20% Rise Seen in Number of Survivors of Cancer

About one in every 20 adults in the United States has survived cancer, including nearly one-fifth of all people over 65, according to new federal data. 

The numbers, released Thursday by the Centers for Disease Control and Prevention and the National Cancer Institute, indicated that the number of cancer survivors increased by about 20 percent in just six years, to 11.7 million in 2007, the latest year for which figures were analyzed, from 9.8 million in 2001. In 1971, the number of cancer survivors was three million.

“There’s still a concept that cancer is a death sentence,” said Dr. Thomas R. Frieden, director of the Centers for Disease Control. But, he said, “For many people with cancer there’s a need for them and their families and caregivers to recognize that this is a stage. They can live a long and healthy life.”

About 65 percent of cancer survivors have lived at least five years since receiving their diagnosis, 40 percent have lived 10 years or more, and nearly 10 percent have lived 25 years or longer. The implications, Dr. Frieden said, are that many cancers are treatable and that it is just as important for people who have had cancer not to assume that they will necessarily die early.

(Continued on page 2)

PSA Screening for Men in Their 70s Double That of Men in Their 50s

Why are men in their seventies being PSA screened at twice the rate of men in their fifties, when it is the younger ones who would benefit the most, while many of the older ones really do not need it, according to an article published 28 March 2011 online ahead of print in the Journal of Clinical Oncology.

According to information from 2000 and 2005, almost half of all males in their seventies had a PSA screening test during the previous twelve months. PSA screening would benefit men in their fifties much more if a prostate diagnosis was made and treated. The authors were even more surprised to find that males aged at least 85 years are being screened at the same rate as fifty-year-old men.

The percentage of patients whose prostate cancer metastasizes has dropped significantly over the last few years – this decline has occurred while PSA screening rates have risen. However, concern about PSA screening use continues.

Senior author Scott Eggener, MD and team from the University of Chicago gathered data from the National Health Interview Survey for the years 2000 and 2005. As part of their research, they worked out the estimated five-year life expectancy of each male aged 40+ who had undergone PSA screening.

(Continued on page 4)

Short Course of Hormone Therapy Works in Prostate Cancer

Men with locally advanced prostate cancer had 40% to 50% reduced risk of progression, metastasis, and mortality with just six months of androgen deprivation (ADT) before radiation therapy (RT), a large randomized trial showed. The risk of PSA and local progression decreased by 43% and 55%, respectively, in men who received six months of ADT versus those treated only RT, as reported online in The Lancet Oncology. The hazards for event-free survival (EFS), prostate cancer-specific mortality (PCSM), and all-cause mortality (ACM) declined by 37% to 51%. The findings showed improved outcomes with a much shorter course of ADT than was seen in earlier trials that evaluated ADT for as long as three years.

“The Trans-Tasman Radiation Oncology Group (TROG) 96.01 trial provides evidence that men with nonmetastatic, locally advanced cancers can be treated successfully and have few late side effects, with as little as six months of neoadjuvant ADT and RT,” James W. Denham, MD, of the University of Newcastle in Australia, and co-authors wrote in the discussion of their findings. Three months of neoadjuvant ADT had a more modest or no impact on the principal outcomes as compared with RT alone.

(Continued on page 5)
“You might think, ‘I’ve had cancer – I don’t have to worry about eating right, quitting smoking, exercising.’ ” Dr. Frieden said. But people with cancer “need to be just as concerned about heart disease and other risks as they would otherwise,” he said.

The study defined a survivor as anyone who ever received a diagnosis of cancer that was alive on Jan. 1, 2007, and it did not indicate if the person was cured, undergoing treatment, afflicted with a chronic cancer-related illness, or in the process of dying at that time.

And the numbers tell only a piece of the cancer story. Some cancers, like lung cancer, are aggressive and difficult to treat. And the death rate from cancer, an indicator that many health experts consider a more accurate measure of progress in fighting the disease, has stayed virtually the same as it was in 1950 – about 200 deaths per 100,000 people a year, and about 1,000 deaths annually per 100,000 people over 65.

Dr. Frieden said the increase in cancer survivors was due to several factors, some of which varied by type of cancer. In some cases of breast cancer and colon cancer, for example, improved treatment and increased follow-up after treatment have helped increase survival. In others, like prostate cancer, an explosion in screening has identified many men with the disease, but the cancer is often so slow-growing that they would be unlikely to die from it. And other cancer diagnoses are simply the consequence of the country’s aging population and improved care for other diseases – in other words, people are living long enough to develop cancer.

