The Survivors Guide to Advanced Prostate Cancer

By

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With Help From the
The Advanced Prostate Cancer On-Line Support Group

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Welcome

Malecare is America’s primary prostate cancer support and advocacy organization. Since we began in 1998, many thousands of men have attended our online and or in-person prostate cancer support groups. Today, many of those same thousands of men are surviving advanced stage prostate cancer.

One of those men is the author of this book, Joel Nowak. There is no prostate cancer survivor on this planet better able to help you navigate your advanced stage prostate cancer than Joel.

This book will help you live longer. It will help you understand your treatment options and their potential side effects. It will help you work with your doctors and care givers. It will teach you some of the truths and break some of the myths about advanced stage prostate cancer.

Whether you have been diagnosed initially with advanced stage prostate cancer, or are dealing with a recurrence of prostate cancer after an initial treatment, you are in good company if you feel shocked, scared, or betrayed.

There’s nothing warm and fuzzy here - just the information necessary for you to feel armed with sufficient knowledge to join with your doctors in fighting the prostate cancer inside you. After reading this book, you will be better equipped to ask focused and life-saving questions about your cancer. You will feel stronger than you feel now, and you will be a more confident treatment choice maker.

This book does not suggest any particular treatment as “best.” When it comes to prostate cancer, each man’s situation is unique. To decide on the best treatment, you must work with your doctors. And that work is hard and tedious. But, you’ve got a version of prostate cancer that could well kill you sooner rather than later. If you want to live longer, you’ve got to work harder.

Register in the advanced prostate cancer program at malecare.org to receive notices when updates are available. Meanwhile, grab your favorite beverage, sit back and spend the next hour or two reading about advanced prostate cancer.

To your health!

Darryl Mitteldorf, LCSW
Executive Director
Malecare Cancer Support

Please email any comments or factual errors:
darryl@malecare.org
Important note:

Do not use any of the information contained and or referenced in this book without first consulting a qualified medical professional. The author and the staff of Malecare are not Medical Doctors, and do not offer any medical advice. Our goal is to help patients, caregivers, and others interested in developing an understanding of prostate cancer, its treatment options, and the treatment of the side effects that often accompany treatment. By reading this book, we hope that you will develop talking points and questions for you to bring to your doctor. Always make sure that you have a full and complete discussion with the medical professional/physician providing your prostate cancer care.
FORWARD

I have written this survivors guide from my personal perspective, as a man who has been diagnosed with four different primary cancers including advanced prostate cancer. My first cancer diagnosis goes back nearly 30 years, so I have a lot of firsthand experience being a cancer survivor. I know that it is vital for anyone with any serious chronic illness, including advanced prostate cancer, to become an empowered patient, or perhaps I should say an empowered survivor.

Becoming an empowered survivor involves very hard work. Some of you might remember the television show “Dr. Welby.” Marcus Welby was a great doctor, a terrific advocate; he knew everything about medicine, had unending time to spend with each of his patients and he cared about all of his patients as if he was a family member. The sad news is that Dr. Welby is no longer taking new patients! This shocking news means that we as patient survivors must step fully into his shoes and become our own medical advocates.

Being an advocate requires us to become educated about our illness. Like it or not, we must completely understand our treatment options, their possible side effects and their possible benefits. We must become the CEO of our own health, actively collaborating with our physician consultants. We are the boss of our treatment decisions. It is our own body that we are making decisions about. Our doctors experience their lives independent of ours. We alone return to our homes and experience the negatives and the positives of our decisions.

Ask questions of your doctors and then ask some more. Keep asking until you understand what everything means. Learn about and then teach your doctor about new options for treatment. This will require you to do some homework, but it will enhance all of your medical decisions and guarantee you cutting edge treatments. Since you are ultimately responsible for making your medical decisions, arm both yourself and your doctor with the latest evidence based information available.

Once you have decided on a treatment, own your decision. First educate yourself about all your options, weigh the pros and cons of the options, and then make a decision. There is a feeling of power from making a choice.

There are not right or wrong decisions. If a treatment doesn’t work out or the side effects become overwhelming, you can choose to change your treatment. Agonizing and regret will only make you miserable, so make your educated decision and then move on with your life. Remember, every day is a new day and a new chance to make a different choice if you need.

All advanced prostate cancer treatments have undesirable side effects, so learn about them and anticipate them. The only treatment that is free of side effects is no treatment -- if you believe that dying from prostate cancer is not a side effect.

This book can be used in two different ways. You could choose to read it from beginning to end or you can search for the specific topics that interest you. Use it in any way that will help you understand the treatment options you face.
It is up to you to decide how you want the rest of your life to go. You could let your feelings of anger take over your life, or you could choose to be happy. I decided I had no interest in living the remainder of my life as an angry person, so I decided to let go of the anger. It worked for me: I am a happy person. My multiple cancer diagnoses are a part of my life, they are potholes on my life road, but potholes can be jumped over or walked around. Avoiding them is part of the journey.

Thank you to Darryl Mitteldorf, LCSW, Wendy Lebowitz, PhD, MPH, Craig Pynn, BSEE, MBA and all the members of the Malecare Advanced Prostate Cancer online support group for their collective wisdom and their editorial assistance in creating this guide. Also, thanks to my family, Wendy, Dov, Max, and Charlie-the-mini-Labradoodle, who have served as superior caregivers when I needed them.

Joel T. Nowak
Introduction

On Being Diagnosed with Cancer

I have been diagnosed with multiple cancers. My diagnoses have included thyroid cancer, prostate cancer, renal (kidney) cancer, Reoccurring prostate cancer and melanoma. Believe me, I understand the implications of a cancer diagnosis. I also know the emotional and psychological effects of a cancer diagnosis.

The very worst time in your life is when you hear the three dreaded words, “you have cancer.” But it will get better and easier. The shock and the panic we all experience will diminish and eventually, we will develop a “new normal.” The reality is that we are no sicker on the day we heard our diagnosis than we were the day before. We will also be the same the day after we learn the diagnosis. In reality, you’ve had the cancer for a long time before you were diagnosed. You are still alive today and will probably remain alive for a long time to come.

Being diagnosed can extend your life because you can now start the battle.

The difficult thing is that you must now deal with an unfamiliar world. Your health, and even your life, depends on it. The vocabulary is different; expectations are different—all along with underlying fear. Taking time to educate yourself will not only reduce fear, but will help you survive longer. Read all you can and speak with others who have already walked the path. Ask questions; examine options; get second and third opinions; carefully choose which doctors you bring on to your team. Finally, always remember that over your life’s journey, cancer is little more than a rock, or perhaps just a pebble, on the path.

Many of us find that when we have been given a cancer diagnosis we spend more time thinking about life. Not bad idea.

You have more time than you may think. Never allow artificial time limits to pressure you into making decisions you are not yet comfortable making. Take all the time necessary to learn all you can so that all your decisions are the best-informed ones you can make. Except for the most aggressive cancers you have ample time to educate yourself as much as possible so that you are able to make good decisions.

Once you have made an informed decision and carried it out, never look back. Looking back in regret about what is past is pointless and will only drive you crazy. The path is always forward: continue to learn about your disease and always look ahead. What counts is today and what lies in the future.
Yesterday is gone, so forget it.

If you educate yourself as completely as possible and you took the time you needed, you will always know that no matter the outcome of a particular choice, you made the best possible decision. That knowledge that you have thought your decisions through carefully is what is really important—and may be more important than the decision itself. An occasional “pity party” might be healthy as long as it is only occasional and brief. It is important to get over it in time to continue to live your life happily and take the next step in dealing with your cancer. Never feel bad for yourself about a poor outcome. You will never know if a different decision might not have actually been worse. Again, the only thing that matters is today and tomorrow. Let go of yesterday and live only in the present.

You always have choices so choose to always be positive.

Remember: Treatment decisions can be changed. When you begin a particular treatment you have not signed a lifetime contract to continue it. Just because a treatment is supposed to last for one year never means that you are required to do it for one year. Possibly, its side effects are so overwhelming that you no longer have an adequate quality of life. Also, new options continue to come along. Some of them may be a better choice. You don’t need to continue to stick it out. Just make sure you are completely informed about the possible consequences of changing your treatment decision.

You are in charge. Not your doctor and not your family. They need to be consulted and their opinions and ideas should carry weight as you make your decisions. But never forget: it is your life, your today, and your future. Make the best possible, fully educated decision that makes sense for you. But to repeat: make sure that you have taken the time to learn all you can and that you understand the full implications of your decisions. Remember, you are in charge.

There is never room for should haves or could haves.

All treatments have side effects. Some of them may be difficult. Just take one day at a time. Keep your life in a manageable perspective, one that you can get through and finish. Break things down to a manageable level, even if it means taking a week a day at a time and a day an hour at a time. As each hour passes and each day passes, you are that much closer to the end of treatment. We don’t eat our dinner in one gulp; we eat it bite by bite, each in a manageable portion. Cancer treatment is no different.

On Being Diagnosed with Advanced Prostate Cancer

Advanced prostate cancer occurs when the cancer escapes the confines of the prostate gland itself. Men may be diagnosed with advanced prostate cancer in one of two ways: Some are diagnosed initially with advanced disease, while others experience Reoccurring prostate cancer after having had a primary treatment failure. Although they aren’t, for simplicity, this book uses the terms Reoccurring prostate cancer and advanced prostate cancer interchangeably as the treatments are much the same.
Advanced prostate cancer often occurs without physical symptoms. This may sound surprising, but feeling healthy is not a good indicator of how life threatening your prostate cancer may be. In fact, many men in our support groups learned of their advanced stage disease from elevated PSA scores or a suspicious image revealed by scans rather than having experiencing any physical symptoms.

About 30% of men who have had a primary treatment for prostate cancer eventually experience a return of the cancer, or Reoccurring prostate cancer. Even after our doctors assured us that our treatment worked and that we were cancer-free, it comes back. Truth is, prostate cancer never left us. The initial treatment simply failed to remove or destroy all the cancer cells in our bodies. It's not anyone's fault. In almost every case, your doctor treated you properly. But, it is a sad, although rarely discussed, fact that prostate cancer treatments are not foolproof. Their long-term effectiveness is unpredictable. Given the state of current medical science, that permanent "cure" that we all hope for is impossible to guarantee.

Cure is not a word that should be in our vocabulary – long-term remission and a chronic illness is our goal.

The most common concern is whether the prostate cancer cells have journeyed to distant parts of the body. When cancer cells have moved out of the prostate gland, we refer to this state as metastatic prostate cancer. Metastatic cancer is not a death sentence, though without proper understanding of the disease it can sound that way.

This is the main goal of this book: Helping you to understand the disease and how to work hand-in-hand with your doctors so that you live a long, happy, and healthy life with the chronic illness called prostate cancer. Our goal is simple: to live long enough to die from some other cause. Many men live many years after their prostate cancer is determined to have metastasized. Even men who are experiencing physical symptoms may benefit from treatments that can add many months and years to their lives.

Men experience advanced prostate cancer along a continuum of symptoms. In its more advanced stages prostate cancer can be accompanied by physical symptoms, including stiffness in the lower back, upper thighs or hips. Some men feel aches and pains in their bones, which is the most common site for the development of metastasized prostate cancer tumors. Others experience swelling in the ankles (edema) caused by obstructions in blood vessels or lymphatic system, as well as weight loss, and an insufficient number of red blood cells (anemia).

So, that is most of the bad news.

Now, the good news: you can learn to live a long and enjoyable life with prostate cancer. Our goal is to teach you about advanced disease so you can get on with enjoying your life. Advanced stage prostate cancer is serious, but there are excellent treatments available today, and many more in the FDA approval pipeline coming in the next few years. Like me, many of us are already living longer and are happier than you might imagine. This book will help you join us.
Being active in my treatment decision making is the way I fight my cancer.

Much of the information in this booklet - especially the insider tricks - comes from the Malecare Advanced Prostate Cancer On-Line Support Group. You can join this group by going to: http://health.groups.yahoo.com/group/advancedprostatecancer/join.

About Fighting Advanced Prostate Cancer

Every man experiences prostate cancer differently. Our bodies are different. Even the shape and the size of our prostate glands are unique to each man. Each of us will respond differently to treatment and each of us will experience a different disease progression.

That's why it's so important to listen to your body, regardless of which type of treatment you have elected. That's also why it's important to understand what makes you happy, and to decide how you want to live your life. This decision includes insisting on getting the tests and treatments that your body tells you are required. Your doctors are there to advise you. Your family and your friends are there to encourage and assist you. Men, who have walked this path before you, are there to tell you what they have experienced. But none of them are there to decide on your treatment. That's your decision—and yours alone.

