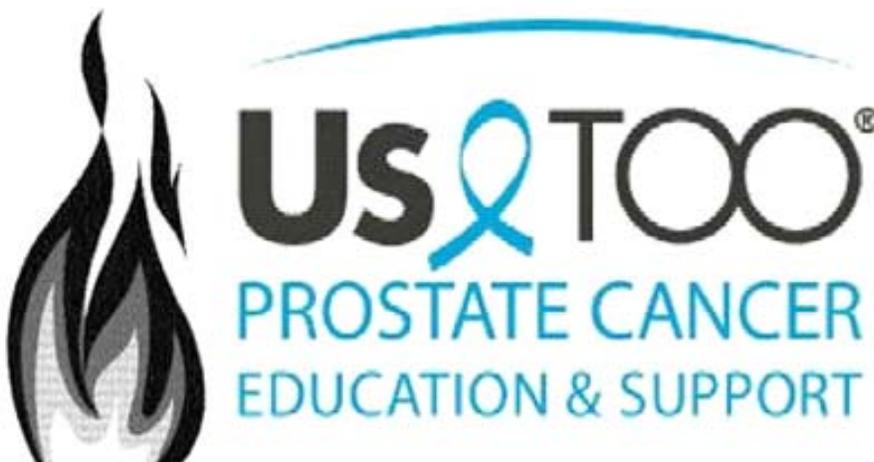


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# HOTSHEET

November 2008

## RADIATION ADDED TO ANDROGEN DEPRIVATION THERAPY HALVES RISK OF PROSTATE CANCER DEATH

Adding radiation therapy (RT) to androgen deprivation therapy (ADT) in older men with locally advanced prostate cancer reduces the risk of dying from the disease by half. These results, from a randomized clinical trial, suggest that men should be offered this additional option, says lead researcher Anders Widmark, MD, professor in RT oncology at Umea University in Umea, Sweden. Dr. Widmark presented the results at a plenary session during the American Society for Therapeutic Radiology and Oncology (ASTRO) 50th Annual Meeting in Boston, Massachusetts.

The trial involved 880 patients, median age 67 years, the majority of whom had stage T3 disease. All of the patients underwent 3 months of intense ADT to achieve total androgen blockade, followed by continuous ADT, but one group also received RT.

After a median follow-up of 7.5 years, death from prostate cancer had occurred in 79 (18%) of 437 patients in the ADT group vs 37 (8.5%) of 436 patients in the combined ADT and RT

*(Continued on page 5)*

## DENDREON ANNOUNCES INTERIM DATA FROM PHASE 3 PROVENGE IMPACT TRIAL

Dendreon Corporation announced that it has completed the planned interim analysis of the Phase 3, randomized, double-blind, placebo-controlled IMPACT (IMmunotherapy for Prostate AdenoCarcinoma Treatment, also known as D9902B) clinical trial designed to assess the safety and efficacy of the investigational active cellular immunotherapy Provenge® (sipuleucel-T) in men with metastatic androgen-independent prostate cancer. While Dendreon remains blinded to the data, the independent data monitoring committee (IDMC) reported to Dendreon a 20 percent reduction in the risk of death in the Provenge arm relative to placebo (Hazard Ratio= 0.80; 95% Confidence Interval [0.610-1.051]). The IDMC observed no safety concerns and recommended that the study continue to its final analysis.

The hazard ratio is an estimate of the treatment effect in the treated versus the control group in a trial. The hazard ratio reported means that a Provenge patient who at the time of the interim analysis has 0.80 times the chance of dying compared to someone in the placebo group. Its reciprocal, 1.25,

*(Continued on page 8)*

## NOVACEA HAS NO PLANS TO DEVELOP PROSTATE CANCER DRUG AFTER FDA LIFTS HALT ON CLINICAL TRIAL

Novacea Inc. announced that it has no plans to develop the failed prostate cancer drug candidate Asentar® (vitamin D3, or calcitriol), despite the FDA’s move to lift an order halting late-stage clinical trials.

In November, the company ended the program after patients taking the drug candidate had a higher rate of death compared with those taking the standard treatment. In April, partner Schering-Plough Corp. pulled out of a development deal on the drug.

Novacea, in May, said it would cut the company’s staff to 15 from 37.

