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The Prostate Cancer Prevention Trial

A Low-Risk, High-Accrual Study

by Jennifer O'Connor

Peter Johnson*, a 71-year-old Michigan man, entered the Prostate Cancer Prevention Trial after reading an article in a newspaper. He enrolled in the study through the Grand Rapids Clinical Oncology Program in Michigan because he was curious about a disease he knew he was at risk of getting. Johnson also believed he had nothing to lose since the trial drug, finasteride, has no serious side effects. With the exception of a prostate biopsy at the end of the trial, participation in the study is convenient and painless, demanding only the daily ingestion of finasteride or a placebo, six-month follow-ups, and a yearly physical exam.

"If they think the drug can prevent prostate cancer, I want to be involved," Johnson said about his reasons for joining the trial.

The Prostate Cancer Prevention Trial is a seven-year double-blind study launched last October by the Southwest Oncology Group (SWOG) in collaboration with the Eastern Cooperative Oncology Group, the Cancer and Acute Leukemia Group B, affiliates of the Community Clinical Oncology Program, and various NCI-supported cancer centers.

As of June 22, 1994, 13,757 men were enrolled in the first phase of the trial nationwide, with 7,680 having been randomized. These figures have exceeded researchers' expectations, said National Project Manager Anne Ryan, R.N., who works at SWOG's Statistical Center in Seattle, Wash. She said project planners expected to lose about 30 percent of the initial enrollees due to early withdrawal from the trial and elevated PSA levels, when in actuality only about 25 percent were eliminated. Researchers also hoped to randomize 18,000 people over three years; in the first nine months, they randomized almost half that figure.

The trial will test whether finasteride, approved by the Food and Drug Administration in 1992 for the treatment of benign prostatic hyperplasia, will prevent prostate cancer.

The trial will also address the necessity of prostate cancer screening, which usually consists of a digital rectal exam and prostate specific antigen (PSA) testing.

Because many prostate cancers do not secrete much PSA, screening can result in a 30 to 40 percent error rate in detection, according to Otis Brawley, M.D., program director in the Division of Cancer Prevention and Control at the National Cancer Institute (NCI). Moreover, prostate cancer screening has not been shown to save lives, and some experts fear it may even lead to a net harm.

Trial researchers hope to find a way to make screening more sensitive and specific (or more accurate). According to Brawley, ancillary studies may make it possible to differentiate lethal prostate tumors, which should be aggressively treated, from indolent tumors that need no treatment.

Ironically, Brawley said, the same technology that brought screening into the forefront of prostate cancer detection is the same technology that has hampered efforts to effectively treat the disease.

"Society is overdiagnosing prostate cancer and treating many men who, while they have cancer, need no aggressive treatment," he said. "Technology is very cruel to us. We have the technology to detect the disease, but not the technology or the wisdom to determine if our detection is necessary.

"The treatments for prostate cancer have considerable morbidity," Brawley continued. "A large number of men who are treated for prostate cancer end up wearing diapers, have incontinence and impotence. Two-thirds who are diagnosed with prostate cancer don't need to be treated; indeed they don't need to be diagnosed."

Some researchers suggest that not all patients should be put through the physical and emotional rigors of the cancer treatment regimen, which usually consists of radiation, hormone therapy, chemotherapy, or surgery.

Trial researchers also want to examine the screening process and its relation to African-American men. Historically, the black community has seen higher incidence rates for prostate cancer than the white community, and the death rate from the disease is twice as high among black men as it is among white men.

More recently, diagnosis among white men is rising. Brawley theorizes that the screening process does not hold the same attraction for black men and other minorities as it does for white men. Thus, white men, who are more concerned about early detection, are more likely to be diagnosed than minorities, particularly black men.

"The middle class white culture is a culture that is very interested in cancer and in some segments fixated on cancer," Brawley explained. "Black men, on the other hand, don't go to the doctor as much as white men for screening."

APPEAL, ALTRUISM, AND COMMITMENT

The launch of the trial is particularly encouraging to prostate cancer survivors like Richard Howe, Ph.D., a 65-year-old retired Penzoil

*Not his real name

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president from Houston. Howe, who spends his days talking to prostate cancer support groups, understands all too well the fears and concerns of cancer patients and believes the low risk of taking finasteride gives men added strength and courage to participate in such prevention trials.