It's Your Decision, Yours Alone

A few years ago, I had a small spot on my leg that my body kept telling me meant trouble. I went to two different dermatologists to have them examine the spot. Both thought I was over-reacting and I should go home and forget it. While I was still lying on the examining table at the second doctor's office I told her that I needed to have a biopsy. When she refused, I told her that she had two choices: she could perform the biopsy or, she could call the police, have them handcuff me and then drag me out of her office while I was still dressed in my paper gown. She finally understood my insistence, relented, and performed the biopsy. The results revealed melanoma, a cancer that could have killed me if the biopsy hadn't been performed at that point.

Listen to Your Body – It Knows Best. Be the boss of your own body.
My own life is proof that men can live full and reasonably healthy lives even though they have advanced prostate cancer.

I was diagnosed with prostate cancer 13 years ago. Eight years ago, I experienced a recurrence of the cancer. Today, despite being diagnosed with four other cancers in addition to advanced prostate cancer, I am as happy and as healthy as I was when first diagnosed!

Men diagnosed with prostate cancer become more aware of their own mortality. Up until we have to confront a disease like cancer, many of us men tend to see ourselves as being permanently healthy. But in acknowledging the possibility of death, we become more introspective about life and its value. Now, we begin to think about how we want to live and enjoy life. Seeing what is most important to us, we begin to set new priorities. We think, too, about how we wish to be remembered, and what impact we may have on the world. Many men report that after they absorb and reflect on their diagnosis, and put their lives into true perspective, they feel far more fulfilled. They learn to appreciate every day as the gift it is.

As the saying goes, “if you have to have cancer, there’s no better time than right now.” Ongoing research, new treatments and drugs are transforming cancers of all kinds from death sentences into manageable chronic illnesses. Nowhere is this truer than with prostate cancer. The treatment goal is simple: learn to live with the chronic illness called prostate cancer, not to die from it. Today this is not only possible it is highly probable.

Defeating cancer involves every aspect of our being: our minds, our bodies and our souls. Understanding and accepting that cancer is just one of the many steps along our life’s journey—and no more than that—puts cancer into the framework of day-to-day reality. Cancer is no more than a part of living; it is not a curse, and it is not a punishment. There is no shame in cancer and no embarrassment. It is time that we push cancer out of the shadows. It is time to call it out for what it is and defeat it.

- Be honest with yourself about your feelings. Saying them out loud helps.
- Then consciously decide to move on and live your life.
- Don’t do what you cannot do, but do what you can.

At Malecare’s advanced prostate cancer blog (www.advancedprostatecancer.net/?p=2-88) there is a post, "Learning from the Regrets of the Dying," listing some of the regrets other men have shared about how they lived their lives:

- “I wish I'd had the courage to live a life true to myself, not the life others expected of me.”
- “I wish I didn't work so hard.”
"I wish I'd had the courage to express my feelings."

"I wish I had stayed in touch with my friends."

"I wish that I had let myself be happier."

In one sense, a cancer diagnosis is a wake-up call. It’s an opportunity to step back and examine how we are going to live our lives going forward. As we’ve said, yesterday is over; there’s nothing we can do to change the past. But today and many tomorrows still lie ahead of us. We can learn from this collective wisdom and decide to make changes in our life now. Our attitude has an enormous impact on how we will live with this disease.

**Now is the time to dissolve regrets.**

**What Kind of Life Can I Expect?**

Most men with advanced prostate cancer can enjoy many healthy years with an excellent quality of life. Living a healthy, happy and extended life has just a few simple requirements.

- Learn as much as possible about this disease;
- Work hand-in-hand with our doctors in shaping our treatments;
- Be flexible in our treatment decisions;
- Think out of the box;
- Always advocate for ourselves, and make our own decisions;
- Always give ourselves ample reasons to continue to enjoy life.

That is why you are reading this booklet, so keep reading.

**What You Can Do, Starting Today.**

The place to begin is education. Here are six simple ways to start:

**Educate yourself - Ignorance can be a blessing, but ignorance can also kill you.**

1. Know that there is no such thing as a stupid question about prostate cancer.
2. Ask your questions at a support group, or email them to other men fighting advanced prostate cancer.
3. Join the Malecare Advanced Prostate Cancer On-Line Support Group by emailing your request to join to Joel@malecare.org
4. Read the Advanced Prostate Cancer Blog at www.advancedprostatecancer.net

5. Sign up to receive the Prostate Flashes (information@prostateflash.com) and the Advanced Prostate Cancer Newsletter on the Advanced Prostate Cancer Blog (www.advancedprostatecancer.net).

6. Learn to read and evaluate ongoing research articles on the Internet.

Along with education, here are three other important life issues to consider:

1. Try to adopt a "heart healthy" diet. Limit your consumption of red meat, dairy products, and foods containing processed sugar. While the research is not completely clear on why this helps, most guys who follow through on adopting a healthier diet report feeling livelier, and often experience fewer treatment side effects. Consider purchasing organic vegetables and fruits—and eat a lot of them. Healthy eating can help you feel better, have more energy and feel less depressed. It can also help your overall health, and protect your ability to resist or manage other illnesses—particularly cardiovascular diseases and diabetes. And, if you feel better, you will be more motivated to fight your cancer.

“Everything you put in your mouth affects your life,”
Darryl Mitteldorf.

2. Along with diet, add exercise to your daily routine. Regular exercise has been shown to increase longevity, as well as quality of life. Even just walking each day helps a lot. If your treatment for advanced prostate cancer includes hormone therapy, resistance exercises such as weights and bands help reduce the effects of muscle and bone mass loss caused by the lack of testosterone in your body.

3. If you have advanced prostate cancer, you really want to have a medical oncologist on your team. Try to find an oncologist who focuses on treating men with advanced and Reoccurring prostate cancer. General oncologists are good, but oncologists specializing in advanced or Reoccurring prostate cancer are best.

Let’s look at the issue of choosing your medical team in more detail...

Your Doctor — Who Should It Be?

Urologists are almost always the doctors who diagnose men with prostate cancer. Typically, most men remain under the care of their urologist through primary treatment and follow-up PSA monitoring. But when you have been initially diagnosed with advanced prostate cancer or you have a recurrence, you should add a medical oncologist to your team, preferably one with considerable experience dealing with patients with advanced prostate cancer.
There’s an on-going debate in the medical profession between urologists and oncologists about the typical urologist’s qualifications to treat men with advanced prostate cancer. Choosing the doctor to spearhead your treatment is a very personal decision. My personal opinion is that if you elect to have your urologist head your treatment team, make sure that he or she has received significant additional training and has ample experience treating advanced disease. Above all, don’t be afraid to ask your urologist about special training; this is a very important question.

Finding the right doctors is a critical task and will involve a substantial investment of time and energy. When we go to the supermarket we often spend time reading the ingredients in the things we’re considering buying. We may try on many different suits from the rack in order to find one that looks good on us and is comfortable. Think of finding the right doctors in the same way. Don’t be afraid to “try on” a number of them before making a decision. Even after you’ve made a decision you can always choose to change your doctor.

Keep looking until you find the doctor that fits you.

Just as important as your doctor’s expertise and experience is how well his or her philosophy and attitude aligns to yours. There are doctors out there who feel they "know it all” and you, the patient, are basically ignorant and should just follow directions. Condescension has no place in a doctor-patient relationship. You must feel comfortable and know that you are a person, not a number. The doctor should be willing to spend the time needed to thoughtfully address your concerns and answer your questions. (Which is another reason why educating yourself about your disease is so important.) The best doctors appreciate good questions that also demonstrate you’re taking the time and effort to learn everything you can about this disease, its treatment, and how it may affect you.

Always get a second and even a third doctor’s opinion, no matter what type of doctor you have or how famous they are in the trade. Much of medicine is subjective, and different doctors may offer different views of your condition and how to treat it. If possible, consult with different medical oncologists and urologists from different medical practices at different institutions. Some institutions develop standardized protocols that they follow despite the individual nature of your disease. Meeting with doctors at different institutions is also useful because some doctors are not happy contradicting a colleague with whom they work. Always remember: you and your disease are different from every other man and his disease. Standardized protocols have a valuable place in medicine, but mainly as a jumping off point, not as a cookbook recipe on how to treat you.

It is important to me that my doctor listens to my concerns and seems to care about what I have to say.

Every doctor wants a satisfied patient. You can build your peace of mind by getting second and third opinions. Seeing another doctor for a second opinion should not offend the original doctor; this practice is common and expected. Insurance almost always covers a second opinion. A doctor who gets angry or upset that you are seeking a second opinion is not the doctor for you...or for anyone else. That said, not everyone lives in a large urban area where “doctor shopping” is practical. Wherever you live and whatever your economic circumstances are, do your best to consult with several doctors. But, don't beat yourself over the head if this proves difficult because of your location.
Until I read my medical records, I didn't really understand what was wrong with me.

Your medical records belong to you. Having your records in your personal possession is key to being able to understand and manage your disease and treatment—and to ask questions at every doctor visit. If you haven't already gathered these records you need to do so, today. You will want a record of every visit you make to a doctor, as well as every test and scan you have ever had. Ask all of your doctors, past and present, their nurses or office staff for copies of these records. Include all of your blood tests, progress notes, surgical notes and scan reports, etc. You may have to pay a small duplication fee but it's well worth it.

Don't be afraid to ask for your records. Don't be worried that you will insult your doctor when you go for a second opinion. A competent and educated doctor will not be threatened by a second opinion, which will require your complete records.

The Affordable Care Act (ACA) now requires most doctors’ practices, labs and hospitals to implement Electronic Medical Records (EMR) systems. Some of these systems include the ability for patients to set up a personal account via the Internet, log on, and access and print out their records and lab results from their home computer. However, earlier paper records may not have been scanned into the EMR system and often one hospital's EMR system cannot talk with a different facility's system. So, be sure to ask for physical copies of those older records when you are compiling your personal set of records.

Electronic medical records do not replace hard the hard copies you must get and keep.

When you receive your records keep all of them in chronological order in a loose-leaf binder. If you go to a new doctor or for a second opinion, copy the entire contents of your medical history file and give the copy (keep the original for yourself) to this doctor, ideally before your first appointment. (If you’re computer-savvy, scan them in and save them as pdf files, they can then be printed out as required.) Most physicians will want to see these records before they will even agree to set up an appointment.

Each time you have a new blood test, an appointment with a doctor, or a scan, obtain a physical copy of the results and add them to your personal medical history binder.

Many labs allow you to send the results to as many doctors as you name at the time the test is performed. However, never assume that your doctor already has a copy; bring a copy of the most recent labs and scan reports with you on your next visit. In states where lab and scan results are supposed to be released only to the doctor ask your doctor to write on the prescription an order for the lab to “release results to the patient.”
Most of us see several different kinds of doctors: dentists, cardiologists, podiatrists, etc. Be sure to send all of your prostate cancer doctors a copy of every test and scan from any doctor you see as soon as you receive them yourself. Don't assume that treatment of one part of your body is unrelated to another part. Your prostate cancer doctors want to know about all of your treatments, tests, and medications, as well as the reasons for them. Make sure that every medical provider you use knows about your prostate cancer and your treatments.

My best tool is my digital voice recorder...I record everything when I meet with my doctors and it never forgets, like I often do.

From now on, you are the one in charge of your own health; you are your own captain. Try to learn about and understand everything in your records. Ask your doctor to set aside time to sit down and explain anything in the record that you don't understand. After your doctor explains something, if you still do not understand, ask again, and again, if necessary. When you get home, search the Internet for the names of all of your blood test results, treatments and medications. Use YouTube to find and view videos about the treatments that have been suggested or recommended. As with any internet use, seek out reputable resources; if it is too good to be true, it's probably not true. Join the advanced prostate cancer online support group (http://health.groups.yahoo.com/group/advancedprostatecancer/join), read the blog (www.advancedprostatecancer.net), sign up for prostate flashes (http://malecare.org/prostate-cancer-news-flash/), subscribe to the Advanced Prostate Cancer Monthly Newsletter at the blog (www.advancedprostatecancer.net), listen to the Malecare teleconferences (www.malecare.org/teleconferences) and don't forget to review the Malecare web site (www.malecare.org).

Bring a tape recorder or, if you use a smartphone (iPhone or Android) use a recording app such as SuperNote or iTalk, when you meet with your doctors. As is the case anytime you are recording a conversation, be sure to ask permission before turning on the recording function.

Even better than a recorder is to bring your caregiver or other loved one to your doctor meetings. Another pair of ears and the brain between them is an invaluable resource. Have them join the conversation and ask questions. They will often ask questions or bring up issues that haven't occurred to you, but which turn out to be crucial.