“We welcome the FDA’s response regarding their release of the clinical hold on Asentar,” said Chief Executive John P. Walker, in a statement. “Following the exciting news last week regarding our proposed merger with Transcept Pharmaceuticals, and the related new direction for Novacea, we have no plans for further development of Asentar.”

On September 2nd, the company said it would sell to Transcept in a stock

*(Continued on page 8)*

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**UNDERSTANDING SCIENTIFIC STUDIES & REPORTS:  
A GUIDE TO DETERMINING WHAT'S GOOD & WHAT'S NOT**

Gerald W. Chodak, MD

Many things are changing in medicine, including the increasing desire for patients and family members to learn as much about a disease as possible. This often results in reading on the Internet and listening to news reports. Too often, however, the news media almost exclusively focuses on the study results, paying little attention to the study design or quality of the study. For those reading the scientific study itself, the average person will find the information from the medical journals difficult to understand or critique. This article will focus on some general information about scientific reports and studies that should help individuals without medical training determine if the medical information is good or bad.

**Prospective, Randomized, Controlled Trial:** The best of the best – this study design has been called the ‘Gold Standard’ for research study designs. So, what do all those words mean? *‘Prospective’* means that the information is collected going forward once the study begins; *‘Randomized’* means that neither the patient nor the physician can determine which treatment will be given; usually a computer randomly selects the treatment and makes that decision and *‘Controlled’* means that the study is restricted to patients with similar specific characteristics meaning that not everyone can join. Why is this design the best? Because using it to compare two different treatments is the only way to truly prove that one treatment is better than another. If two groups of patients are essentially identical in every way possible except that one group received a different treatment and had a better outcome, then it is reasonable to conclude that the better result occurred *because* of the treatment given. For example, suppose a new drug has been developed for men with advanced prostate cancer. If it is tested in a prospective randomized, controlled trial and is compared to a placebo or inactive drug and the average survival is longer, then one may conclude that the drug improves survival. Based on that result it can be recommended for pa-

tients with the same characteristics as those tested in the study. **This is the only study design that permits such a recommendation.**

In an ideal world, all research trials would use this design. Unfortunately, that does not occur. You are probably wondering why not. The reasons are cost and time and patient acceptance. These studies usually cost several hundred million dollars to perform and take a number of years to complete. They are just too costly and time-consuming to be done. Drug companies do them because that is the only way a drug can be approved. But in the case of other therapies like surgery or radiation, they are much less likely to be done. The other reason is that in the case of surgery or radiation, too few patients would be willing to let a computer choose the therapy. They want to help make that decision which is not permitted in this study design.

**Retrospective Study:** Not good enough! In a retrospective study, someone decides to look back at patients treated at one or more institutions over many years. Specific characteristics are tabulated including the treatment they received. The results are then reported. As an example, in a retrospective study of men treated for localized prostate cancer at Hospital X, 100 men received surgery and 80 received radiation. Alternatively, all the men at Hospital X received radiation and the results were compared to another report published last year from Hospital Y in which the patients were treated by surgery. The 5-year survival for the radiation patients was 85% but only 80% for the men treated by surgery. So, does that prove that radiation is a better treatment? Absolutely not! You are probably wondering why not. There are many reasons why a retrospective study is not valid. First, the patients may be different due to general health issues their Gleason score or PSA results at diagnosis are different. There may be other differences between the groups that are not known. Second, there is the bias of how patients chose their treatment.

(Continued on page 5)

## THE PATIENT AS HEALER – HOW TO ALLEVIATE YOUR PAIN AND STRESS

Rabbi Ed Weinsberg, EdD, DD

**Editor's note:** Although *Us TOO* doesn't endorse any one treatment type, product, service or book, we felt this subject was of high interest to our readership, and thus included an excerpt from the author's new book, "Conquer Prostate Cancer: How Medicine, Faith, Love and Sex Can Renew Your Life." Five percent of the book's net proceeds will benefit *Us TOO* International, and if you order it through a special link with Amazon.com, *Us TOO* will receive an additional 4-6% of sales. To place your order, either visit the *Us TOO* website at <www.ustoo.org> or the author's website at <http://conquerprostatecancer.now.typepad.com/us\_too/>.

