every hot flash.

And what hot flashes! If they were visible, my friends would have to wear dark glasses. If they were palpable, seismologists would worry. If I were a bell, I'd be ringing.

But here's the truth; I love this study. I love being part of the Sibley study group. I've met four of the other women and they're great, all very different from each other, and all alike—upbeat, handsome, articulate, hovering somewhere in their sixth decade. Like me, they perspire freely. Like me, they confess to be working all the signs to figure out which drug they're on.

And I love knowing that at the study's end, I will have counted for something. I don't know in which statistical column my name will fall, but I know absolutely that something good will come out of this for all women. I know that, if something sorry should befall me or my study fellows, someone will detect it good and early. And I know we have a rooting section of wise and wonderful people who would follow our progress with the kind of attention you give to people who are endlessly and without exception ***...interesting!***

1999-2000 NSABP Publications

P-1
Weighing the Risks and Benefits of Tamoxifen Treatment for Preventing Breast Cancer
By.....Gail MH, MD, PhD, *et al*
Published in...Journal of the National Cancer Institute 91:21:1829-1846, 1999

P-1
National Surgical Adjuvant Breast and Bowel Project Breast Cancer Prevention Trial: A Reflective Commentary
By.....Fisher B, MD
Published in.....Journal of Clinical Oncology 17:5:1632-1639, 1999

P-1
Validation Studies for Models Projecting the Risk of Invasive and Total Breast Cancer Incidence
By.....Costantino JP, DrPH, *et al*
Published in...Journal of the National Cancer Institute 91:18:1541-1548, 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.....Fisher B, MD
Published in.....CA - A Cancer Journal For Clinicians 49:3:159-177, 1999

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Health-Related Quality of Life and Tamoxifen in Breast Cancer Prevention: A Report From the National Surgical Adjuvant Breast and Bowel Project P-1 Study
By.....Day R, PhD, *et al*
Published in.....Journal of Clinical Oncology 17:9:2659-2669, 1999

B-04, B-05, B-06, B-18, B-24, & P-1
From Halsted to Prevention and Beyond: Advances in the Management of Breast Cancer During the Twentieth Century
By.....Fisher B, MD
Published in.....European Journal of Cancer 35:14:1963-1973, 1999

B-04, B-06, B-09, B-13, & B-14
Differences in Breast Cancer Prognosis Among African-American and Caucasian Women
By.....Dignam J, PhD
Published in.....CA - A Cancer Journal For Clinicians 35:14:1963-1973, 1999

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Breast Cancer Prevention: A Review of Current Evidence
By.....Vogel V, MD, MHS
Published in.....CA - A Cancer Journal For Clinicians 50:3:156-170, 2000

P-1
Editorial: Cancer Prevention: From Concept to Practice
By.....Vogel V, MD, MHS
Published in.....CA - A Cancer Journal For Clinicians 50:3:140-142, 2000

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