After the meeting, review together what was said and what was recommended. Personally, I am always shocked when I review my meetings; I seem to get so much wrong. Remember, we are under extraordinary stress. We are subject mishearing, misunderstanding, and forgetting.
The Role of PSA in Men with Prostate Cancer

PSA is not a reliable measure of prostate cancer before a man is diagnosed. However, once you have been diagnosed and have received a primary treatment, the PSA test becomes one of the best available surrogate measures of your cancer’s progress or decline.

Your PSA measure is now your best friend.

Always know your PSA number. Plot your PSA on a graph so that you can see changes in its trend and calculate your PSA velocity (how fast it is changing) and PSA doubling time. For men with advanced prostate cancer, we recommend that you have a PSA test at least every three (3) months. The more points you can graph, the more useful the graph will become. Also, we believe that PSA anxiety (the fear some men experience prior to learning their PSA results) is reduced by frequent PSA tests. The sooner you can determine changes in your PSA, the sooner and more effectively you and your medical team can adjust your treatment. Show your PSA graph to your doctor at every visit and ask about the meaning of your graphic representation of your PSA—especially any changes in PSA value.

Why and How to Graph Your PSA Scores at: http://www.advancedprostatecancer.net/?p=4411

When Are You Considered to Have A Prostate Cancer Recurrence?

No matter how many years may have passed since your primary treatment (surgery, radiation, HIFU, etc.) for prostate cancer, if your PSA begins to rise, or if your PSA never became very low following primary treatment, you have Reoccurring (advanced) prostate cancer. This means that your cancer has returned, or was never brought under control.

The medical profession has very specific definitions as to when you have experienced a prostate cancer recurrence.

If your primary treatment was any type of radiation, including electron beam radiotherapy (EBRT, IMRT, IGRT), proton beam radiotherapy (PBRT), brachytherapy (including HDR brachytherapy) you are considered to have Reoccurring prostate cancer IF:

- You experience three (3) consecutive rises in your PSA score after having reached your nadir* score. (This is the “ASTRO [American Society for Radiation Oncology] definition.”)

**OR:**

- After you have reached your nadir* score, and your PSA increases by 2.0 over any period. Example: If your nadir* is 1.2, after which your PSA rises to 3.2 or more, you have experienced a recurrence. (This is the "PHOENIX definition.")
*Nadir score is defined as your lowest PSA achieved after completing radiation. Be aware that it may take a fairly long time for radiation to achieve its full effectiveness, sometimes as long as 18 months, to reach a stable PSA nadir. Generally, the longer it takes for your PSA to reach its nadir, the greater the likelihood you will experience prostate cancer recurrence. (Citation: Cancer, 2009 March 1; 115(5): 981-987, Time to PSA nadir independently predicts overall survival in metastatic hormone sensitive prostate cancer patients treated with androgen deprivation therapy; Toni K. Choueiri et al).

After receiving radiation treatment, it is entirely normal for some men to experience a “PSA bounce” or jump for a short period of time. Don’t panic if this happens to you; it has no significance for your long-term health outlook.

If your primary treatment was any type of surgery (open, laparoscopic, robotic-assisted) you are considered to have Reoccurring prostate cancer IF:

- Your PSA rises above 0.2 and continues to increase, confirmed by at least one additional PSA score above the 0.2 threshold. (This is the “AUA [American Urological Association] definition.”)

The most desirable PSA score after radical prostatectomy surgery is: "undetectable,” usually shown in lab results as “<0.01” or “<0.015”

CAUTION- From a post on the advanced prostate cancer blog:

(http://advancedprostatecancer.net/?p=1900) warns about common medications that alter PSA levels and interfere with your ability to accurately monitor your PSA for a recurrence. These include NSAIDS, 5 AR-Inhibitors, statins, and thiazide diuretics—all of which are capable of reducing PSA score by clinically relevant amounts. The specific impact of these drugs on monitoring PSA levels in unknown. (Citation: J Clin Oncol. 2010 Sep 1;28(25):3951-7. Epub 2010 Aug 2. PubMed Abstract, PMID: 20679596—also: “Impact of common medications on serum total prostate-specific antigen levels: analysis of the National Health and Nutrition Examination Survey Chang SL, Harshman LC, Presti JC Jr.)
What Should I Do If My PSA Begins to Rise?

First, be sure to note that in the definitions already cited, several PSA tests taken over a period of time are required to confirm a recurrence. A single PSA rise does not define recurrence.

Your next step would likely be a series of scans to determine if you have developed any identifiable metastases (new tumors large enough to be detected by current technology). These scans can include: a bone scan, an MRI, a PET scan and a CT scan. There is a complete description of each of these scans later in this document.

What is a PSA Only or Biochemical Recurrence?

Some men’s scans return with negative reports, meaning there were no visible tumors, but their PSA continues to rise. This is called a PSA only recurrence or “biochemical recurrence.” Doctors refer to this as micro-metastatic prostate cancer, meaning that the growth of the cancer is too small to be seen by currently available scanning technology.

All scans have limited sensitivity and can only detect what is visible above certain sizes or tolerances. Regardless of their sensitivity, scans report only the “here and now” and cannot predict what might develop in the future. However, scan technology continues to improve. A negative scan is still good news. However, just don't drop your guard by believing that the good news is durable. It isn’t.

Scanning technology is improving, so in the future we will be able to visualize smaller and smaller tumors.

What is a Metastasis?

A metastasis, or a "met," is a tumor, or an abnormal growth, that has developed in another part of the body other than where the cancer originally began (for our discussion here, the prostate gland). We do not fully understand how metastases spread from one part of the body to another. Some scientists think that the cancer moves through the blood stream while others think it travels through the lymph system. In the end, it doesn’t matter how it travels. What does matter is that it has traveled beyond the prostate gland itself.

The most common target for a prostate cancer metastasis is bone, particularly in the pelvis, spine, thighs, and ribs. Prostate cancer can also travel to soft tissue organs such as lymph nodes, the liver, lung, and brain. Over time, the metastases will continue to grow, weakening and breaking bones, eventually pushing aside surrounding organs, causing pain, disability, and ultimately, organ failure. That is how many men actually die from prostate cancer.

I tell my doctor about every one of my aches and pains, just in case I am developing a metastasis that will need quick treatment. Sometimes I feel like all I do is complain.
What Is A Bone Scan?

A bone scan* (sometimes called a nuclear bone scan) determines if you have visible metastases in any of your bones. Bone scans are performed by first injecting a small amount of a radioactive marker into your arm. Three hours after receiving the injection (you can have lunch while you wait), you will lie on a table that will slowly move you under a scanner that will record any areas of your bones that have a high concentration of the marker, which collects at areas of metastases, making the mets visible to the scanner.

Bone scans are painless and not at all claustrophobic since the scanning machine is totally open. The actual scanning process takes approximately 35 to 45 minutes.

Bone scans are highly sensitive, so sensitive they also pick up infections, arthritis, and very small bone fractures, as well as mets and tumors. Since bone scans cannot discriminate among a tumor, an infection, arthritis or a break, your doctor may order a CT scan, PET scan or MRI to better characterize the finding.

*Do not confuse a bone scan with a “bone density scan,” (sometimes referred to as a "DEXA scan"), which is used to determine whether or not you have lost bone mass and may have osteopenia or osteoporosis. Bone density scans cannot detect bone metastases.

What Is an MRI Scan?

An MRI (Magnetic Resonance Imaging) is a non-invasive method of scanning soft tissue. It uses only magnetic and radio waves, so there is no exposure to any form of radiation.

To perform the scan, you will lie on a movable table that will slide into a cylindrical tube that is actually a large magnet. Once you are inside, radio waves that are between 10,000 to 30,000 times stronger than the magnetic field of the earth are broadcast through your body. These are harmless and you will not feel anything. These waves force the nuclei of the atoms inside your body's cells into a different position. As they shift back into their normal position, their movement emits radio waves of their own, which a computer uses to assemble an image. Depending on what is being scanned, an MRI scan may take anywhere from ten minutes to almost an hour.

An MRI is a noisy procedure, and some people may feel claustrophobic while in the tube. I recommend two methods to counter this claustrophobic feeling. One is to close your eyes and picture yourself somewhere else that is pleasant. Also, you may be able to manage to look up behind your head and see outside the tube. Sometimes, for parts of the procedure, you may be able to relax your body and take a short nap, so that when the MRI is completed you feel rested. Since the sound of the machine is very loud, you may be offered earplugs, or in some facilities, headphones with music to block out the sound. If your facility offers the headphones, bring in a CD of your favorite relaxing music.

You can tell the MRI operator to pull you out of the tube at any time

An MRI scan is capable of creating images of almost all the different types of tissue in your body, as
well as tissue that is surrounded by bone. Even the tissue in your skull (your brain) and spinal column can be visualized.

An MRI procedure may also use contrast agents to highlight a particular organ or specific type of tissue. (The contrast material is often also called “dye.”) Make sure you tell your doctor when prescribing the MRI if you have ever had an allergic reaction to other contrast materials; shellfish; or if you have any metal in your body or kidney problems. Tell the technician the same thing as well before starting the MRI. Certain MRI procedures will also use a coil that is inserted into the rectum to better visualize that area of your body. This is increasingly common when the prostate area is being imaged.

The good news is that MRI technology is getting better. Many facilities now have machines with greater sensitivity and use new, significantly more sensitive contrast materials (dyes). Contrast media such as Radioactive Choline (Choline C-11) is available at the Mayo Clinic (www.advancedprostatecancer.net/?cat=1101) and Feraheme-based MRIs are available at Sand Lake Imaging in Orlando Florida. Both of these represent a forward step in improving imaging of prostate cancer cells.

What Is a CAT Scan?

A CAT Scan or Computed Axial Tomography, also known as Computed Tomography (CT Scan), is another painless method used to scan your body when trying to determine if you have developed any metastases. CT scanning uses x-rays to rapidly obtain multiple images taken in "slices," which are then compiled by computer into an image. The CT scan produces a picture of a cross-section of soft tissue, blood vessels and bones.

Although considered safe, CT Scans employ x-ray radiation that may increase your risk for the development of another primary cancer. Be sure to tell your doctor if you have had any prior CT scans. Be sure to ask if the CT is really necessary when perhaps an MRI could accomplish the same task without the radiation exposure.

Like MRIs, CT Scans may also use contrast agents to highlight an organ or specific tissue. Follow the same procedure mentioned in the MRI discussion above by letting your doctor and the technician know about any allergic issues you might have with contrast materials.

Like MRIs a number of newly developed CT contrast materials have been developed. However none of these new contrast agents are FDA-approved and may not be covered by your insurance. The most common contrast agent is: [18F] fluorocholine- based PET/CT.

What are the Significant Differences Between an MRI and a CT Scan?

An MRI allows the doctor to create images from any angle, while a CT Scan allows only a cross-sectional (transverse) view of the body. MRI systems do not employ x-ray radiation and they yield more detailed images.
What is a PET Scan?

Unlike bone scans, MRIs and CT scans, a PET scan, or Positron Emission Tomography, is an imaging test that aids visualization of how organs and tissues inside your body are actually functioning.

The PET scan often includes the injection of a small amount of a radioactive material linked to a glucose-based substance, called a radiotracer, into a vein of your arm. Your organs and tissues absorb the tracer. You will then lie down on an examination table that is moved into a doughnut-like shaped machine (that looks very much like a CT scanner). This machine detects and records the amount of energy given off by the tracer substance as the glucose is metabolized over time. Three-dimensional images reveal the degree to which the tracer is being metabolized, locating possible tumor activity where it may be taking place because tumor cells tend to metabolize glucose more quickly than nearby normal cells.

The doughnut-shaped PET scanner is usually open, and rarely induces claustrophobia. PET scans are not used often to visualize prostate cancer because prostate cancer cells tend not to metabolize glucose as aggressively as other types of cancer cells, thereby making the prostate cancer difficult to distinguish from normal cells.

Many modern machines combine a PET scan with a CT to get the best possible view (with minimal exposure to radiation) of your internal functioning.

What Types of Treatments for Advance Prostate Cancer Are Appropriate?

As we have seen, advanced prostate cancer has spread from the prostate gland to other areas or parts of your body, be those bones or soft tissue. Prostate cancer that is no longer confined to the prostate gland needs to be treated with systemic treatments that affect your entire body, not just the targeted or localized area that primary treatment is designed to accomplish.