"When you're told you have prostate cancer or any type of cancer, it's like someone has dropped a thousand-pound rock on you," he said. "The Prostate Cancer Prevention Trial is a win-win deal. If it works, it would be extremely important, but if it doesn't work, not much is lost but some time and bookkeeping."

What is most remarkable about the participation, say trial coordinators, is the commitment men have in participating in such a lengthy study.

"I thought I knew the way men think," said Marilyn Zack, project coordinator at the Grand Rapids Clinical Oncology Program. "Because of the way the trial was set over seven years, I thought a lot of men might not want to deal with it. I was also surprised about the concern over health issues. Usually women are concerned, not men."

According to James L. Wade III, M.D., a medical oncologist at the Decatur Memorial Hospital Cancer Institute in Decatur, Ill., men want not only to help find a cure for prostate cancer, but also to help improve the quality of life for those already afflicted with the disease (see "What's It All About" on page 24).

"What is remarkable is the tremendous interest in prostate cancer and the willingness of these men to participate in the screening process," Wade said. "They are willing to go through the trial to protect themselves, for altruism, for their fellow men. There is a spirit in these men in doing something for their community. They are also blood donors and volunteers in their communities."

Although finasteride has possible side effects of incontinence, impotence, and decreased libido and ejaculatory volume, these problems are worth the investment in time for men like Johnson.

"Participating in the trial is a form of contribution," Johnson said. "It's not harmful so I couldn't lose much with involvement. Maybe I can win."

Medical staffs are finding this attitude refreshing. With management of health care costs weighing heavily on the industry, medical personnel are faced with the challenge and stress of providing quality service with fewer dollars. The tension has created a need for an emotional and professional reprieve that the prostate trial seems to offer.

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"I think the trial has put some fun back into the work place, which I think we've been losing because of everything that is happening in the medical field," said Deborah Ware, B.S.N., R.N., trial coordinator and oncology director at the Michigan-based Battle Creek Health System, an affiliate of the Grand Rapids Clinical Oncology Program. "It's fun taking care of people who are not sick, but who are trying to be concerned about their health.

"I think the trial is bringing physicians and patients together in a more relaxed setting," Ware continued. "Physicians are more likely to open up and discuss things when they are not experiencing the stress of dealing with a chronically ill population."

Connie Szczepanek, R.N., B.S.N., of the Grand Rapids Clinical Oncology Program agrees, adding that healthy patients are able to offer support and an emotional lift to medical staffs in ways sick patients are not.

"Participation in the trial is something that's totally optional, so it takes a different kind of mentality," Szczepanek said. "These men have an extreme level of commitment. If we're having difficulty finding information, they're usually the ones we can call for help."

The trial is helping to enlighten residents about the health care system and about health issues. Through the trial, participants are given yearly exams and free PSA tests, plus the medical staffs advise participants on general health issues. Because of these services, residents are becoming aware that there is a cancer program in their area and that the staffs at those centers care about their general health.

"I think some of the men on the trial are seeing this as a benefit to themselves," Szczepanek said. "Participation in the trial will help them stay on track, be on the cutting edge. They're part of something big. The trial is about men's health, not just the prostate gland. It has at least opened the door to planning strategies about how men can be more healthy."

This concern over men's health creates a stronger relationship between residents and hospitals that is vital for all communities, particularly small communities and clinics that don't always have the financial resources of the larger conglomerates.

"It's not often that a community of our size gets to participate in something this big," said Zack. "It certainly shows a commitment on the part of the hospitals that they're interested in preventing a possible health problem. It shows that our hospitals can commit to bringing the most up-to-date technology to our community."

AGGRESSIVE PUBLIC RELATIONS

Community awareness about the trial has been heightened through an aggressive public relations effort that is being played out across the country. Many community cancer centers responded enthusiastically to a national press conference October 13, 1993, held by scientists from SWOG and the NCI to announce

the start of the Prostate Cancer Prevention Trial. In conjunction with the national announcement, for example, the staff at Grand Rapids Clinical Oncology Program formed a public relations committee with eight consortium hospitals, each of which targeted a specific television, newspaper, or radio station for publicity. The committee's efforts, along with a letter writing campaign to local physicians for referrals, resulted in 500 inquiries at Grand Rapids Oncology alone. One hundred twenty-five men wound up attending the center's information meeting, with 80 actually enrolling in the trial. The response has been so overwhelming that the Grand Rapids staff are still enrolling the initial group from their first meeting. However, Zack is considering another media blitz this fall to attract a second group of participants.