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Reducing or eliminating pain and stress is as much a matter of the patient's resolve as it is the result of scientific progress. We patients must do our part in the healing process. If we ourselves do not demonstrate a strong will, we may end up with a strong won't!

Precisely what can we do as patients? Trust me, no matter how infirm you are, you can do a lot to de-stress. At the very least you can literally take in a big breath! Consciously breathing in and-out in various patterns takes your mind off your pains, at least some of the time. Just ask any woman who has used the Lamaze method for breathing her way through childbirth. Most patients, regardless of their maladies, can quickly learn to breathe in this manner. Almost anyone can adapt a breathing practice to offset whatever causes pain and stress before or after surgery or some other treatment.

Doing your favorite things in spite of your pain can also work wonders. You can rise above your pain by reading a good book, listening to your favorite music, or eating good food (but watch those calories!) You can also go for a swim or take a hot bath in a spa, like my wife and I have done from time to time on our lanai at the back of our house. The heated, whirling water helped reduce her severe back and leg pain due to her spinal stenosis and fibromyalgia. At the same time, the water eased my tensions, including some post-operative issues I had in the weeks after my robotic surgery.

Self-hypnosis is another means toward the same end. Not having any clinical

training in hypnosis did not stop me from trying it. I believe that self-hypnosis is just a fancy phrase for planting a suggestion in your mind and following through. As such hypnosis can be directed by a trained clinician or self-directed by a person who intuitively knows how to redirect his mind-set. For instance you can focus on beautiful images and hear music, or you can recall a beautiful film sequence and transport yourself to that scene. You can also concentrate your thoughts on someone or something you love very much or a beautiful sight you've seen, and keep it in mind until your stress or pain passes.

Of course not everyone is open to the power of suggestion, whether induced by others or themselves. So if you have prostate cancer or another illness and want to prepare for surgery, what's a fellow or gal to do? One of the best approaches to reduce and at least momentarily eliminate pain and stress is to **take every opportunity to laugh**. Tell jokes or watch funny TV shows or movies.

Laughter doesn't always reduce pain, but it sure helps, as journalist Norman Cousins famously wrote while suffering from a painful degenerative spinal disease, described in his 1979 book, *Anatomy of an Illness*. This message is implicit in the ongoing *Reader's Digest* column, "Laughter – the Best Medicine." It's clear that laughter may not always be curative for the long-term, but clearly laughter can't hurt – unless you happen to suffer from broken ribs or severe asthma!

No matter what the disease - cancer, liver damage, brain injury, or spinal stenosis - laughter can reduce or eliminate pain at least momentarily, either because it kicks in endorphins or distracts us from our stress and sorrows.

One example of humor which helps people rise above their medical hardships pokes fun at death. For example I recall a story about reporters who interviewed a man who had just turned 107 years old. They asked him, "What do you think is the best thing about being your age?" His reply: "There's no more peer pressure!"

Many find they can reduce stress by reciting the well-known "Serenity Prayer." This prayer was attributed to 20th Century theologian, political analyst, and Protestant minister Reinhold Niebuhr, who before his passing taught at New York's Union Theological Seminary, across the street from the seminary where I was ordained as a rabbi. However, Reverend Niebuhr was unsure of its actual origins, which have now been traced to two 18th-century deacons in the German town of Weinsberg – from which I am descended! Many who repeat this universally appealing prayer find momentary relief from various stresses and conflicts. Here's a version that is known and recited by millions around the world:

**God grant me the serenity  
to accept the things I cannot change;  
courage to change the things I can;  
and wisdom to know the difference.**

Apart from serenity, we all need to rely on our resiliency - our inherent power to bounce back. I'm not suggesting you deny how difficult your life may be; rather I would encourage you to figure out how to respond with greater creativity and less passivity. Don't fault yourself or others for your illness or related problems. It may be tempting, but don't even fault your clergyman or God. Seriously! Instead seek your own solutions to your concerns. Commit to getting beyond the issues that bother you. Tell others openly what's on your mind.

If you like to write, use a journal to write down your worries as well as

*(Continued on page 6)*

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## PROTON RADIATION FAILS TO IMPRESS IN PROSTATE CANCER STUDY

Proton radiation for early prostate cancer had an acceptable tolerability profile but produced little evidence of a “gee whiz” impact to support its cost, according to preliminary results from a phase I/II clinical trial.