Exceptions would be:

* You still have your prostate gland after non-surgical primary treatment such as radiation or received seeds (Brachytherapy), cryosurgery or HIFU (High Intensity Focused Ultrasound), and the subsequent PSA rise is due only to lingering cancer cells that remain active in your prostate gland. Here additional focused treatment to the gland itself may help.

* Or, you may have some prostate cancer cells remaining in the area close to where the gland had been prior to surgery. It is possible to treat these “hot spots” with external beam radiation and halt the cancer’s progress.

I no longer think of my prostate cancer as curable, but as chronic...something I can fight until I am in my nineties and
Treating Reoccurring Prostate Cancer

Reoccurring prostate cancer, when caught early after primary treatment, is sometimes treatable with another locally focused procedure, such as radiation or cryotherapy, but it must be caught very early in its progression, in cases of failed surgery prior to the PSA making it to 1.0. This second, locally focused treatment is often called “salvage therapy.”

After your treatment, always remain vigilant in monitoring your PSA so you could catch a reoccurrence very early.

If the primary treatment you had was surgery, and your PSA begins to rise, or if the PSA fails to become undetectable following surgery, beginning radiation salvage therapy and hormone therapy may still beat the cancer and provide you with a good outlook. If the primary treatment was radiation, surgery or focal surgery may beat the cancer.

If you find yourself in this position, it is best to identify where the cancer is located in order to develop an optimum treatment plan. Scans are the best way to accomplish this. In addition to glucose-based PET scans, one other FDA-approved method, a PET scan using c11 Choline PE, is available only at the Mayo Clinic in Rochester, Minnesota. Unlike glucose, Choline is rapidly taken up by prostate cells so Choline-based scans will indicate a significant metabolic uptake in areas where the cancer has spread. Unfortunately, these scans also have a high rate of false positives, so confirmatory tests should be performed. (To learn more about Choline-based PET scans go to the advanced prostate cancer blog at:

http://advancedprostatecancer.net/?p=3433;
http://advancedprostatecancer.net/?p=681; and
http://advancedprostatecancer.net/?p=3439

If the scan identifies four or fewer lesions, the disease might actually be considered oligometastatic (meaning "isolated distant metastases") and may still be treatable with “curative intent” (Citations at www.ncbi.nlm.nih.gov/pubmed/23151910 and http://jnumedmtg.snmjournals.org/cgi/content/meeting_abstract/52/1_MeetingAbstracts/35.)

For details, and to request an appointment at the Mayo Clinic for a Choline C-11 PET scan in conjunction with evaluation for Reoccurring prostate cancer, call 507-284-5052 from 8 a.m. to 5 p.m. Central time, Monday through Friday.
In addition to the FDA-approved choline-based PET scan, there are other as yet unapproved contrast agents being used to identify prostate cancer outside of the gland (in the prostate bed). The best known is USPIO nanoparticles with Feraheme (ferumoxytol) that is used only at the Sand Lake Imaging Center in Orlando, Florida (9350 Turkey Lake Rd, Orlando, FL 32819, 407-363-2772).

This procedure uses ultra-small super-paramagnetic iron oxide (USPIO)-enhanced MRI/CT fusion study of chest, abdomen and pelvis. The scan examines lymph nodes as well as other soft tissue sites and organs for any abnormality. The procedure requires a slow infusion of USPIO nanoparticles with Feraheme (ferumoxytol) on day one and then a CT scan of the abdomen and pelvis day two.

Ferumoxtran-10 (aka Combidx MRI in the United States and Sinerem MRI in Europe) is another alternative scan contrast. Currently it is only available at Radbound University in Holland. In 2004 the FDA did not approve it, stating that there were insufficient clinical data to support a broad indication for use of ferumoxtran-10 to differentiate metastatic from non-metastatic lymph nodes across all cancer types.

Ferumoxtran is highly sensitive, being able to discriminate lymph nodes down to 2mm (as opposed to C11 that discriminates down to 4mm and a PET Scan that discriminates down to 10mm). A Combidx MRI is done over a two day period: day one involves having an infusion of the contrast and day two having the actual MRI procedure.

If you missed catching a post-surgical recurrence prior to a PSA score rising above 1.0, or if your cancer is not oligometastatic, there are still many available treatments that will slow the progress of the cancer, reduce symptoms, and extend your life for many years. Always remember: the treatment goal is to turn Reoccurring prostate cancer into a chronic, long-term illness, while still maintaining a great quality of life.

The Treatment Process

**Salvage Therapy** - If your PSA is less than 1.0, your first treatment endeavor when you experience a recurrence will be salvage therapy. The objective of salvage therapy is to reduce or eliminate any lingering prostate cancer cells. Salvage therapy must begin as soon as possible after you know that the cancer has recurred. The appropriate salvage therapy depends upon the primary treatment you received.

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<th>If The Primary Therapy That Failed Was</th>
<th>Your Possible Salvage Therapy Can Be</th>
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<td>Radiation</td>
<td>Surgery; HIFU or Cryosurgery</td>
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With most salvage therapy attempts, you should consider including androgen deprivation therapy (ADT), also called “hormone therapy.” There is extensive research, especially in the case of failed primary surgery, suggesting that a course of ADT can extend your life.

We now have significantly improving scanning technology that might allow your doctor to identify precisely where there is a recurrence, allowing a targeted treatment directed to the actual site of the recurrence.

**Androgen Deprivation Therapy (ADT)**

ADT is a systemic modality that treats—and affects—the entire body, not just the localized area of the prostate gland. This treatment impedes the production of hormones (androgens) and blocks the body from absorbing any androgens such as testosterone produced naturally in your body.

ADT is effective because prostate cancer cells develop and grow in the presence of testosterone, the male androgen produced mostly by the testes. Limiting production of testosterone and preventing any androgen that is produced from interacting with the cancer cells, forces the cancer cells into stasis, possibly delaying their harmful effects by years. In effect, ADT, when it employs medications (see below) causes the male body to experience castration without surgery.

Unlike surgery, when chemically induced ADT is no longer required the positive emotional and physical benefits of testosterone may return. However, there is no guarantee that the testosterone will eventually return and no way to know how long the return might take.

ADT is often called “hormone therapy.” This is an inaccurate description. In fact, ADT should be called "anti-hormone therapy" because its function is to halt production of the hormone testosterone in a man’s body.

Your doctor will usually recommend ADT if:

- Salvage therapy fails, or
- You are initially diagnosed with advanced prostate cancer with a PSA above 10.0, or
- There is other evidence that the cancer has already moved beyond the prostate gland (such as positive scans or symptoms such as blood in the urine), or
- There a bio-chemical recurrence with a PSA greater than 10.
Prostate cancer that responds to ADT is said to be hormone- or androgen-dependent. Unfortunately, in most cases, the cancer eventually “learns” how to grow without requiring testosterone derived from the testis making the ADT ineffective. At this point, the cancer is called “castrate resistant prostate cancer” (CRPC). Many studies in the literature have suggested that ADT will only work for a short period of time, probably not much longer than 18 to 24 months, before the cancer becomes castrate resistant. However, in my experience (not scientific) most men benefit from ADT for many years before becoming castrate resistant. I know many men who have been successful for over ten years, with one man now approaching his 16th year. In a study that looked at long term ADT using Lupron 90% of the subject men still remained hormone responsive at 10 years (J Clinical Oncol 32 2014; (suppl; abstr e16077; Peter Hammerer, Manfred Wirth)

On the flip side, there are individuals who never achieve a good response from ADT.

So, why is there this discrepancy? My best guess is that the drugs used in ADT have improved greatly over the past few years and that we are now able to employ intermittent therapy (which is discussed later) successfully. Although there is no way of knowing, it’s not unreasonable to anticipate many years of successful ADT.

I have been on ADT for over 9 years and I continue to be successful with the treatment.

What is Testosterone & How Can You Control Its Production?

Testosterone, the male androgen, is mostly (though not exclusively) produced in the male testes when they receive a signal via another hormone called leutinising hormone (LH), which is generated in the pituitary gland located in the brain.

LH production is controlled by yet another hormone, leutinising hormone releasing hormone (LHRH) (which is different than “plain” LH), which is produced in the hypothalamus, a gland located adjacent to the pituitary gland in the brain. This complex interaction of the pituitary, hypothalamus, and the testes regulates the production of testosterone. Whether via drugs or surgery, altering the interactions between these three glands can substantially decrease or even halt the production of testosterone in the testes.

Normal testosterone levels can range from around 250 to 800 nanograms per milliliter (ng/ml). ADT’s goal is to lower your testosterone levels to less than 20 ng/ml. Some doctors feel that a level less than 50 or 30 ng/ml is sufficient, but experience in our support groups suggests that bringing your testosterone level to below 20 ng/ml is a better goal for more effective ADT.


There are different methods to obtaining a castrate level of testosterone. They are:
Surgically Controlling the Production of Testosterone

Testosterone production can be permanently reduced via a surgical procedure known as an orchiectomy. This is commonly known as surgical castration. Orchiectomy consists of the removal of the gonads and the spermatic cord through an incision in the abdomen. An orchiectomy is not reversible.

GnRH Agonists- Chemically Controlling the Production of Testosterone

Testosterone production can be controlled chemically by a class of drugs known as gonadatropin-releasing hormone (GnRH) agonists. These drugs are:

- Eligard
- Lupron (The most widely administered GnRH agonist)
- Trelstar
- Viadur
- Zoladex

All these drugs slow down testosterone production by interfering with the LHRH signaling process. They are the most common method of administering ADT in economically advantaged regions.

*CAUTION - Evidence has confirmed that these drugs, as well as surgical castration, increase your risk for developing metabolic syndrome, including diabetes, heart problems, and vascular complications. As of November 2010, the FDA has required a "Black Box" warning on these drugs because they have been linked to increased cardiovascular risk, i.e. myocardial infarctions (heart attacks) and death. If you are already taking, or are considering starting any of these drugs, consider making an appointment with a cardiologist for an initial exam, and make sure that your doctor regularly monitors your blood sugar and possible signs of any heart damage.

Side Effects Caused By Reduced Testosterone (ADT)

Many men mistakenly believe it is the orchiectomy or the LHRH drugs themselves that cause the negative side effects of ADT. This is not true. These negative effects are caused by the loss of testosterone in the body. The degree, incidence, and frequency of these side effects will vary greatly from man to man. Some men report that they "barely" experience any side effects, while others report that the side effects of being deprived of testosterone has a substantial negative impact on their quality of life. There is no way to predict how you might experience any of these side effects, which may include:

- Increased risk of developing cardiovascular complications
- Increased risk of developing metabolic syndrome and diabetes
- Increased risk of developing Colorectal Cancer (Journal of the National Cancer
• Hot flashes (sometimes called hot flushes) and night sweats
• Loss of muscle mass
• Loss of libido
• Shortness of breath
• Increase of blood pressure
• Feelings of confusion
• Disorientation
• Weight gain
• Neuropathy
• Breast growth

According to a 2010 report from the American Society of Clinical Oncology “endurance, upper extremity strength and the physical components of the QOL are affected within 3 months of starting GnRH agonists.” Ask your doctor if you should start an exercise program at the beginning of ADT in order to reduce the potential for physical deterioration associated with living without testosterone.

PSA FLARE

When you first start a GnRH agonist, your testes will attempt to compensate for loss of signaling created by the ADT drug and will over-produce testosterone. This testosterone “flood” will do exactly what you don’t want: cause the prostate cancer to grow. This is especially dangerous for men with very advanced disease, but never a good thing for any man with prostate cancer. This situation can result in significant disease progression and increased pain. When the testosterone flood happens, there will be a “PSA flare,” as the PSA increases due to progression of the disease.

Ask your doctor if you should take an anti-androgen medication such as Casodex, at least ten days prior to starting a GnRH agonist.

I chose to use medications instead of surgery for my ADT so that I could periodically go off the treatment and improve the quality of my life (aka Intermittent ADT.)
GnRH Receptor Antagonist—Another Chemical Way to Control the Production of Testosterone

Degarelix (Firmagon), recently approved by the FDA for the treatment of advanced and Recurring prostate cancer, has an immediate onset of action, binding to gonadotropin-releasing hormone (GnRH) receptors in the pituitary gland. This induces a fast and profound reduction in testosterone without a PSA flare and the need to use an anti-androgen such as Casodex (See discussion of anti-androgens below).

The most serious of its possible side effects are:

• Difficulty breathing
• Swelling of the face, lips, tongue or throat
• Dizziness, fainting or pounding heartbeat
• Pain or burning during urination
• Swelling in your hands, ankles, or feet
• Injection site reactions
• Dangerously high blood pressure (severe headache, blurred vision, buzzing in your ears, anxiety, confusion, chest pain, shortness of breath, uneven heartbeats or seizures

If you experience any of these symptoms, immediately see your doctor or go to an emergency room.