About a million more of the survivors were women than men, partly because women live longer than men, and partly because breast and cervical cancers are often diagnosed and treated at younger ages. About 22 percent of the survivors had breast cancer, about 19 percent had prostate cancer, and about 10 percent had colorectal cancer.

The study identified only the type of cancer first diagnosed in each person; additional tumors or cancer diagnoses were not recorded.

Health authorities urged families and physicians to be aware of the health needs of cancer survivors. “Having cancer may be the first stage, really, in the rest of your life,” Dr. Frieden said. “We need to continue to scale up” the services available for cancer survivors.

The New York Times, 10 March 2011
**STATINS MAKE RADIATION MORE EFFECTIVE AT CURING PROSTATE CANCER, STUDY SUGGESTS**

Men with high-risk prostate cancer who take statin drugs commonly used to lower cholesterol while receiving radiation therapy are less likely to have their cancer return than patients who do not take these medications, according to a study published in the March issue of the International Journal of Radiation Oncology•Biology•Physics, an official journal of the American Society for Radiation Oncology (ASTRO).¹

In the study, 1,681 men with high-risk, localized prostate cancer were treated with radiation therapy between 1995 and 2007. Of them, 382 (23 percent) were taking statin medication at diagnosis and throughout the treatment. Statins are a class of drugs used to lower the cholesterol level in people with or at risk of cardiovascular disease. The median follow-up time was approximately six years.

Researchers found that the men taking statins were less like to relapse than other patients. At five years, 11 percent of men taking statins saw their cancer return compared to 17 percent of patients not taking the medication. At eight years, 17 percent of men on statins had a relapse compared to 26 percent not taking the drug.

“In our retrospective study, we have demonstrated that statin use during radiotherapy is associated with improved biochemical tumor control among high-risk patients,” said Michael J. Zelefsky, MD, the senior author of the study and a radiation oncologist at Memorial Sloan-Kettering Cancer Center in New York. “This study, along with other emerging studies, strongly suggests that statin use improves outcomes in patients treated with definitive radiation therapy.”

Reference:
*ScienceDaily, 23 March 2011*

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**NEW CANCER DRUG HEADS TO CLINICAL TRIALS**

Researchers at the University of Michigan Comprehensive Cancer Center have developed a new drug called AT-406 that has the potential to treat multiple types of cancer.

A study, published online ahead of print in the *Journal of Medicinal Chemistry*, showed that AT-406 effectively targets proteins that block normal cell death from occurring. Blocking these proteins caused tumor cells to die, while not harming normal cells. The researchers believe the drug could potentially be used alone or in combination with other prostate cancer treatments.

The normal cell death process, called apoptosis, is what keeps normal cells in check. When apoptosis is disrupted, cells reproduce uncontrollably, which is a hallmark of human cancer.

“Removing key apoptosis blockades in tumor cells is a completely new cancer therapeutic approach and could have benefit for the treatment of many types of human tumors,” says study author Shaomeng Wang, PhD, Warner-Lambert/Parke-Davis Professor in Medicine and director of the Cancer Drug Discovery Program at the U-M Comprehensive Cancer Center.

Wang’s laboratory has been pursuing new cancer treatments aimed at this cell death pathway since 2003. His team designed and made AT-406 and tested it in the laboratory in 2006. The small-molecule drug hones in directly on the proteins -- called inhibitor of apoptosis proteins or IAPs -- that block cell death. The researchers found that AT-406 destroyed these proteins in cancer cells. Meanwhile, the drug had little to no effect on normal cells.

In animal models, the drug shrank tumors but caused few side effects. The drug is designed to be taken by mouth, which researchers say will make it easier than traditional intravenous chemotherapies to administer.

Patent applications covering the drug are exclusively licensed to Ascenta Therapeutics, a privately-held, clinical stage biopharmaceutical company co-founded by Wang. After extensive testing, Ascenta began the first clinical trial in 2010 testing AT-406 for cancer treatment. This trial, which is being tested in all solid tumors, is offered at the U-M Comprehensive Cancer Center, Duke University and the Mayo Clinic. Ascenta has also recently opened a second trial of AT-406 in high-risk acute myeloid leukemia at the U-M Comprehensive Cancer Center. Several more clinical trials are planned.