Two-thirds of patients had acute genitourinary (GU) or gastrointestinal (GI) toxicity, and a third had late GU/GI toxicity, Anthony Zietman, MD, of Harvard and Massachusetts General Hospital, reported at the American Society for Therapeutic Radiology and Oncology meeting.<sup>1</sup> Although most of the toxicity was grade 2 in severity, the overall profile provided little reason for enthusiasm.

At the ASTRO meeting, Dr. Zietman reported safety data on 85 patients with localized prostate cancer treated with proton radiation. The patients had stage T1-2a disease and PSA values 15 ng/mL. The treatment protocol delivered a total radiation dose of 82 Gray Equivalent (GyE) in 2-GyE daily fractions – 50 GyE to the prostate and seminal vesicles (including 0.5 to 1 cm margin) and 32 GyE to the gross tumor volume. The primary endpoint was GI/GU toxicity and morbidity.

At a median follow-up of two years, the rates of acute GI/GU toxicity were 50% grade 1, 14% grade 2, and 1% grade 3. Late toxicity was grade 2 severity in 25% of patients, grade 3 in 7%, and grade 4 in 1% (one case of hemorrhagic cystitis and rectal ulcer). The two-year actuarial risk of grade 3+ toxicity was 6.1%. No patients died. Follow-up has been too brief for assessment of secondary endpoints, said Dr. Zietman.

“The bottom line is that the treatment was safe, it was reasonably well tolerated, but probably no better tolerated than any other form of radiation that we give,” Dr. Zietman said. “I think it’s true that if I were looking at this data for the first time, I would say, ‘What’s the big deal? I didn’t see a home run here,’” he added.

1. Zietman AL, et al. *Int J Radiat Oncol Biol Phys* 2008; 72(1 Suppl): S77, abstract 169.

*MedPage Today*, 26 September 2008

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

**“The latest blockbuster drug(s) for weight loss stink (I could have said “suck” but I did not) and that is why they will never get approved so back to the fiber and fish oil I guess.”**

Mark A. Moyad, MD, MPH

University of Michigan Medical Center, Department of Urology

### Bottom Line:

There are several drug companies that have weight loss drugs that help you lose a lot of weight, but they also increase the risk of depression and cause other mental health problems, so they are no good and have no chance of getting approved. Also, I have a political statement at the end of this column - please read it!

Over the past 10 years, several drug companies have invested 100s of millions of bucks (not the animals) to find a new and great weight loss drug. We have only had three weight loss pills in my lifetime that were good enough to write home to mommy about.

The first one was an over-the-counter medication known as “ephedra,” but that caused heart attacks so it is now off the market, thank goodness. The other two weight loss pills are prescription medications, Xenical® and Meridia® (I like Meridia more but that is for a different column). These drugs work okay and seem to be safe, but never caused dramatic weight loss. “Alli” is a “new” over the counter drug that is actually a lower dose version of Xenical (nice marketing job) so in reality you can see why a blockbuster weight loss product would really be a blockbuster because there is not much competition.

Anyhow, back to my story boys and girls about the latest and greatest drugs. Several companies identified a way where people can lose lots of weight by taking a pill that impacts the brain and you end up eating a lot less.

However, these drugs also impact other areas of the brain that can significantly increase your risk of depression. So, Merck was the latest company today that pulled their experimental weight loss drug off the market and there will be more casualties soon I promise you that my friends. What does all this mean for you and your weight or waist?

The only things that have helped with weight loss (besides the obvious of eating less and moving more) in the past year has been a study of a couple of fish oil pills daily with exercise and a study of men and women also getting 20-30 grams of fiber a day. However, recently in the *New England Journal of Medicine* there was some dramatic weight loss with the Mediterranean diet and we will cover that study next month because I have run out of room and I want to keep you interested in this column so stay tuned.

Oh and by the way if any of the presidential candidates mention that they are going to increase funding for cancer research when they are elected please let me know because I have not heard anything about this issue! If you ever wonder why we do not have a cure for cancer, please keep in mind for example that the proposed 750 billion dollar Wall Street bail out is approximately 150 times (I am not kidding here) more than the annual government research budget for cancer!!!!!! I need a beer and some blood pressure medication... see you next time my friends!