Anti-Androgen Medications - Blocking Testosterone from Accessing the Cancer Cells

Many doctors choose to add another drug to the GnRH agonist/antagonist drug, whose function is to block the androgen receptors, which are located on every cancer cell, from accessing any testosterone that might still be produced in your body. These drugs are called anti-androgens. When used in combination with the GnRH drugs that restrict the testosterone production, the treatment is called “combined hormonal therapy,” or in shorthand, ADT2. ADT2 provides a more complete form of hormone therapy.

As discussed above, when first starting GnRH agonist medications (e.g. Lupron) the testes respond to the termination of the signals from the pituitary gland and over-produce testosterone that can be detrimental, especially for a man with serious disease, indicated by PSA flare. To prevent this, ask your doctor if the anti-androgen drugs should be started at least ten days prior to the first administration of a GnRH agonist in order to prevent this damaging situation. (A GnRH antagonist such as Firmagon does not require the earlier anti-androgen since it does not produce a testosterone flood.)
The commonly used antiandrogen drugs are:

- Casodex (bicalutamide)
- Eulexin (flutamide)
- Nilandron (Nilutamide)
- Androcur (cyproterone acetate)

Anti-androgens also have their own side effects, which will vary from man to man. These drugs may:

- Negatively affect the liver
- Cause hot flashes
- Cause breast tenderness or growth (gynecomastia)
- Cause a loss of libido

I always ask my doctor and my pharmacist about the side effects of all of my medications. ...I am often surprised at the possibilities

**A Long Simmering Controversy — The Use of a 5-alpha-reductase Inhibitors**

An enzyme called 5-alpha-reductase is responsible for the conversion of testosterone to 5a-dihydrotestosterone (5a-DHT). 5a-DHT is three times more potent than testosterone in causing prostate cancer cells to grow because of its greater affinity for androgen receptors. *(Citation: Wright, A. S., L. N. Thomas, et al. (1996) and Relative potency of testosterone and dihydrotestosterone in preventing atrophy and apoptosis in the prostate of the castrated rat. J Clin Invest 98(11): 2558-63.)*

Nevertheless, some doctors will recommend that their patients use 5a-reductase inhibitors (5-ARIs) such as finasteride (Proscar, Propecia) or dutasteride (Avodart) because 5-ARIs are thought to be a better testosterone blockade, as well as being able to extend the "off" periods during intermittent hormone therapy (IHT). We struggle to find evidence to supports this recommendation.

As with any other drug, the 5a-reductase inhibitors have side effects. The most common side effects include gynecomastia (breast enlargement) and loss of ejaculate. The 5-ARIs are metabolized in the liver and should be used with great caution by anyone with any sort of liver disease.

**Anti-Androgens as ADT Mono-Therapy**

Some doctors will start you out on only an antiandrogen drug, as a ADT "mono-therapy." As we’ve seen, anti-androgen drugs block testosterone from interacting with the androgen receptors on the prostate
cancer cells, thus depriving the cancer cells of testosterone. However, it’s important to note that this protocol does not prevent the production of testosterone. Therefore, side effects from anti-androgen mono-therapy are not as significant as when ADT is coupled with a GnRH drug or orchiectomy, so mono-therapy may be a good choice for someone concerned with quality of life.

Although it is rare that a doctor in the United States will offer antiandrogen mono-therapy, the 2007 guidelines from The American Society of Clinical Oncologists (ASCO) for initial ADT states, “non-steroidal antiandrogen mono-therapy merits discussion as an alternative to combined androgen blockage (CAB) (50 mg Casodex with a GnRH agonists).” Translated, an anti-androgen along with the GnRH agonist or antagonist may be more effective than the GnRH drug by itself. So, if the doctor does not offer you an anti-androgen ask about it.

Casodex (150 mg daily) mono-therapy has become the established alternative treatment in Europe. In men with biochemical recurrences only, this dosage of Casodex may provide comparable outcomes, while preserving bone mineral density and muscle strength, as well as other quality of life advantages. In men with demonstrated metastases, mono-therapy is not as effective as combined androgen blockage. A doctor might prescribe Casodex (150mg daily) mono-therapy for a month or two before undergoing a radical prostatectomy (primary treatment) since it can help shrink the prostate gland, simplifying the surgical procedure. (http://www.nejm.org/doi/pdf/10.1056/NEJM198908173210702)

Timing of Hormone Therapy — When to Start and How to Structure It

Data from the National Cancer Institute (NCI) Intergroup Trial showed longer survival times with combined therapy (CAB) for men with metastatic disease. This observation and other studies suggest the benefits of using ADT early. It is possible that early treatment with CAB in men with metastatic disease will improve survival time compared to waiting until symptomatic metastasis occurs. There appears to be a recent trend to treat men earlier using CAB, before metastatic symptoms develop. (http://www.nejm.org/doi/pdf/10.1056/NEJM198908173210702)

However, in a recent study involving men who have a PSA only (bio-chemical) recurrence starting hormone therapy immediately doesn’t provide any additional survival benefit over delaying the start of hormone therapy (http://advancedprostatecancer.net/?p=4602). So, if you have PSA only recurrence you should discuss with your doctor the possibility of delaying the start of hormone therapy. Delaying the therapy will allow you to put off having to deal with the side effects of the therapy.

Timing of Hormone Therapy- Intermittent (IHT) vs. Continuous Therapy

Traditionally, ADT has almost always been administered on a continuous basis; once on ADT a man stayed on it indefinitely. Unfortunately, ADT itself poses significant risks to a man's life as well as to his quality of life (QOL).

Many doctors now suggest using intermittent hormone therapy (IHT), except for those patients
with very aggressive prostate cancer. Instead of keeping a man on therapy continually and indefinitely, they start and stop ADT by monitoring PSA levels. Most survivors refer to the off ADT period as being "on vacation." For the most part, research has shown that intermittent ADT is not inferior to continuous therapy (or stated in lay terms, "just is as good"). A recent exception to this was a study done by Dr. Maha Hussain from the University of Michigan (http://abstract.asco.org/AbstView_114_92516.html) concluding that intermittent ADT was inferior to continuous therapy. This was a very large study performed over many years, but it may have enough design flaws to render its conclusions invalid. (A complete explanation of the author’s conclusions about this study may be viewed at: http://advancedprostatecancer.net/?p=3274).

With respect to IHT, here are excerpts from the Advanced Prostate Cancer Blog:

An intermittent androgen blockade appears to delay the progression from treatable androgen-dependent cancer to untreatable androgen-independent disease (castrate resistant prostate cancer).

"Side-effects were more pronounced in those on continuous ADT. Men on intermittent therapy reported better sexual function."
The conclusions of the researchers was that IHT should be considered for use in routine practice because it is associated with no reduction in survival, no clinically meaningful impairment, better sexual activity, and considerable economic benefit to the individual and the community at: http://advancedprostatecancer.net/?p=539.

"Comparing Intermittent To Continuous Androgen Deprivation For Advanced Prostate Cancer", http://advancedprostatecancer.net/?p=386 concluded that IAD appears feasible for patients with locally advanced, hormone sensitive prostate cancer.

"Intermittent Hormone Blockade is Safe & Effective"; http://advancedprostatecancer.net/?p=73_The study showed that IAS is safe. The men on IAS experienced a 40% "off time" while also experiencing an increase in a positive "quality of life.

"Intermittent Androgen Deprivation (IAD) provides similar outcomes to continuous therapy with the potential for fewer side effects and less disruption to quality of life."- No Longer Considered Experimental for Treating Men with Advanced Prostate Cancer" http://advancedprostatecancer.net/?p=2729

Managing the Side Effects of ADT

The potential side effects of ADT can be both bothersome and serious. These side effects include:

- Hot Flashes and “the sweats”
- Loss of Libido and erectile dysfunction
- Fatigue and weakness accompanied with loss of muscle mass
- Weight gain
MALECARE PROSTATE CANCER SUPPORT www.malecare.org

- Breast tenderness and growth
- Memory loss and confusion
- Increase risk for metabolic and cardio problems
- Mood swings and depression
- Bone thinning (osteoporosis)

You should work closely with your doctor on developing strategies to maintain or even improve the quality of your life (QoL) by keeping you as free as possible of undesirable side effects. The advanced prostate cancer blog has a number of posts specific to managing these side effects:

"How to Manage the Side Effects of Hormone Therapy MDT in the Treatment of Prostate Cancer"
http://advancedprostatecancer.net/?p=803

"Long-Term Effects of Intermittent Androgen Suppression on Testosterone Recovery and Bone Mineral Density: Results of a 33-Month Observational Study" reported that the bone mineral density partially recovered in men who recovered their testosterone levels during a vacation or "off period“ at:
http://advancedprostatecancer.net/?p=547

Although not the side effect that puts a man at risk, hot flashes seems to be the most reported side effect as being bothersome. To counter them members of the Malecare Advanced Prostate Cancer On-line Support Group have reported good results using a 400 mg intramuscular injection of of Depo Provera. Read more about this at: www.pubmed.gov with a search Pub Med ID 16006929.

Recent evidence suggests that the use of estrogen, either to mitigate hot flashes or as a second line ADT, can pose additional risks for men who have breast cancer in their families as well as men who are at a higher risk of developing Melanoma. (www.advancedprostatecancer.net/?p=2996)

Another common treatment for hot flashes is the drug Gabapentin. Research shows, however, that Gabapentin offers only a moderate benefit. (Citation: Ann Oncol. 2009 Jan 6. Epub ahead of print. doi:10.1093/annonc/mdn644, PMID:19129205)

Some advanced prostate cancer support group members report success with acupuncture, weight loss, hypnosis, reducing alcohol consumption, smoking cessation, biofeedback and also drinking a tea of Pueraria root (Chinese name Ge Gen). Talk to your doctor about all of these, before you try them yourself.

Hot flashes that we experience from ADT are similar to the hot flashes experienced by postmenopausal women. These women have pioneered ways to deal with the flashes, so ask someone you know what they find helpful.

Other tricks you might want to consider are avoiding stress, caffeine, spicy foods and alcohol. Dress in layers so that you can shed some cloths as needed. Carry a personal fan, use cooling pads, a bag of frozen peas on your pillow as well as on your neck, head and wrists. These are all simple, inexpensive tricks that do not come with any side effects of their own.
Breast Enlargement- Gynecomastia: What Is It & How To Cope With It

Gynecomastia, breast enlargement, is a common side effect of some treatments such as ADT, anti-androgens such as Casodex, and 5-alpha-reductase inhibitors. For many men, gynecomastia can be difficult to talk about. In addition to the embarrassment caused by the cosmetic issues, gynecomastia can cause breast tenderness, discomfort, and in some cases, pain.

Some men have larger breasts simply because they are overweight or were born with larger breasts. Gynecomastia is not extra fat tissue; it is caused by expansion of the breast's glandular tissue that is located under the nipple. It is not distributed around the entire breast, as is fat tissue.

Several potential treatments are available for men with gynecomastia. Radiation, prior to commencing an ADT drug, surgery and taking the drug tamoxifen (an anti-estrogen drug used in the treatment of breast cancer) may reduce gynecomastia. However, all of them have potential negative side effects. Malecare urges you to consider passing on these treatments if you can cope with the psychological and social issues of gynecomastia. In any case speak with your doctor about these treatments prior to making a decision.

If you are interested in radiation therapy to prevent gynecomastia, it must be administered prior to starting the hormone therapy. The typical dosing is 300-400 centigrays (3-4 GY) per day administered each day for 4 days.

If you become unhappy with your breast size you can use body-shaping underwear that can be ordered from [http://tinyurl.com/yvvja9](http://tinyurl.com/yvvja9). A tight T-shirt under looser clothes can also help.

What is Osteoporosis and How Is It Related to Hormone Therapy (ADT)?

Osteoporosis is a general loss of bone mass that can lead to fractures. (A related condition, osteopenia refers to bone density that is lower than normal peak density but not low enough to be classified as osteoporosis.) ADT increases a man's risk of developing osteopenia or osteoporosis. The longer a man remains on ADT, the greater our risk for loss of bone mass (bone mineral density). (Citation: Michael G. Oefelein, Vincent Ricchuiti, et.al, J of Urology; Volume 166, Issue 5, Pages 1724-1728 November 2001)

In normal bone, two types of cells called osteoclasts and osteoblasts work together to rebuild and strengthen bone:

- osteoclasts that destroy old bone
- osteoblasts that build new bone.