“Our research goal and passion is translating our science and discovery into new and effective medicines for patients,” Wang says. “I am delighted to see the drug we have designed, made and tested in our laboratory now being given to patients right here in the same building.”

**Note to patients:**

AT-406 is still in early stages of testing. To learn more about clinical trials opportunities at the U-M Comprehensive Cancer Center, please go to website <UMClinicalStudies.org> or call the Cancer AnswerLine at 800-865-1125.

*ScienceDaily, 29 March 2011*
NCT01090765: A PHASE I/II STUDY OF TRC105 IN METASTATIC CASTRATE RESISTANT PROSTATE CANCER

Background:
Currently, there is no curative therapy for metastatic castrate-resistant prostate cancer (CRPC). However, new drugs that prevent angiogenesis (new blood vessel formation) that can slow or prevent tumor growth are being explored. TRC105 is an experimental drug that blocks angiogenesis, and has been studied for possible use in treating different kinds of cancer. However, it has not been validated to treat prostate cancer in general or CRPC in particular.

Objectives:
- To determine the effects of TRC105 as a treatment for CRPC
- To determine the safety and effectiveness of TRC105 in treating CRPC

Eligibility:
- Men at least 18 years of age
- Progressive, metastatic CRPC
- Normal bone marrow, liver and kidney function
- Life expectancy 3+ months
- ECOG PS less than or equal to 2
- No brain metastases

DIGOXIN – A POSSIBLE PROSTATE CANCER TREATMENT?

Scientists have identified digoxin as a possible therapy for prostate cancer, using a combination of laboratory science and epidemiology that is unprecedented in its cooperative nature.

The paper was published in Cancer Discovery by lead author Elizabeth Platz, ScD, MPH, professor of epidemiology and Srinivasan Yegnasubramanian, MD, PhD, assistant professor of oncology at Johns Hopkins. Platz said the team collaborated to identify existing drugs that might treat prostate cancer in a process called drug repositioning. This avoids a need for safety studies, allowing testing to determine if the drug will actually work in a new setting, said Platz.

Each branch of scientific inquiry before had flaws but at Platz explained “When we combined the basic science and the epidemiology approaches, the flaws were not the same and were covered by their respective strengths.”

Platz, Yegnasubramanian and colleagues from Johns Hopkins and Harvard combined a high-throughput laboratory-based screen and a large, prospective cohort study.

In the first stage, an in vitro prostate cancer cell toxicity screen revealed that digoxin, a known heart failure drug was a leading candidate due to its potency in inhibiting cell proliferation in vitro.

In the second stage, the epidemiology team observed the drug’s use in a cohort of 47,884 men followed from 1986-2006. Two percent of all study participants reports regular use of digoxin at the start of the study, and those men had a 24 percent lower relative risk of getting prostate cancer compared to men who did not use the drug. Those who used digoxin for more than 10 years had about half the risk of developing prostate cancer as those who did not.

Platz said the team is identifying pathways digoxin targets in prostate cancer to help design a trial that will confirm whether or not digoxin has utility as a prostate cancer treatment.

UroToday, 4 April 2011

SCREENING IN OLDER MEN (Continued from page 1)

They divided the men into two main groups, males aged at least 70 and males aged 40 to 69 (controls). The older men were divided into five groups – ages 70-74, 75-79, 80-84 and 85+. There were nearly 12,000 men aged 40 to 69. The following PSA screening rates by age group were revealed:

- Ages 40-44 – 7.5%
- Ages 50-54 – 24%
- Ages 70-74 – 45.5% (the highest rate)
- Age 85+ – 24.6%

Among those aged 70+, screening rates were higher for men with a life-expectancy of more than five years. 47.3% of males whose chances of dying within five years were “unlikely” (15% or less) were screened, compared to 39.2% with an “intermediate” chance and 30.7% with the highest chance.

Extrapolating data to the general population, the authors estimated 777,000 men with a high five-year mortality risk underwent testing. Screening rates were similar across age groups for men with low and intermediate life expectancies.

Elder men tend to visit their doctor more often because of other health problems, this could explain their high PSA screening rates, while younger men see their physicians less frequently, Eggener wrote as a possible explanation.