Arizona Update

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## RT+ADT HALVES RISK OF PROSTATE CANCER DEATH

(Continued from page 1)

group. "It was rather surprising that the addition of RT cut by half the risk of death from prostate cancer," Dr. Widmark commented. The absolute cumulative difference in the prostate cancer death rate increased from 2.9% at 7 years to 12% at 10 years, with a relative risk of 0.44 ( $P = 0.00003$ ).

In addition, significant reductions were seen in two other outcome measures. Overall mortality rate was 30% in the ADT group vs 21.6% in the ADT+RT group ( $P = 0.004$ ). Plus, recurrence of high levels of serum PSA occurred in 65% of the ADT group but in only 17.5% in the ADT+RT group ( $P = 0.00001$ ).

Quality of life, as reported both by patients and by clinicians, was "slightly worse" in patients who received ADT+RT vs those in the ADT group but "only marginally," Dr. Widmark commented. Adverse events included moderate to severe urinary leakage (reported by 6% of patients in the ADT+RT group vs 3% in the ADT group 4 years after treatment) and pain on urination (reported by 2% vs 4%, respectively). Erectile dysfunction was also more common, reported by 85% of patients in the ADT+RT group vs

72% in the ADT group ( $P < .001$ ).

"This trial will change clinical practice," predicted Anthony Zietman from Massachusetts General Hospital in Boston, who was moderating a press briefing at which the results were highlighted. "At present, there is a bit of a fatalistic attitude towards locally advanced prostate cancer, as it generally considered to have already quietly spread elsewhere," Dr. Zietman commented. "Often the only treatment often offered to older men with this stage of disease is ADT," he continued. "The thinking is that the cat is already out of the bag... but "the results from this trial prove that this is not the case."

"This randomised trial is the first to show that men with locally advanced prostate cancer will survive substantially longer when RT is added to their treatment plan," Dr. Widmark told journalists. "Considering the substantial survival benefit, the increase in symptoms seems to be acceptable and of small influence on quality of life 4 years after treatment," he concluded.

Presented at ASTRO's 50th Annual Meeting, plenary session, 22 September 2008  
*Medscape, 23 September 2008*

## GTx CITES FAVORABLE TREND IN PROSTATE CANCER STUDY

GTx Inc. has reported that its experimental drug toremifene showed favorable safety and efficacy trends in a late-stage trial tested in patients with advanced prostate cancer. The drug was studied to see if it could help lessen worrisome side effects, including bone loss and bone fractures, caused by a standard means of treating advanced prostate cancer called androgen deprivation therapy (ADT).

ADT helps treat prostate cancer by reducing levels of the male hormone testosterone. But it can weaken bones and leave men at high risk of fractures.

Almost 1,400 patients were studied in the Phase 3 trial sponsored by GTx. While continuing with ADT, they were also given either toremifene or

placebo and followed for two years. Among men who began the trial with detectable levels of PSA, 27 percent of those given toremifene saw levels of PSA rise during the study. That was statistically better than the 37 percent of patients receiving placebos whose PSA levels progressed.

Toremifene is an oral selective estrogen receptor modulator (SERM) which helps oppose the actions of estrogen in the body. Licensed in the US under the brand name Fareston®, toremifene citrate is FDA approved for use in advanced (metastatic) breast cancer. It is also being evaluated for prevention of prostate cancer under the brand name Acapodene®.

*Reuters, 16 September 2008*

## UNDERSTANDING STUDIES

(Continued from page 2)

Perhaps healthier patients chose the radiation or their disease was less aggressive. Also, the doctor could have recommended radiation because they felt there was not much cancer present. Another shortcoming is there is no way to validate the accuracy of the information gathered about each patient. There are many examples showing that when information is gathered from medical records and rechecked, there are often errors. For example, the Gleason scores on the biopsy may be inconsistent if different pathologists interpret them. In a prospective study, however, a single pathologist usually will review the biopsies leading to better consistency. Another example is the cause of death, which is sometimes misinterpreted when not done by someone involved in the study.