ADT and prostate cancer causes an imbalance between these two cell types resulting in more bone being destroyed than rebuilt, leading to weakening and thinning of the affected bone.
Make sure that you do have a regular bone density test if you are on ADT, no matter the schedule.

This can cause pain and means that the bone can fracture or break more easily. Men may not even know they have osteoporosis or experience any significant problems with this condition until a fracture occurs. When osteoporosis is present, fractures of the spine are common and may occur while merely bending, lifting, standing, sudden movements, or from other minimal stress. Pain results from the collapse of the small bones of the spine that may have been weakened by osteoporosis. More severe spinal fractures can cause paralysis. Early diagnosis and treatment can prevent these potentially disabling injuries.

How is Osteoporosis Diagnosed?

Early diagnosis is helpful for men on ADT. You can be tested for osteoporosis by having your bone mineral density (BMD) evaluated by a dual energy x-ray absorptiometry (DEXA) scan. DEXA readings can be overly optimistic (i.e., indicate greater BMD than actually exists) because this scan misreads calcification and calcium in the blood vessels close to the bone as being bone itself. DEXA is by far the most common BMD test, but a better scan is a Quantitative Computerized Tomography (QCT). QCT distinguishes vascular calcifications and degenerative joint disease - a common effect of aging on bones - as something different from osteoporosis. (Citation: Smith et al, Cancer 9:2238, 2001). Both scans are safe and painless.

Dexa scans should not be used once there has been a development of confirmed bone metastases. A man with bone metastases should insist on a QCT scan.

How Is Osteoporosis Treated and Prevented?

- Stop smoking and reduce drinking alcohol.
- Taking calcium and vitamin D3.
- Regular exercise with weight-bearing or resistance exercises.
- Talk to your doctor about taking an oral (not IV) bisphosphonate.

Oral bisphosphonates are commonly used to treat bone thinning (osteoporosis). Bisphosphonates are often given alongside other treatments.

Zoledronic acid (trade name: Zometa), the most commonly prescribed bisphosphonate, targets areas of bone where osteoclast activity is high. It helps bring the balance of osteoclast and osteoblast activity back to normal by reducing the activity of the osteoclasts, in turn reducing pain and helping strengthen the bone. It also means that less calcium will be lost from the bones. Zoledronic acid is
given by a drip (infusion) into the vein through a fine tube called a cannula. It's usually given in the outpatient department at the hospital. The infusion takes at least 15 minutes and is given every 3-4 weeks.

**CAUTION**- The experience of many men is that the first infusion of Zoledronic acid must be slowed down to take at least an hour. A too-fast first infusion has been reported to exacerbate the negative side effects, notably “flu-like symptoms.”

Traditional practice has been to give Zometa for as long as it provides a positive outcome. However, a recent study has cautioned that extended use of Zoledronic acid may in certain cases cause an unusual and serious fracture of the femur bone in the leg. (Citation: [http://www.johnshopkinshealthalerts.com/alerts/osteoporosis/Bisphosphonates-for-Osteoporosis_6795-1.html?s=W1R_140125_001&st=email](http://www.johnshopkinshealthalerts.com/alerts/osteoporosis/Bisphosphonates-for-Osteoporosis_6795-1.html?s=W1R_140125_001&st=email)).

A newer bisphosphonate is now available. The FDA has approved Denosumab, marketed as Xgeva, for men on ADT. It has been shown in clinical trials to increase bone density and prevent fractures in men who develop osteoporosis as a result of androgen deprivation therapy. It has also been shown to delay the onset of bone metastases. Denosumab has been demonstrated to be more effective in reducing bone fractures than zoledronic acid (Zometa).

If your doctor offers you Zometa instead of Xgeva ask him or her why they have made that decision. Generally, Xgeva is a superior drug, but many oncologists remain loyal to the older standby because of their familiarity with the drug.
Castrate Resistant Prostate Cancer [CRPC] (Formerly Called Androgen Independent Prostate Cancer)

Usually, after a long period of time, prostate cancer cells will stop responding to the absence of testosterone that has been caused by ADT, and the cancer will begin growing again. It is not clear why this happens, but there are several theories.

- Some researchers believe that prostate cancer consists of many different types of cancer cells; some are killed by ADT, but others are able to survive, even thrive, on very low levels of testosterone. Eventually, those cells that survive begin to proliferate and become the dominant type of cancer cells.

- Other researchers believe that during the course of ADT some cancer cells will mutate in such a manner that they may be able to grow on lower levels of testosterone and then replicate themselves, eventually becoming the dominate cell type.

- Some believe that it is the androgen receptors on the cancer cells that mutate and become able to take better advantage of the low levels of testosterone.

- There is even a theory that the cancer cells themselves find a way to produce their own, low levels of testosterone, which then enable further cancer cell growth and proliferation.

Regardless of the actual reason or reasons as to why ADT eventually fails and the cancer cells begin growing again, developing castrate resistant prostate cancer is a significant and worrisome development in the progression of your disease.

At this juncture, despite your being on ADT, your PSA will begin to climb, signaling that the cancer has begun to progress. When facing this moment, your essential first response should be to confirm that your ADT has actually achieved a castrate level (less than 20 ng/ml) of testosterone production. Testosterone levels should be monitored on a regular basis the entire time you are on ADT. If your testosterone is still at a castrate level and your PSA is climbing, you have developed castrate resistant prostate cancer (CRPC).

After developing CRPC, some doctors will recommend that you move on to chemotherapy using docetaxel (Taxotere). However, many of us believe that rather than moving to chemotherapy, this step should be delayed by either a second-line hormone therapy or an immunotherapy called Provenge, which is described later on in this guide. Despite this, a recent study from National Institute of Health (http://www.nih.gov/news/health/dec2013/nci-05.htm) showed that early chemotherapy for men with very aggressive and advanced prostate cancer can extend life.

Second-Line Hormone Therapy

Many commonly prescribed second-line hormone therapies are not formally approved for advanced prostate cancer, but many doctors believe that they can control PSA and perhaps extend life for many men. However, each of the second-line therapies has unique side effects themselves.
Use an experienced prostate cancer oncologist so they are familiar with the potential “off label” uses of some treatments.

- Antiandrogen withdrawal (AAW) (stopping the drug) is considered an excellent first option for men who have been taking an anti-androgen drug such as Casodex, Eulexin, Nilutamide or Androcur. There are no side effects associated with AWW, but its response is often short-lived and PSA begins rising again.

- For those men who have not taken antiandrogen drugs, adding them to the ADT protocol can help suppress the cancer because they block cells from metabolizing the androgens. Possible side effects of antiandrogens can include liver damage, hot flashes, breast growth and tenderness, loss of ejaculate, breast cysts, and the loss of libido. Men who only took an antiandrogen drug (antiandrogen mono-therapy) can add a GnRH agonist (Firmagon).

- Estrogens can also control testosterone levels in the blood, and may even directly kill castrate resistant cancer cells. Problems with estrogen therapy include risk of developing blood clots, increased risk for cardiac events, and breast growth and associated pain. Estrogen therapy may be administered via injections, IV, pills, gels, or patches. The optimum method is by patches because it allows superior dosing control and avoids any stomach-related complications.

**CAUTION**- Men who have a family history of breast cancer or have an increased risk of developing Melanoma proceed with great caution before beginning an estrogen regime. These men should make sure that their doctor knows of the increase in their risks as well as undergoing genetic screening and testing for the BRCA mutation before starting an estrogen regime.

**CAUTION** — Diethylstilbestrol (DES), which is an inexpensive synthetic form of estrogen, is thought to cause blood clots, which can kill you. If you do use any estrogen, especially DES, be sure that you also have your doctor prescribe an anticoagulation medication, possibly Coumadin or Heparin. Do not take aspirin or aspirin-related medications while taking any anti-coagulation medication.

- Ketoconazole (Nizoral) (Keto) is an antifungal drug that has been shown to be effective by temporarily decreasing testosterone levels. Normally administered in higher doses (200mg to 800mg/day) together with hydrocortisone, it can produce an effective, albeit temporary, hormone blockade. Since it has a different action than ADT or anti-androgens, it also blocks the androgens that are generated in the adrenal gland. However, Keto can cause nausea, vomiting and abdominal pain. If high doses create bothersome quality of life (QOL) issues, it is possible to take it at lower doses and still receive a benefit. Keto must be taken with an acid stomach (drink orange juice along with the pill), and it must be taken religiously every eight hours without fail. Do not drink grapefruit juice with keto as it nullifies much of keto’s action.

Keto can be toxic to the liver so bilirubin and albumin levels in your blood must be monitored on a
regular basis. Some doctors will administer drug called Ursodial to protect the liver.

Keto has a similar mode of action as the newer, FDA approved drug abiraterone (Zytiga). A question has been raised if prior exposure to Keto will prevent abiraterone from being effective. A study found that a significant proportion of the men with prior Keto exposure still demonstrated a clinical response to Zytiga. So, if you have already had Keto in your treatment protocol you should still try Zytiga as a treatment.

However, if you have not started Keto you should discuss with your doctor the risks of possibly interfering with future treatments of abiraterone. (http://advancedprostatecancer.net/?p=4399 )

Citation re Keto and abiraterone: J Clin Oncol 32, 2014 (suppl 4; abstr 53), Won Kim, John Wilton, Li Zhang, Amy M. Lin, Lawrence Fong, Terence W. Friedlander, Andrew Caleb Hsieh, Rahul Raj Aggarwal, Tammy J. Rodvelt, Allison Morse, Jeffrey Bozeman, Vivian K. Weinberg, Arturo Molina, James Mohler, Gerald J. Fetterly, Russell Zelig Szmulewitz, Eric Jay Small, Charles J. Ryan)

Other second-line hormone therapies include:

- Leukine, a granulocyte macrophage colony-stimulating factor (GM-CSF), is a hormone therapy that has no effect on a man's testosterone production. It works by increasing overall production of white blood cells and increasing their biological activity.

  Dr. Eric Small has reported (Rini, etaL Journal of Clinical Oncology) on using Leukine to treat men with advanced prostate cancer. Dr. Small found that Leukine slowed and sometimes even arrested the progression of prostate cancer cells. (http://advancedprostatecancer.net/?p=1966)

  There have been reports of a mild skin reaction to Leukine. Over the counter treatments such as Claritin or Benadryl usually resolves these issues.

- Celebrex, which is used to treat arthritis, blocks a protein called "akt." Akt, when inhibited, causes the death of prostate cancer cells. Celebrex has fallen into some disfavor by the rheumatology community because it has been reported to increase the risks of strokes. Discuss this issue with your doctor to see if it may be a good alternative for you.

- Revlimid (lenalidomide) is approved to treat Multiple Myeloma and has also been used by some of the "out of the box" oncologists to treat advanced prostate cancer. However, a recent clinical trial using Revlimid with taxotere and prednisone was halted early because
it did not significantly increase the overall survival of men with castrate resistant prostate cancer. However, the actual implications of this trial, specific to using Revlimid alone as a second line treatment, is not clear because it was not tested as part of the study.

- Low dose Thalidomide (30 mg) along with 300 mg of vitamin B6 (to prevent peripheral neuropathy) taken daily also appears to have an anti-prostate cancer effect. But there are no formal studies to support this observation.
Immunotherapy: Treating Cancer by Enhancing Your Own Immune System

Your immune system identifies foreign organisms that invade your body and then eliminates them. Cancer is the out-of-control growth of your own native cells, so your immune system does not recognize your cancer as a foreign organism and does not attack it.

There has been great effort and cost expended over the years to create ways for the immune system to respond to cancer. The goal is to develop immunotherapy that “tricks” your immune system into recognizing your cancer cells as “invaders” and then attacking and destroying them. Immunotherapy is at the leading edge of cancer treatment.

We men are fortunate because prostate cancer has gleaned a significant portion of immunotherapy development dollars. In May 2010, the FDA approved Sipuleucel-T (Provenge), the first immunotherapy approved for the treatment of any type of cancer.

What we have learned is that immunotherapy takes time to work. This is very different than in other therapies here we expect to see immediate responses in both our PSA and in evidence of slowed disease progression in our scans.

Immunotherapy takes time to “recruit” the immune system to go into high gear and attack the cancer. This means that the earlier in the prostate cancer disease stage the more time it will have to kick into gear. Immune therapy should be started as soon as possible when there is evidence that you have become castrate resistant.

Immunotherapy uses your own natural immune system to fight the cancer.

Following immunotherapy, do not expect to see a decline in your PSA and a halt in disease progression on scans. These markers will not tell you if the treatment will be effective, all we have is the knowledge from the clinical trial data that it does extend life. Six months or a year into your treatments you will still not know if you would have had even worse numbers without the treatment. Remember what we said at the beginning of this guide: it’s pointless to ponder what might have been. Yesterday doesn’t matter, only today does.