At the Medical College of Virginia (MCV) in Richmond, staff members of the hospital's minority-based CCOP participated in a TV news story about the trial. They also worked to produce a 10-minute public service announcement, wrote an article for the college's alumni magazine, and manned telephone lines at a Cancer Survivor's Day telethon.

According to MCV Study Coordinator Gwendolyn Parker, R.N., M.S., media campaigns must be followed up with personal contact so that prospective participants can be advised as to the personal relevance of the trial.

"The best way to get enrollment is to sit down one on one, establish rapport, and get clarification on issues of concern," she said.

Establishing rapport and explaining the trial's relevance are particularly important for minority recruitment, according to many trial coordinators who travel to minority neighborhoods to explain the reasons for and the benefits of the trial.

Edward DeAntoni, Ph.D., an assistant professor of urology at the University of Colorado Medical Center, works with 67 men in his trial group. He agrees with Parker about the importance of personal contact in these neighborhoods, adding that, in his experience, white men are more responsive than black men to traditional recruitment methods like newspaper advertising, and as a result, do not need the personal sales pitch.

"We are getting health conscious, well-educated, upper class white men in our trial group," said DeAntoni, who is also research director for the independent Prostate Cancer Education Council, which promotes nationwide public awareness of prostate cancer. "These men are the ones who will read the papers thoroughly and respond."

Although publicity has generated a lot of response to the trial, some professionals believe timing also played a crucial role.

"The incidence of prostate cancer is really high; it always has been, but now it may be getting the attention it has always deserved," Zack said. "Its time has come."

Yet, only time will tell if finasteride works. No matter what the results, researchers and other health care professionals believe the seven-year nationwide trial is worthwhile.

"There is no scientific evidence that finasteride will prevent prostate cancer, but it's not an unreasonable hypothesis," said Peter T. Scardino, M.D., chairman of the department of urology at Baylor College of Medicine in Houston. He is also co-chair of the Prostate Health Council, a group of specialty physicians and patient cancer survivors who distribute information on prostate disease and prostate cancer.

"Finasteride might work," said Scardino. "It may not be the home run drug, but it might get us to first base.

"No doubt, we will learn a lot from this trial. That information, however, may not be what we expect."

WHAT'S IT ALL ABOUT?

The $60 million intergroup Prostate Cancer Prevention Trial, which was launched in October 1993 by the Southwest Oncology Group (SWOG), calls for the recruitment of 18,000 men in the high risk category of age 55 and older who will have a life expectancy of at least 10 years after the completion of the study. All trial participants must have normal digital rectal exams and prostate specific antigen (PSA) determinations of less than 3.

The seven-year double-blind study focuses on the use of finasteride, an inhibitor of 5-alpha reductase, which is an enzyme in the prostate gland that converts testosterone into the stronger androgen dihydrotestosterone. The study will test whether finasteride can reduce the point prevalence of prostate cancer by reducing dihydrotestosterone.

Participants are being randomly assigned a 5 mg. finasteride tablet or a placebo and will receive annual digital rectal exams and PSA blood tests. The men will be contacted at six-month intervals to verify that they are taking the prescribed dosages. At the end of the study, all surviving participants will undergo a prostate biopsy. A complicated algorithm is being used to equalize the likelihood that PSA screening will identify prostate cancer.

"The plan is to determine if there is evidence in the change of the point prevalence of prostate cancer in men treated with the placebo versus finasteride," said SWOG Chairman Charles A. Coltman, Jr., M.D. "There are a group of kindreds (families) in which some of the men have a hereditary deficiency of 5 alpha reductase. These offspring develop sexual ambiguity, undetectable prostate glands, and they never develop prostate cancer."

Because androgen plays an important role in prostate cancer, and because finasteride can reduce dihydrotestosterone, researchers hypothesize that finasteride will reduce the chances of males developing prostate cancer.

Prevention isn't the only focus of the trial, however. Researchers will also study quality of life by using, among other tests, the American Urologic Association Symptom Score, a series of 18 questions about health status, pain, and social, emotional, and sexual function. By using the score's numerical rating system, participants will be able to explain the effects of finasteride, including the possible side effects of incontinence, impotence, decreased libido, and decreased ejaculatory volume. Interestingly, these side effects can often be resolved through the continued use of finasteride.