In summary, in a retrospective study there are too many possible factors that could have affected their survival than the treatment they received. Without randomly assigning patients to surgery or radiation, a valid conclusion about which is better is just not possible. In some ways it is like comparing apples and oranges!

Because of the problems of a retrospective study design, the FDA does not approve treatments based on this approach. Unfortunately, the news media rarely reports which study design was used or the study's weaknesses. The public is led to believe the study provides important information that should influence their treatment decision. However, if you find out the study was done retrospectively, you can now appreciate that the conclusions and any recommendations made may not be valid. Only a prospective study can provide valid results.

**Case-controlled Study:** Also not good enough. Another study design with similarities to the retrospective study is the case-controlled study. A case-controlled study can be done either retrospectively or prospectively. With this design, data about patients from an institution who will be or were treated in a similar fashion are collected and then compared to another group with the same disease

(Continued on page 7)

## THE DOCTOR'S NOTE

Gerald Chodak, MD <www.ProstateVideos.com>

There are three important areas to cover from this month's *HotSheet*. A very important paper recently presented from Sweden looked at the effect of adding external radiation therapy (RT) to hormone therapy (ADT) in men with locally advanced prostate cancer. Previous randomized studies had shown that men receiving RT for this stage of disease had a significantly improved survival if they also received ADT for 36 months. A question not previously answered, however, was whether ADT alone would be sufficient. In this study, ADT was given to both groups and one also received RT to determine the RT added any value.

The answer was YES it did help improve survival. So, going forward, there is good evidence from randomized studies that the best way to treat locally advanced prostate cancer is a combination of ADT+RT. In this study, ADT was given continuously without stopping it and the question that now remains is whether men will have a better survival by taking ADT

indefinitely or limiting its duration to just 36 months. Another study will be needed to answer that question. For now, however, stage T3 disease should be treated with both RT+ADT.

Another RT study cited looked at the complications of Proton beam therapy that has been in used for many years at a few centers in the US. It is likely to become even more available as new sites are in development at a considerable cost. Unfortunately, there is little good scientific data in the published literature although testimonials do exist. The question is not whether the treatment can produce acceptable results, but whether the results are sufficiently better and/or the side effects are significantly lower to warrant it being a better, though more costly alternative to conventional RT. Given the advances in IMRT, it may be very difficult to satisfy either of these two goals.

Results of a phase I/II toxicity study of Proton beam RT are discussed showing a significant rate of grade 2 toxicity. Although no long-term outcomes were

presented, the presence of this toxicity is actually worse than conventional RT. Since randomized trials are unlikely to be conducted any time soon, these data raise serious questions about whether this therapy is a better way to go than the conventional RT or even radioactive seed implants, especially for low risk disease which occurs now in over 60% of all new cases.

Lastly, the article about Novacea, the maker of the Vitamin D related drug Asentar®, is important for the following reason. Preliminary studies and news reports suggested that men were doing better and lay groups suggested that men might benefit from vitamin D therapy. These encouraging studies led to the phase III randomized study. As the article states, mortality was higher in the men that received the experimental drug vs. placebo.

This is yet another excellent example of the need for properly designed, prospective randomized studies to truly determine if a drug or supplement is both safe and beneficial.

## THE PATIENT AS HEALER (Continued from page 3)

your successes. Journaling can help you let go of your anxiety and ease your pain even if you spend just ten to twenty minutes a day in reflective writing. Months after my prostate cancer surgery I admittedly didn't journal consistently. However in some ways writing these thoughts and the rest of my book, *Conquer Prostate Cancer*, was a form of extensive journaling.

Those who don't care to write may find some useful approaches listed in a Harvard publication called *The Relaxation Tool Kit*. It advocates that one should literally smell the roses and use aromatherapy - although care should be exercised for cancer patients who are on specific medications. You can also drink your favorite beverage every day, read regularly, go to the movies and theater, or listen to your favorite music. Eating dark chocolate, within limits, usually won't hurt either! And, of course, hugging someone you love makes a big difference.

In my personal experience those of us

who are pet lovers can de-stress by petting our cats or dogs or other animals at home. My family has twin cats, Oreo - a girl, and Taski - a boy, which belong to our daughter. Just looking at such calm, magnificent animals gave me increased enjoyment and lowered my stress level before and after my robotic surgery. Rubbing their tummies until they purred was even more gratifying. All too often, we get along better with our pets than with people, and both we and our pets derive pleasure and relaxation as they curl up around us—or on top of us.