Sipuleucel-T (Provenge)

Provenge, the first FDA approved immunotherapy for any cancer, is considered a vaccine, but it differs from traditional vaccines. Most vaccines are a defensive treatment, to prevent our developing an ailment. Provenge, like all other cancer vaccines, is administered after prostate cancer has developed. Provenge is a personalized treatment that teaches your immune system to recognize your prostate cancer as a foreign body and then fight it.

The approval of Provenge is very specific. It is limited to men with castrate resistant prostate cancer, who have metastatic disease, and who experience minimal or no symptoms (pain) from their cancer.
Provenge is administered in a unique fashion. A process called leukapheresis removes dendritic cells, (T cells) a type of white blood cell, from your body. This is accomplished by drawing blood from your arm or via a catheter that has been surgically placed in one of your veins. A special machine extracts the dendritic cells from your blood and returns the remainder of your blood product to you. Your body quickly replenishes dendritic cells, so you will experience no long-term effects from their removal.

The removed dendritic cells are then shipped to a manufacturing plant where a prostate cancer antigen and some immune stimulating molecules are attached to the surface of your own dendritic cells. These "supercharged" dendritic cells are then shipped back to the leukapheresis center to be returned to you via an infusion.

Provenge is administered using three separate leukapheresis removal and replacement sessions over about a one-month time period.

The fact that Provenge has no effect on PSA or disease progression causes great confusion about the viability of the treatment. Many men do not believe that Provenge works since their PSA will continue to climb after treatment. But the clinical trials were clear: Provenge does extend life, which is the "gold standard" of all cancer treatments. We believe Provenge works best for men with low PSA scores and disease burden since these will continue to progress while undergoing treatment.

Additionally, Provenge needs time to build up your immune system. Despite the unclear evidence for this statement, it may make sense during the time it takes to have immunotherapy treatments as well as for a period after the treatment has been administered for you to avoid undergoing any other type of treatment such as chemotherapy that may compromise the immune system. Whether to decide to delay an additional treatment or move directly to it should be a decision that is based on your general physical health, how far your cancer has progressed and a complete discussion with your doctor.

The most common side effects of Provenge are minimal and brief in duration: chills, fatigue, fever, back pain, nausea, joint ache, and headache (flu-like symptoms). These would develop within a day or two of the infusion and usually last for only a day or two.

As we noted above, many men are concerned because there is no clear metric to know if Provenge is helping. This is especially frustrating because both PSA and disease progression will often continue even while receiving treatment. Yet a new analysis shows that Provenge may have a median survival (life extension) advantage of as much as 7.8 months—the largest thus far observed for any late stage cancer treatment.

Another study showed that the largest immune boost occurred in men in an earlier stage of the disease, underscoring the importance of getting Provenge as early as possible after becoming castrate resistant.

Arrange to have Provenge as soon as you become castrate resistant.

Currently there are a number of studies evaluating Provenge at different disease stages as well
as in combination with other drugs and for the development of biomarkers. The advanced prostate cancer blog (www.advancedprostatecancer.net) will keep you informed about these study findings.

For more information go to: Dendreon on Call at 1-877-336-3736 or go to www.Provenge.com

In addition to Provenge, there have been significant developments of new candidate vaccines and therapeutic antibodies designed to target prostate cancer. As of 2012, around 30 different immunotherapy candidates are in development: 16 prostate cancer vaccines and 14 prostate cancer-targeting antibodies. Of these candidates, eight are in Phase I trials, while nineteen are in Phase II and Phase III trials (9 vaccines and 10 antibodies).

These various investigational vaccines and antibodies are targeting more than fifteen different prostate cancer-associated antigens or other prostate cancer-associated proteins. There are twenty-five companies currently involved in this research: 20 small- and medium-sized enterprises and 5 multinational pharmaceutical companies.

The potential and motivation for pharmaceutical companies is clear and we hope to see new immunotherapy products in the not too distant future.
ZYTIGA® (abiraterone acetate)

Zytiga is an oral, once-daily agent taken together with prednisone. It reduces androgen production in three different parts of the body including the testes, the adrenal gland, and the tumor itself. Zytiga blocks the production of testosterone by inhibiting CYP17A1, an enzyme also known as 17α-hydroxylase/17,20 lyase. CYP17A1 participates in the formation of DHEA and androstenedione, which may ultimately be metabolized into testosterone. Abiraterone (Zytiga), in a phase III trial, extended survival by an average of 3.9 months among men with castrate-resistant metastatic prostate cancer for whom other treatments, including chemotherapy with docetaxel, had failed. The FDA has now also approved Zytiga to be given prior to chemotherapy. However, this trial, which was designed to evaluate Zytiga in the pre-chemotherapy stage was halted early to allow the men who were receiving a placebo to benefit from the Zytiga treatment, so we don’t know what statistical survival advantage it offers.

At this time, abiraterone is by far the most efficient androgen production blocker that we have to use against advanced prostate cancer. To review: Zytiga (abiraterone) is currently FDA approved for men with metastatic, castrate resistant prostate cancer both in the pre-chemotherapy and post chemotherapy spaces.

Another big question lurking in the background is if Zytiga, being an even more potent treatment than our current LHRH antagonists and agonists, should be given as a part of primary ADT? The answer to this question must wait on clinical trial results for guidance.

Zytiga’s mode of action is somewhat similar to the anti-fungal drug Ketoconazole (Keto) described earlier. As we noted, a small study found that a significant number of men who had Keto exposure and eventually failed it still had a clinical response to Zytiga. (Citation: J Clin Oncol 32, 2014 (suppl 4; abstr 53); Kim, Wilton, Zhang, Lin, Fong etal.)

One of the issues we now face is how long to stay on a treatment before deciding it has become ineffective. Given the high cost of many treatments (for example: Zytiga, which is now about US $4,500 per month) as well as the high risk nature of allowing our prostate cancer to run away on us while we wait to see if it is going to work, we need better ways to know if a treatment is working.

At the 2013 European Cancer Congress in Amsterdam Dr. Howard Scher from Memorial Sloan Kettering Cancer Center reported on a panel of biomarkers that could identify the effectiveness of response to treatment with Zytiga + prednisone (abiraterone + prednisone) in men with metastatic, castration-resistant prostate cancer (mCRPC). He stated, “At 12 weeks after initiation of Zytiga therapy the number of circulating tumor cells (CTCs) in combination with serum levels of lactate dehydrogenase (LDH) can predict how well the Zytiga has worked.”

Sher went on to add, “If the combination of abiraterone acetate + prednisone has not provided a substantial clinical benefit at 12 weeks, no further improvement in patient outcome can reasonably be expected.” (Citation: Scher HI, Heller G, Molina A, et al. Evaluation of a composite biomarker panel including circulating tumor cell enumeration as a surrogate for survival in metastatic castration-
Many of the Phase III clinical trials for advanced prostate cancer evaluate an investigational treatment in men with bone metastases, as it is the most common condition. However, these trials do not evaluate the treatment's effectiveness in visceral (soft tissue) metastases (mets). Zytiga was evaluated in this manner, and not tested on men with soft tissue metastases. So, is Zytiga effective for men with soft tissue mets? According to an exploratory analysis of the COU-AA-301 clinical trial of abiraterone acetate (Zytiga) that assessed whether Zytiga improved overall survival (OS) in mCRPC men with visceral disease in the post chemotherapy (docetaxel) stage of treatment, it did. The finding was that post-chemotherapy administration of Zytiga has a beneficial clinical effect on soft tissue prostate cancer metastases. (Citation: Goodman OB Jr, Flaig TW, Molina A, Mulders PF, Fizazi K, Suttmann H, Li J, Kheoh T, de Bono JS, Scher HI. Department of Medical Oncology, Comprehensive Cancer Centers of Nevada, Las Vegas, NV, USA. Reference: Prostate Cancer Prostatic Dis. 2013 Oct 1. Epub ahead of print. doi: 10.1038/pcan.2013.41 PMID: 24080993)

ZYTIGA® may cause serious side effects including:

- High blood pressure (hypertension)
- Low blood potassium levels (hypokalemia)
- Fluid retention (edema)

Tell your healthcare provider if you get any of the following symptoms:

- Dizziness
- Fast heartbeats
- Feel faint or lightheaded
- Headache
- Confusion
- Muscle weakness
- Pain in your legs
- Swelling in your legs or feet

- Adrenal problems may occur if you stop taking prednisone, get an infection, or are under stress.

- Liver problems may occur and you may develop changes in liver function blood test. Your healthcare provider will do blood tests to check your liver before treatment with ZYTIGA® and during treatment with ZYTIGA®.

The most common side effects of ZYTIGA® include:

- Weakness
- Joint swelling or pain
- Swelling in your legs or feet
Chemotherapy

Chemotherapy is the treatment of a disease, including cancer, with any type of toxic chemical. Chemotherapy is designed to kill fast dividing cells (cancer divides more quickly than normal cells); however the drug cannot discriminate against normal cells so numbers of them will also die. Your hair and nails are the fastest dividing normal cells in your body so they are the most visible cells to be affected, along with the cancer cells themselves, by chemotherapy. Treatment of prostate cancer via chemotherapy almost always employs the drugs docetaxel (Taxotere) and cabazitaxel (Jevtana), which are the only FDA approved chemotherapy drugs. However, in some instances where an individual has not been able to use docetaxel, the breast cancer drug taxol can be used “off FDA label”.

Taxotere (docetaxel)

The US Food and Drug Administration (FDA) approved Taxotere (docetaxel) in May 2004 for men with castrate resistant, metastatic disease. Taxotere is administered by intravenous infusion (IV) in combination with the steroid prednisone, every three weeks. Men who experience significant side effects will have a reduced Taxotere dosage administered every week. The higher dosage infusions are considered to be more effective, but the lower dose also works.

Taxotere demonstrated safety and effectiveness in the TAX327 clinical trial of more than 1,000 men, as compared to the previous standard of care for men with castrate resistant prostate cancer who had bone metastases. In this trial, Taxotere provided a mean survival advantage of 2.5 months over the control group receiving the previous standard of care, mitoxantrone.

(Click here to learn more about Survival Advantage — Is It Worth It and What Does It Mean? near the end of this guide.)

Taxotere chemotherapy is systemic, meaning it works throughout your entire body. Taxotere targets and kills rapidly dividing cells. Since cancer cells divide more quickly than healthy cells, more cancer cells are killed by the drug than are healthy cells. Taxotere will also kill healthy cells including the...
Taxotere is administered by infusion together with a steroid such as prednisone or dexamethasone. These steroids are administered because Taxotere interferes with the adrenal production of corticoid-steroids and therefore need to be replaced. Additionally, steroids can control allergic reactions to the drug or its preservatives, prevent nausea and vomiting, help lower blood calcium levels in men with bone metastases and reduce inflammation.

Some men (very uncommon) may experience extreme pain and/or go into shock so, for your first infusion do ask your nurse to slow the normal drip rate to ensure that you are not allergic. If you tolerate the infusion without allergic reaction, the infusion rate can be increased.

It is very common and recommended that you be pre-dosed with an antihistamine to control allergic responses to the drug. In addition, rapid infusion of additional antihistamines generally counteracts any severe allergic reaction. One member of the Advanced Prostate Cancer On-line Support Group reported that he had an extremely painful allergic response within one minute of the start of the infusion. Benadryl was quickly administered to combat the allergic reaction. Others report that they always receive Benadryl prior to the Taxotere infusion.

Each infusion takes a few hours to be completed.

It is common to have an IV port inserted, which makes administering the chemo easier on you. The installation of the port is often performed as an outpatient procedure, although it is still significant surgery. The actual surgery can cost as much as US $10,000 so make sure that your insurance company has agreed to pay for it before you have it done.

Prior to having the port put in, take off your shirt, sit in your car, and use a magic marker or something similar to draw a line across your chest where your seatbelt normally crosses your chest to make sure that when the port is installed it won't interfere with your seatbelt. If the seatbelt does irritate the port area, such that you need to wear the shoulder part of the seatbelt tucked under your arm, carry a doctor’s letter or prescription to avoid an “improper use of seatbelt” ticket.

Since the port is a direct access into your veins it is important to always keep it clean. If you see any sign of an infection of any sort, call your doctor and go to the emergency room. This can be a life-threatening event.

There are on-going clinical trials investigating whether administering Taxotere earlier in the course of the disease will provide additional efficacy. In a trial called E3805 that enrolled 790 men with metastatic prostate cancer between July 2006 and November 2012, the men in the trial received either initial ADT alone or ADT with docetaxel every 3 weeks for 18 weeks.

