LONG TERM RESULTS from the PROSTATE CANCER PREVENTION TRIAL

By Dr. Silvana Martino
Director of Education and Research
The Angeles Clinic Foundation

On August 15, 2013, The New England Journal of Medicine published the long term follow-up of men who participated in the Prostate Cancer Prevention Trial (PCPT). It is an instructive article that causes one to ponder the basic concept of cancer prevention. Many of us believe in the old adage that “an ounce of prevention is worth a pound of cure,” but is that always true? From pure logic, the premise of prevention is sound. However, logic and biology are not always the same.

Examples of the benefits of prevention are certainly available. From the field of cardiology, we have learned that the management of glucose level, blood pressure, lipids and weight has demonstrated improvement in both morbidity and mortality from cardiovascular disease. Similarly, the development of childhood vaccines has demonstrated widespread benefits for large populations. It would seem that the same logic should apply to the field of oncology. It was with these expectations that over two decades ago, our government funded the first breast cancer prevention trial conducted by the National Surgical Adjuvant Breast and Bowel Project (NSABP). The drug tested was the hormonal agent tamoxifen. In designing that study, we questioned whether all breast cancers were under hormonal influence from their onset. If so, we reasoned that we should see a decrease in all types of breast cancer. The alternative hypothesis that was considered was that hormone receptor positive and hormone receptor negative cancer had different origins and we might only see a decrease in hormone positive breast cancer. Though this question may not yet be entirely resolved to everyone’s satisfaction, the results of the tamoxifen prevention trial favored the second hypothesis. Only a decrease in hormone positive breast cancer was noted. Hormone negative cancers were neither increased nor decreased. Interestingly, in subsequent tamoxifen literature, there have been reports of more hormone negative second cancers developing in women taking tamoxifen in the adjuvant setting. Subsequent breast cancer prevention studies with tamoxifen, raloxifene and exemestane have confirmed that hormone receptor
Prostate Cancer Prevention Cont’d …

positive breast cancer risk can be reduced by about one-half using these hormonal agents. In spite of these demonstrated benefits, the clinical application of these agents as primary prevention for breast cancer has never become a dominant medical practice.

The Prostate Cancer Prevention Trial was designed in part based on the favorable results from prevention trials in breast cancer. Breast cancer and prostate cancer share many common properties. They are both very common, they can both behave in an indolent or aggressive manner and both can be treated with hormonal therapy. The PCPT was designed in 1992 by the National Cancer Institute, the Southwest Oncology Group (SWOG) and other participating cooperative groups. The trial included 18,882 healthy men who were enrolled from January 1994 through May 1997. Approximately half were assigned to receive seven years of finasteride (Proscar) a 5-alpha-reductase inhibitor hormone, and the other half were assigned to receive placebo. The median age at time of entry was 63.2 years for the entire group.

The results of this trial were originally presented and published in 2003. As a member of SWOG, I had the opportunity to be among the first to hear the results. As expected, finasteride reduced the overall number of prostate cancers relative to placebo. However, the types of prostate cancer reduced were those of low grade. In contrast and unexpectedly, the group of men treated with finasteride was found to have a higher incidence of high grade, presumably more aggressive lesions than the placebo treated group. These findings led to a standstill in the field of primary prevention of prostate cancer and attention was turned to early diagnosis using PSA screening, which in turn has met with considerable scrutiny.

In 2005, two years after the publication of the original report from the PCPT trial, a long term follow-up study was initiated. The objectives of the extension trial were to update prostate cancer events and to evaluate survival in participants of the original study. No further treatment was planned. Survival data was supplemented by searching the Social Security Death Index.

The updated results were published in a recent issue of The New England Journal of Medicine by Dr. Ian M. Thompson, Jr. and colleagues. Similar to the original report from 2003, long term follow-up demonstrates that men given finasteride experienced a 30% reduction in relative risk of any type of prostate cancer and a 43% relative risk reduction of low-grade prostate cancer. There was again noted an absolute higher incidence of high-grade prostate cancer in those on finasteride of 3.5% versus 3.0% in those given placebo.