Researchers said that their findings confirm a worrying trend of over-screening using PSA, and potential for needless treatment in older patients. Elderly men who are treated have a much higher risk of urinary incontinence, bowel dysfunction and erectile dysfunction.

The American Cancer Society advises males who expect to still be alive in ten years’ time to discuss the risks and benefits of PSA screening with their doctor. Those with an average prostate cancer risk should talk to their doctors when they are fifty, while those with a higher risk (close relative with the disease) should do so when they are 45. The authors say that doctors should be more discriminating about who should be recommended for PSA screening, favoring more those patients who are expected to live longer.

Medical News Today, 30 March 2011
NCCN CONTINUES TO MODIFY PROSTATE CANCER GUIDELINES

“More rigorous” monitoring of active surveillance (AS) is one of the big changes to the prostate cancer guidelines from the National Comprehensive Cancer Network (NCCN), said James Mohler, MD, from Roswell Park Cancer Institute and chair of the NCCN prostate cancer panel. Although PSA screening is problematic, it is also vitally necessary, he stated at the NCCN 16th Annual Conference.

AS is a strategy to reduce the overtreatment of prostate cancer and its related morbidity, said Dr. Mohler. In 2010, the NCCN issued a new prostate cancer guideline calling for AS to be the sole initial approach for all men with very low-risk and low-risk disease. The revised guidance tightens up the monitoring recommendations. Much is unknown about the watch-and-wait strategy, and some new data from AS cohorts in North America are troubling, Dr. Mohler reported.

The NCCN guideline now advises clinicians that, when the initial biopsy is more than 10 cores, repeat biopsy may be performed within 18 months. When the initial biopsy is fewer than 10 cores, a repeat biopsy may be performed within 6 months of diagnosis. However, physicians should “consider” a repeat prostate biopsy as often as annually for all patients “to assess for disease progression, because PSA kinetics may not be reliable as monitoring parameters to determine progression of disease” said Mohler. This insight about PSA kinetics comes from research at Johns Hopkins, in Baltimore, Maryland, one of the AS cohorts in the US. In addition, guidelines state that a digital rectal exam should be performed as often as every 6 months, and at least every 12 months.

“It’s very hard to provide concrete guidance because of the lack of Level 1 evidence,” he admitted. “We hope to do more for patients and urologists to establish the best possible schedule to detect prostate cancer progression,” he said. Evidence will eventually come from the phase 3 “Surveillance Therapy Against Radical Treatment” (START) trial comparing AS with mainstay treatments.

Medscape Medical News, 15 March 2011

ADT BEFORE RT WORKS IN PROSTATE CANCER

(Continued from page 1)

Findings should provide reassurance to clinicians concerned about the risks of long-term ADT evaluated in earlier trials. “Many clinicians and patients are reluctant to use prolonged ADT because of its cost and adverse sequela, which include permanent hypogonadism, osteoporosis, muscular atrophy, various features of metabolic syndrome, anemia, gynecomastia, and prolonged sexual dysfunction,” the authors added.

Clinical trials conducted in the 1990s established the efficacy of ADT as an adjunct to RT for prostate cancer. However, the trials produced mixed results with respect to the duration of ADT, although some trials suggested superiority of long- vs. shorter-term ADT.

Investigators in TROG 96.01 sought to establish a role for short-duration ADT and to compare three versus six months of ADT with RT alone. The trial included 818 men with locally advanced prostate cancer (T2b-T4, N0, M0), enrolled from June 1996 to February 2000. All patients received a total RT dose of 66 Gy to the prostate and seminal vesicles and were randomized to three or six months of ADT (ADT3 or ADT6) or to no additional therapy. ADT consisted of goserelin and flutamide. Men randomized to ADT3 began treatment two months before the start of RT, and patients randomized to ADT6 began treatment five months before RT started.

Primary endpoints were PCSM and ACM. Five-year data from the trial suggested that ADT6 improved PCSM by reducing the risk of metastasis. Denham and co-authors extended the findings with 10-year follow-up data. TROG 96.01 eliminates much of the uncertainty surrounding neoadjuvant ADT and has two clear messages for clinical practice, according to Chris Parker, MD, of the Royal Marsden Hospital in Sutton, England in an invited commentary. “First, it confirms that neoadjuvant ADT significantly reduces mortality after RT for high-risk prostate cancer and is a standard of care,” wrote. “Second, it helps to resolve the uncertainty regarding neoadjuvant ADT duration and strongly suggests that men receiving neoadjuvant ADT should have at least six months of treatment.”