Other simple but helpful recommendations for reducing stress include meditating and visualizing; exercising and moving around, even if you do so for as little as thirty minutes a day; resting and eating sufficiently; going easy on alcohol; not eating excessively; not isolating yourself from friends or others who are willing to lend their support; and balancing work with play.

Some but not all of these pain and

stress "busters" worked for me before and after my prostate surgery. You have to experiment in order to determine which approach works best for you. It's not quite clear why some avenues will raise your spirits more than others, but this varies from one individual to the next. Practice whatever method benefits your mental and physical health. This will help you develop a more positive outlook, with heightened immunity and reduced toxicity.

To sum up, it's important to take a proactive stance to reduce your pain and stress, supplemented by whatever relief your doctor may provide. Doing your share to control your personal well-being is in your best interest. No matter how ill you feel, it's largely up to you to make your life more livable.

To learn more, please go to <www.ConquerProstateCancer.com>.

## UNDERSTANDING SCIENTIFIC STUDIES & REPORTS—WHAT'S GOOD & WHAT'S NOT

(Continued from page 5)

who were treated by a different method at a different institution. The weaknesses of a case-controlled study are the same as the retrospective study; the potential bias in how the treatment was selected, recognized or unrecognized differences in the patient groups and potential inaccuracies in the data collected. Even if done prospectively, these problems still exist. The bottom-line is no conclusion is justified and a treatment recommendation cannot be made.

**Epidemiological Study:** Garbage in, garbage out. Have you ever heard a news report presenting the results of an epidemiological study saying food X or vitamin Y is good for you and then you hear about another report saying food X or vitamin Y is bad for you? Why such confusion and how should you interpret these reports?

The best advice is to ignore them. Why? The reason is that epidemiological studies prove nothing. They may be correct or they may be incorrect. There is absolutely no way to know the truth. They are conducted by collecting lots of information from a group of individuals such as what they ate, how often they ate it, what vitamins and supplements they ingested, how much they exercised, etc or what treatments they received. The patients are then divided into groups, based in part on how long they lived, or what diseases they developed. The researchers then try to determine whether any particular characteristic or characteristics was (were) associated with living longer, or getting a disease, or avoiding one. They may find that food X was associated with a particular disease; those eating a lot of it were more likely to develop cancer than those eating little or none of it. The greater the amount people ate, the greater the likelihood of getting the disease.

There are many problems with trying to make conclusions and recommendations based on epidemiological studies. Some of it is the accuracy of the data gathered. There may be other unknown factors that influenced someone getting or avoiding a disease. The most significant criticism of an epidemiological study is that it does not

prove cause and effect. There is no way to conclude that the reason a result occurred is because of any particular intervention. Epidemiological studies are useful, however, for designing prospective studies. They generate an idea for a prospective study to prove or disprove the theory.

The next time you hear the result of an epidemiological study presented, say thank you very much and be hopeful that a proper prospective study will eventually be done to determine if the result was correct. Is there any harm in incorporating the findings from an epidemiological study about a food or supplement into your own life? No, of course not, as long as you realize that it may good for you or it may be bad for you and there is no way to know if there are any harmful effects. But if you do hear about the results of an epidemiological study, realize that nothing has been proven.

**Commentary:** There is much more to learn about research study designs but this information should begin to make it possible for individuals who are not doctors to be a little more critical about what you hear on the news or read in the papers or on the internet. If at all possible, try to determine how the study was performed. If the report is discussed in a news article, send an e-mail to the author or try to search for that article on the Internet. That is quite easy to do these days and then look specifically at the study design so you can decide if the results are valid and useful. While all studies do provide some useful information, they do not all provide patients with guidance on the best form of treatment. Only a prospective randomized controlled trial can do that.