Perhaps the most important information available from this follow-up is that at 15 years, overall survival rates were identical for the two groups; 78.0% for the finasteride treated men versus 78.2% for those given placebo. Ten year follow-up of men who were diagnosed with prostate cancer demonstrated a survival rate of 83.0% in the finasteride group and 80.9% in the placebo group. Ten year survival rates for those with high grade lesions on finasteride were 73.0% and 73.6% for those in the placebo group. Specific cause of death was not known for most patients, so we cannot infer how many died from prostate cancer. An important consideration, especially when dealing with an older population such as in prostate cancer, is the reality of competing causes of death. Specific efforts need to be made to record cause of death. This is rarely available in a reliable manner unless specified in the original protocol. The conclusions that can be reached based on the long term results of the PCPT is that finasteride does reduce the overall incidence of prostate cancer, but it has no beneficial effect on overall survival.

A valuable lesson from the data obtained from the PCPT is that long term follow-up that includes survival data provides considerable value and insight. I believe this is particularly true in trials of early detection and primary prevention.

So, how are we to consider the field of cancer prevention? How do we measure its value? Several thoughts come to mind. We must recognize that prevention is most necessary when treatment of a disease is inadequate. If we could cure those with a cancer diagnosis, then prevention would have less importance. We must understand the complex biology that drives the development of cancer to interrupt the process before it has full expression. A single type of therapy such as a hormone for example, suggests a simple understanding of biology. We must be clear on what endpoints we intend to measure. Is it simply prevention of a diagnosis of cancer or is survival our primary target? If it is survival, is it sufficient to decrease cause specific mortality or is overall mortality the true meaningful endpoint? Shall we ignore this target simply
**HONORS AND AWARDS**

DR. LAWRENCE D. PIRO was awarded the BEST OF 2013 SANTA MONICA-INTERNIST by the SANTA MONICA AWARD PROGRAM

DR. LAWRENCE D. PIRO was honored by the SWISS-AMERICAN CHAMBER OF COMMERCE on Wednesday, October 23, 2013

---

**EDUCATIONAL EVENTS**

**CALIFORNIA BRAIN TUMOR UPDATE**

Presented by: SAINT JOHN’S HEALTH CENTER and JOHN WAYNE CANCER INSTITUTE

Date: Saturday, November 16, 2013
Time: 8:30 am—4:00 pm
Location: Annenberg Community Beach House
415 Pacific Coast Highway
Santa Monica, CA
RSVP: (805) 300-9154
Speakers: DR. ANI BALMANOUKIAN & DR. PETER BOASBERG

---

**CELEBRATING OCTOBER BREAST CANCER AWARENESS MONTH**

**By Nick Belardo**

**Administrative Director**

**The Angeles Clinic Foundation**

The Angeles Clinic Foundation made quite the impression on many passersby at The Original Farmers Market in Los Angeles on October 25th, 2013. We placed, in the middle of a busy shopping center, the following: male models, a live action photo booth and information that could save countless lives. MANOGRAMS FOR MAMMOGRAMS was an event that put flash marketing to the test—with the charm and good looks of The Angeles Clinic Foundation models, many people stopped by to take a look. What they were not expecting was to receive information from the male models regarding the importance of being proactive with one’s health and the lifesaving value of screening mammography. Combining fun and an important message, The Angeles Clinic Foundation is thrilled to see this event grow.

*See pictures on next page.*

---

**LIFE AFTER PROSTATE CANCER TREATMENT — PATIENT INFORMATION SEMINAR**

Presented by: USC INSTITUTE OF UROLOGY

Date: Tuesday, November 19, 2013
Time: 6:00 pm—7:30 pm
Location: Catherine & Joseph Aresty Conference Center- Room LG 500
Norris Cancer Center
1441 Eastlake Ave. Los Angeles, CA
RSVP: Regina @ (323) 865-3594
Speaker: DR. LAWRENCE D. PIRO
Manograms for Mammograms
10.25.2013
Spreading the importance of early detection in support of Breast Cancer Awareness presented by The Angeles Clinic Foundation