MedPage Today, 24 March 2011

<table>
<thead>
<tr>
<th>Outcome measure</th>
<th>ADT3 vs. RT only</th>
<th>ADT6 vs. RT only</th>
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</thead>
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<tr>
<td>↓ PSA progression</td>
<td>0.72 0.003</td>
<td>0.57 &lt;0.0001</td>
</tr>
<tr>
<td>↓ Local progression</td>
<td>0.51 0.0005</td>
<td>0.45 0.0001</td>
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<td>↑ EFS</td>
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<td>↓ PCSM</td>
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<tr>
<td>↓ ACM</td>
<td>0.84 0.180 (NS)</td>
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</tr>
</tbody>
</table>

MedPage Today, 24 March 2011
ASK DOCTOR SNUFFY MYERS

I live in Sydney, Australia. I had a radical prostatectomy in 2000. My Gleason score was 7. I had salvage radiation in 2004. My PSA doubling time over the past 2 years has been 1.25 is now 0.40. I have been following your diet for prostate cancer on my doctor’s advice for the past 18 months. Most restaurants here in Australia use various vegetable oils (canola, sunflower, sesame) and not olive oil. Most commercial food products also use these oils. Should I avoid them altogether or use them sparingly?

It is important to recognize that this is a diet, not a religion. You do not have to be perfect. As a patient, I have to deal with these issues all the time. When I cannot be sure of the oil used in a restaurant, I generally choose menu items that do not include a lot of oil. Here in the US, most restaurants have chicken or salmon on the menu. I just ask them to grill it with nothing on it. If I am hungry and nothing appropriate is available, I do my best. One bad meal will not do you in.

While I have a special love of olive oil, oils from almond, hazelnut, macadamia nut or avocado would be fine. Avocados and macadamia nuts are major products of Australian agriculture. New Zealand provides the world with the best avocado oil. Perhaps avocado or macadamia nut oil would be available?

Some of my patients carry a flask with olive oil in it for just such emergencies.


DOC MOYAD’S WHAT WORKS & WHAT IS WORTHLESS COLUMN, ALSO KNOWN AS “NO BOGUS SCIENCE” COLUMN

“An aspirin a day can keep the prostate cancer away, or it can put you into the local emergency room if you do not qualify for aspirin!”

Mark A. Moyad, MD, MPH
University of Michigan Medical Center, Department of Urology

Bottom Line: Low-dose baby aspirin continues to show that it may reduce the risk of being diagnosed with and/or dying from colon cancer, but whether or not it prevents aggressive prostate cancer from growing is still controversial, but getting more interesting.

Heart healthy = Prostate healthy right?! Aspirin has to be the most misunderstood over the counter (OTC) product I have ever watched people deal with over time. Heck, it seems natural (originally came from willow bark), it is cheap, and it is touted as a miracle drug, so why not have everyone take it?

Hold the phone Batman! Aspirin also can cause serious internal bleeding and ulcers (not fun my friends). Ergo, just like any pill, aspirin comes with good things for those that qualify and really bad things for those that do not qualify for it. You and your doctor that you trust the most should decide if you qualify for daily aspirin to reduce your risk of cardiovascular disease.

In the meantime, take a look at this website <www.reynoldsriskscore.org> to help determine your cardiac risk and whether aspirin could provide a benefit. In order to benefit from this wonderful web site you have to know your health numbers/health history and also the result of a newer cheap blood test known as “hs-CRP” (ask your doc to get it with your next cholesterol test). Just keep in mind that by reducing your cholesterol, blood pressure, and not smoking that it can reduce your risk of cardiovascular disease to such an extent that you may no longer qualify for aspirin use.

However, recent evidence suggests that individuals may also reduce their risk of cancer death if they can take low-dose aspirin for many years (especially 5 or more). Please keep in mind that most of these positive studies center around reducing the risk of gastrointestinal cancers (like colon cancer).