For those with prostate cancer, the challenge is even greater because treatments can and do become available even without a randomized controlled study. Such is the case for radical prostatectomy, radiation therapy, brachytherapy, cryosurgery, hormone therapy and HIFU. Not one of these treatments was ever compared to a placebo or control before it was used for patients nor have any of them been compared to each other. The FDA did

not have to approve these therapies. As discussed earlier, however, for new medications, drug companies must perform randomized studies because the FDA regulates how drugs can be marketed. In order to claim a drug is effective for the treatment of X disease, they must conduct a prospective randomized trial to prove it. The FDA does have to certify that a new device is safe for patients, but it is not necessary to show how a treatment compares to other treatments in terms of efficacy for treating a disease. That is why there is so much disagreement between doctors as to which option is best for a given patient with localized prostate cancer. **WE HAVE NO PROSPECTIVE RANDOMIZED STUDIES.** This is important for you to recognize when being counseled about your therapy. If a doctor recommends any of these treatments, it is based on his/her opinion and NOT on the kind of study (prospective randomized study) that proves it is really better than any of the other options available. There is physician bias. Unfortunately, this is not likely to change because there is no incentive for those studies to be done.

**In summary,** medical science is making important progress all the time. More good studies are being conducted that truly help guide treatment for patients. Yet, there are still too many studies that are not well designed but we hear about them anyway and they get publicity. It is the nature of news reporting. Patients need to be aware that just because something is in the news or on the Internet does not make it correct or useful. And since no one restricts the kind of studies that can be published or what is written on the Internet, we are far more likely to hear about retrospective, case controlled or uncontrolled studies because they are so common.

In the absence of good studies, what should a patient do who is trying to decide about treatment? Become informed about all the options, learn what are good and bad about each and then share in the choice, recognizing that no one can prove at this time that one is better than the other.

**PROVENGE INTERIM ANALYSIS** *(Continued from page 1)*

means a placebo patient has 1.25 times the chance of dying compared to someone in the Provenge group.

“The treatment effect we have observed in this interim analysis is consistent with that observed in the integrated analysis of our previous Phase 3 trials in this patient population when analyzed at a similar 24-month follow-up time,” said Mitchell H. Gold, MD, president and chief executive officer of Dendreon. “Given the delayed treatment effect we have seen in previous studies, we are pleased to see evidence suggesting a prolongation of survival in the Provenge arm at the time of the interim analysis, as well as a favorable safety profile.”

At the final analysis, which is anticipated in the middle of 2009, if the study

demonstrates approximately a 22 percent reduction in the risk of death, based on 304 events, the company would expect the study to meet its primary endpoint of overall survival. The FDA previously agreed that a positive final analysis for overall survival from the IMPACT trial would be sufficient to meet its request for additional clinical information to support the proposed efficacy claim for Provenge.

“We look forward to the final results next year and the opportunity to make Provenge available to the many men with advanced prostate cancer who currently have few appealing treatment options,” said Dr. Gold.

*Dendreon Corporation, 6 October 2008*

**NO JUDICIAL REVIEW FOR PROVENGE**

The US Court of Appeals has rejected CareToLive’s (CTL) appeal that requested an investigation into the FDA’s decision to delay approval of Provenge® (Sipuleucel-T; Dendreon) in May of 2007. CTL is a non-profit advocacy group for men with late-stage prostate cancer.

CTL requested judicial review after the District Court for the Southern District of Ohio dismissed CTL’s claims that there was a lack of transparency and accountability in the FDA decision. The US Court of Appeals rejected the appeal on the grounds that “the district court did not err in its conclusion”.

Earlier this year the House of Representatives Committee on Energy and Commerce also rejected a request from several House of Representative members to investigate any possible conflicts of interest in the FDA’s decision. Committee Chairman John Dingell declined the request, explaining that the Committee must allow the FDA to make a final decision about Provenge, which was delayed and not rejected by the FDA.

*Nature Reviews Drug Discovery, Vol. 7, pp. 792-3, October 2008*

**NOVACEA HAS NO PLANS TO DEVELOP ASENTAR**

*(Continued from page 1)*

deal, with Transcept shareholders owning 60 percent of the new company and Novacea shareholders 40 percent. The deal is expected to close during the fourth quarter of 2008 or the first quarter of 2009.

After the announcement, shares of Novacea fell 30 cents, or 16.1 percent, to close at \$1.56. The stock reached an all-time low of \$1.50 earlier in that trading session.

*Associated Press, 11 September 2008*

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