So, if you are at a high risk for colorectal cancer or were diagnosed and treated for that cancer you should consider taking aspirin. And, this new metaanalysis also suggests that aspirin may reduce the risk of dying form prostate cancer. I believe that men with more aggressive prostate cancer (high Gleason scores) should consider taking a baby aspirin daily if your doctor thinks the benefit would outweigh the risks. This is because aspirin (like statin or cholesterol lowering drugs) appears to have an impact on more aggressive tumors as opposed to non-aggressive tumors.

So, perhaps a baby aspirin (no greater benefit was observed for larger doses) a day may keep the prostate cancer away, but if you are not careful and do not carefully weigh the benefits versus the risks...well an aspirin a day could put you in the emergency room. Take your time and talk to your doctor about the latest research on aspirin and whether or not adding it to your prostate cancer treatment makes sense.

(Wow, now wasn’t that was an unusually serious Moyad column!)

Reference:

MARK YOUR CALENDARS

The dates have been selected for the 2011 Prostate Cancer Conference. Presented by the Prostate Cancer Research Institute (PCRI), their national annual Conference will be held in Los Angeles on September 9-11, 2011 at the Westin Los Angeles Airport Hotel. Visit <www.pcri.org> for more information.

Want to learn more about local prostate cancer support group activities? Read the CHAPTER NEWS! at www.ustoo.org!
The article about the increase in the number of cancer survivors brings both positive and negative reaction. Clearly having more people survive their cancer is a tribute to advances in treating different diseases. But as often happens with statistics, they do not always tell the whole story. Lung cancer is a perfect example; deaths from the disease have remained mostly unchanged. Prostate cancer patients also distort the results because so many men getting diagnosed do not have life threatening cancer. That makes the survival rate look better.

The BOTTOM LINE: There is no doubt that improvements have been made in treating cancer and that applies to prostate cancer but to really judge what is happening, cancer death rates are a much better way to make that determination.

Multiple articles have appeared in the HotSheet about the merits and risks of screening for prostate cancer. One thing becoming increasingly clear is that the odds of benefiting from screening and treatment are exceedingly small in men with a limited life expectancy. The US Public Health Task Force has recommended against screening men over age 75. Other organizations suggest that screening should not be done in men with a limited life expectancy of less than ten years. The study by Drazer, et al found that at least in 2000 and in 2005, screening was done in a large percentage of men with little chance of benefit. Whether or not that has changed in the last few years cannot be determined without another study.

Before screening men with a limited life expectancy, a careful discussion should take place making men aware of the very small odds that screening and treatment will help improve their survival while putting them at a significant risk of a reduced quality of life.

One of the important advances occurring in the management of prostate cancer is the recognition that hormone therapy combined with RT can improve survival of some groups of men. In this issue, the results of another well-done study from Australia and New Zealand are presented in which men with locally advanced disease getting RT received either no other treatment or three or six months of hormone therapy. The study found that men getting the longer duration of hormone therapy with RT had a better survival than the other two groups. Although the authors conclude that 6 months is an effective treatment, another good study also done in men with locally advanced disease getting radiation found that 6 months of hormone therapy was inferior to 36 months. Another study is planned comparing six months to a longer duration but less than three years.

The BOTTOM LINE: For now, men with locally advanced prostate cancer treated with external RT should be informed that the best way to maximize survival is to use 36 months of hormone therapy. Any side effects should be treated aggressively.

In the past few years, several uncontrolled studies have suggested that men with prostate cancer have better outcomes if they are taking a drug that lowers cholesterol. None of the studies have been randomized and that makes interpretation quite difficult. In this issue, another retrospective, uncontrolled study is presented about men getting external radiation (RT), some of who also received a drug that lowers cholesterol. The authors found that here again, those taking a statin drug had a lower chance of a rise in the PSA several years later. Some would look at this result and conclude that men should take a stain drug when they receive RT.

There are two problems with that conclusion. First, this study does not prove cause and effect, which means that the reason men did well might be from the drug but it also might be from something else. The second problem is that PSA is not a valid predictor of long-term survival. The TROG study also included in this issue is a perfect example of the problem with placing too much emphasis on the changes in PSA because men on short-term hormone therapy had their PSA reduced yet overall survival was not affected.

Although using statins might be good against prostate cancer, a properly designed study is the only way to find out if that is correct.

Like bad neighbors who decide to go wreck another community, prostate and breast cancer usually recur in the bone, according to a new University of Michigan study. Now, U-M researchers believe they know why. Prostate cancer cells specifically target and eventually overrun the bone marrow niche, a specialized area for hematopoietic stem cells, which make red and white blood cells, said Russell Taichman, professor at the U-M School of Dentistry and senior author of the study published online in the Journal of Clinical Investigation.

Once in the niche, the cancer cells stay dormant and when they become active again years later, that’s when tumors recur in the bone. The implication is that this may give us a window as to how dormancy and recurrence take place. Taichman and a team of researchers looked in the bone marrow and found cancer cells and hematopoietic stem cells next to one another competing for the same place. The finding is important because it demonstrates that the bone marrow niche plays a central role in bone metastasis giving researchers a new potential drug target.

Cancer cells act a lot like stem cells in that they must reproduce, so the U-M research group hypothesized that prostate cancer cells might travel to the niche during metastasis. One of the jobs of the niche is to keep hematopoietic stem cells from proliferating – which may be the case for cancer cells, as well, the researchers found.

“Our work also provides an explanation as to why current chemotherapies often fail – in that once cancer cells enter the niche, most likely they stop proliferating,” said Yusuke Shiozawa, lead author of the study. “The problem is that most of the drugs we use to try to treat cancer only work on cells that are proliferating.”

Metastases are the most common malignant tumors involving the skeleton, and nearly 70 percent of patients with breast and prostate cancer have bone involvement. The next step is to find out how tumor cells gets into the niche and become dormant, and exactly what they do to the stem cells when they are there.

ScienceDaily, 24 March 2011
Researchers at the University of Michigan Comprehensive Cancer Center have identified a potential target to treat an aggressive type of prostate cancer. The target, a gene called SPINK1, could be to prostate cancer what HER2 has become for breast cancer. The study appeared online in the 2 March 2011 issue of Science Translational Medicine.

Like HER2, SPINK1 occurs in only a small subset of prostate cancers – about 10 percent. But the gene is an ideal target for a monoclonal antibody, the same type of drug as Herceptin, which is aimed at HER2 and has dramatically improved treatment for this aggressive type of breast cancer.

“Since SPINK1 can be made on the surface of cells, it attracted our attention as a therapeutic target. Here we show that a ‘blocking’ antibody to SPINK1 could slow the growth of prostate tumors in mice that were positive for the SPINK protein,” says study author Arul Chinnaiyan, M.D., Ph.D., director of the Michigan Center for Translational Pathology and a Howard Hughes Medical Institute Investigator.

The researchers additionally found that SPINK1 can bind to a receptor called EGFR. They tested an FDA-approved drug that blocks EGFR, cetuximab (Erbitux®), and found that it also reduced the cancerous effects of SPINK1.

Using mice, researchers first tested a monoclonal antibody – a type of targeted treatment designed to go after a specific molecule (i.e., SPINK1). They then tested cetuximab. Tumors treated with the SPINK1 antibody shrunk 60 percent, while tumors treated with cetuximab shrunk 40 percent. By combining the two drugs, tumors were 74 percent smaller. The effect was seen only in tumors that expressed SPINK1.

Previous studies that looked at cetuximab for metastatic prostate cancer have been disappointing, with only 8 percent of patients showing some benefit. The researchers suggest that the poor results may be because the treatment is appropriate only for patients with SPINK1-positive tumors.

“About 10 percent of prostate cancer patients are SPINK1-positive and strategies to block SPINK1 signaling may have utility in this subset of patients. These studies should stimulate the development of antibody-based therapies against SPINK1 or targeting of EGFR in SPINK1-positive cancer patients,” says study author Bushra Ateeq, a research fellow at the U-M Medical School.

SPINK1 is associated with a more aggressive form of prostate cancer. It can be detected in the urine of prostate cancer patients, making it an easy test for urologists to perform routinely.

“This non-invasive form of screening could be helpful in the molecular categorization of prostate cancer patients and administering therapies in a molecularly guided fashion,” says Chinnaiyan, SP Hicks Endowed Professor of Pathology at U-M Medical School and an American Cancer Society Research Professor.

Side effects in mice appeared limited. Future studies will need to determine whether targeting SPINK1 in humans would affect normal tissue. The researchers will also look to further understand why SPINK1 is elevated in a subset of prostate cancers. Clinical trials testing SPINK1 therapies are not available at this time.

ScienceDaily, 5 March 2011