Early results showed a significant improvement in the overall survival for men who received ADT plus docetaxel compared to ADT alone (3-year survival rates of 69.0% vs. 52.5%, respectively).

However, there is an important caveat, as the majority of benefit was limited to men receiving both ADT and chemotherapy who had significant metastasis (3-year survival rates of 63.4% vs. 43.9%, respectively). As a result, the investigators noted that the use of chemotherapy in combination
with ADT should be limited to only men with high-extent (multiple metastases) metastatic prostate cancer. (http://advancedprostatecancer.net/?p=4246)

CAUTION: Men taking Taxotere who are not castrate resistant should be aware that they are actually on an experimental protocol. A recent FDA warning (http://www.fda.gov/Drugs/DrugSafety/ucm401752.htm) has indicated that some formulations of Taxotere have large quantities of ethanol and could cause an individual to become intoxicated. If you are unable to consume alcohol because of a co-morbidity issue make sure that your doctor orders either the two-vial formulation of the drug manufactured by Sanofi, with 2 grams per 200 mg dose or Docefrez, manufactured by Sun Pharma, at 2.9 grams per dose.

Combination chemotherapy regimens appear to be superior to single agent regimens. There are a number of drugs and supplements that tend to amplify the positive effects of docetaxel (Taxotere). The most commonly used synergistic treatment is carboplatin. However, Sillibinin, Celebrex and Zometa have all been used in combination with docetaxel. (For more information, do a Pub Med search for additional information, if desired.) Preclinical studies showed that treatment with COX-2 inhibitors also augmented the anti-tumor effects of docetaxel. (Citation: Altorki NK, J of Clinical Oncology 21:2645, 2003)

As with all cancer therapies, some men will derive benefit while others will not. Most men have a positive response to Taxotere, including a lowering of PSA, pain relief, and reduction in tumors as evidenced on scans and by pain relief. The duration of response varies. Some men only experience the benefits for a few months, while others have a longer benefit period. Also, many men will require supportive care while taking Taxotere, including the possibility of hospitalization.

The National Cancer Institute (NCI) has a number of web sites about chemotherapy that might be worth exploration. These include:


Eating Hints Before, During, and After Cancer Treatment at: http://www.cancer.gov/cancertopics/coping/eatinghints


Chemotherapy Side Effects

Commonly reported side effects include:

- Nausea
- Hair loss (alopecia)
- Loss of appetite
- Fatigue
- Loss or change of taste
- Eye tearing
Bone marrow suppression (leading to anemia)  
Fluid retention (edema)  
Peripheral neuropathy (tingling feelings in the hands and feet)  
Skin rash  
Fever without an infection  
Low white blood count leading to an increased risk of infection  
Nail changes including color changes and brittleness  
Breathing difficulty

Eye tearing can lead to scarring; so let your oncologist know if you experience this side effect. Ask for a referral to an ophthalmologist who has experience with oncology patients.

One of the major problems experienced by men on taxotere (chemotherapy) is anemia, which is characterized as a low red blood cell count. Anemia is often the cause of significant fatigue, another major complaint from men on chemotherapy. Aranesp and Procrit are both synthetic versions of the naturally occurring hormone erythropoietin that stimulates red blood cell production. Aranesp or Procrit is normally administered every two to three weeks while on chemotherapy. Usually, they will safely maintain an adequate red-blood-cell level.

Edema can become painful and dangerous — see the section below about edema. Edema is an underreported problem. Ask your doctor about any swelling you may experience.

There is a good post about Taxotere chemotherapy, its administration and side effects at: [http://www.advancedprostatecancer.net/?p=306](http://www.advancedprostatecancer.net/?p=306)

Some members of the advanced prostate cancer support group have recommended the use of frozen gloves, hats and slippers while Taxotere is being administered in order to minimize hair, skin and nail side effects. Some oncologists don't believe that these frozen items have any effect, and have observed that if there are cancer cells in your feet, head or hands, will they be able to escape the chemotherapy because you have slowed down the cellular division by icing them? Nevertheless, you could still consider their use; talk to your doctors about whether your particular situation makes you a candidate.

If you do decide to use them, one recommended source for these items is at M&W Sales (888-880-2747). The product number for the gloves is TM7008, the slippers are SL3000 and the cold cap is CAP610.

According to M&S you should have two sets of each to swap them out along with a cooler full of dry ice to keep the items cold. They recommend that you start using the “equipment” 15 minutes prior to the start of the administration of the Taxotere and then swap out the products every 30 minutes for a colder one. It is also stated that the products should be taken on and off every 15 minutes while the infusion progresses. The CVS pharmacy ([www.CVS.com](http://www.CVS.com)) also offers cold packs online.

**NOTE:** Malecare is recommending neither M&W nor CVS; we are only passing along the feedback received from some of the members of the on-line advanced prostate cancer support group.

Those individuals unable to obtain or afford these items may wish to follow the advice given by another member of the support group who viewed a YouTube video that showed how to make...
diaper freeze pads. He took a baby diaper, poured 3 oz. of water and 3 oz. of 100% alcohol on to the diaper and then froze it overnight. The patient would take the frozen diapers to the treatment center to use on his finger and toenails. It is important to leave any cold item on your body for only 15 minutes and then remove it for 15 minutes, repeating the process through the duration of the infusion.

Nausea and vomiting are common side effects of chemotherapy. Untreated nausea and vomiting can have serious consequences. Nausea can cause exhaustion and dehydration. Vomiting can throw off your electrolyte balance. Losing fluids can also increase the toxicity of the chemotherapy and prevent you from continuing treatment.

Some men may experience anticipatory or conditioned nausea before getting the treatment. If you have this experience talk to your doctor about starting antiemetic drugs before you start your treatment. Some men get relief from chewing on ginger, or ice cubes, or using acupressure bands.

Mouth infections, rawness of the tongue and throat (oral mucositis) are also a common side effect of chemotherapy. This may make it difficult to eat, speak or swallow. Some have reported that using Biotene, First Mouthwash BLM, or First Mouthwash BXN, which are moisturizing mouthwashes, can be helpful. It is also possible for your doctor to write a compounding prescription for a specialized mouthwash that will contain at least three of these items:

1. An antibiotic to kill bacteria around any sores.
2. An anti-histamine or local anesthetic to reduce pain and discomfort.
3. An antifungal to reduce fungal growth.
4. A corticosteroid to treat inflammation.
5. An antacid to coat the mouth.

Usually, the mouthwash is intended to be used every 4 to 6 hours and to be held in your mouth for 2 to 3 minutes before being spit out or swallowed. It is also recommended that you don’t eat or drink for 30 minutes after using any of these mouthwashes so the medicine has time to produce an effect. It is unclear how effective these mouthwashes are in treating oral mucositis since there is a lack of standardization in the formulations of these mouthwashes making it impossible to gather adequate data. They also have been known to create problems with changing perceived taste, a burning sensation in the mouth, drowsiness, constipation, diarrhea and nausea.

On the Advanced Prostate Cancer online support group several individuals have recommended using glutamine powder. One individual said that he takes 1 teaspoon of the powder mixed into juice 2 to 3 times a day, every day. They also have reported that the powder has successfully combated their low energy level and fatigue during chemotherapy. There are online references to the use of glutamine powder to reduce peripheral neuropathy during chemotherapy.

However, no one on chemotherapy claims to have avoided many of the common chemotherapy side effects altogether.

One participant in the advanced prostate cancer online support group has made the following recommendations
to deal with various side effects:

- To treat nausea: Zofran (ginger tea) or chew on ginger
- To treat tear duct scarring: eye drops and cold and warm compresses
- To treat oral problems: Biotene or another dry mouth mouthwash
- To treat Edema: compression stockings
- To treat constipation: Sennelot, Miralax, or Normacol
- To Treat fatigue: exercise
- To treat stomach effects: Glutamine, ginger tea, or Zantac
- To treat skin rash: moisturizing or antifungal creams depending on problem

It is possible for a man to go through chemotherapy with minimal side effects and then unexpectedly, several months later, experience some side effects.

For more information on how to manage the side effects of Taxotere go to:

http://advancedprostatecancer.net/?p=1915

http://advancedprostatecancer.net/?p=1918

http://advancedprostatecancer.net/?p=1920

One man summed up his personal experience during chemotherapy, day by day. He reported:

- Day of the infusion – He felt well
- Day 2- He felt a little weak
- Day 3 through Day 5 – He feels like “crap,” reported that couldn't sleep but was tired (probably due to the steroids that accompany the medication) and had some pain.
- Day 6 – He reported that he begins to feel better each day thereafter until he has the next infusion.

He also commented that the chemotherapy does “suck.” However, he makes it a point to walk at least one hour per day, every day.
Cabazitaxel (Jevtana)

Another chemotherapy agent, Cabazitaxel (Trade name: Jevtana) is administered together with the steroid prednisone. It was approved by the FDA in June 2010 as a second-line chemotherapy to be used in advanced castrate resistant prostate cancer in men who have already been treated with docetaxel and then failed. Cabazitaxel is the first and only chemotherapy agent to have shown any survival benefit for men with advanced castrate resistant prostate cancer since the approval of docetaxel.

Like Taxotere, cabazitaxel is a semi-synthetic analogue of paclitaxel, an extract from the bark of the rare Pacific Yew tree. There is an interesting mechanism that allows cabazitaxel to work when Taxotere has stopped working. Prostate cancer cells learn how to eventually "pump out" the key ingredient of Taxotere—taxane--from the cells. Cabazitaxel disables this pumping process, allowing the taxane to remain inside the cancer cell and effectively kill the cancer cell.

FDA approval of cabazitaxel was based on data from the single company-sponsored phase III TROPIC clinical trial, conducted with 755 men. All who participated in the trial had advanced castrate resistant prostate cancer and all had previously been treated with, and failed, docetaxel. They were randomized to receive either cabazitaxel or mitoxantrone, in combination with prednisone. In this setting, the cabazitaxel demonstrated a median survival advantage of 2.4 months over the mitoxantrone. (Refer to "A Survival Advantage — Is It Worth It and What Does It Mean?" later in this booklet.)

Cabazitaxel presents significant side effects. The most common adverse reactions, seen in 10% or more of the men in the trial included:

- neutropenia (Reoccurring periods of a very low white blood cell count)
- anemia (low red blood cell count)
- leukopenia (low white blood cell count)
- thrombocytopenia (low levels of blood platelets that cause clotting)
- diarrhea
- fatigue
- nausea
- vomiting
- constipation
- asthenia (lack of muscle strength)
- malaise (dizziness and fatigue)
- abdominal pain
- hematuria (presence of red blood cells in the urine)
- back pain
- anorexia (loss of appetite)
- peripheral neuropathy (pain, numbness and tingling in your arms, hands and feet)
- pyrexia (fever)
- dyspnea (shortness of breath)
- dysguesia (distortion of the sense of taste)
- cough
- arthralgia (joint pain)
The most common adverse events leading to discontinuation of the cabazitaxel were neutropenia and renal failure.

*Warning* - Cabazitaxel has caused neutropenic deaths (an abnormally low count of neutrophils, a type of white blood cell that helps fight off infections, particularly those caused by bacteria and fungi).

As with most chemotherapy drugs, cabazitaxel kills many white blood cells that then leave a patient significantly more susceptible to life-threatening infections. It is very important that you monitor your blood count assiduously to avoid any dangerous occurrence of neutropenia.

**Because of its possible harsh side effects many men choose to use abiraterone and prednisone, or enzalutamide, prior to using cabazitaxel.**
Enzalutamide (Xtandi)

Xtandi, which is taken orally, is an androgen receptor inhibitor, which blocks the ability of androgens from accessing the cancer cell’s nucleus to fuel its growth. The FDA approved it in 2012 to treat metastatic castration resistant prostate cancer in men who have received and failed docetaxel. This is the same disease stage for which both abiraterone and cabazitaxel are also approved. Sometimes enzalutamide is referred to as a “super Casodex” as it has a similar, but much more powerful, antiandrogen effect.

Unlike abiraterone, enzalutamide does not require simultaneous administration of a steroid such as prednisone.

Additional phase III trials have been conducted, and there is a pending application at the FDA to approve the drug for use before chemotherapy in addition to its current approval for post-chemotherapy use. Malecare believes by the end of 2014 enzalutamide will be approved for pre-chemo use joining Provenge and Zytiga at this stage. This raises the same question I asked about using abiraterone as a primary ADT treatment: should enzalutamide be used as an alternative to Casodex? Only additional research will answer this question.

The most common side effects reported in the clinical trial of enzalutamide were:

- Fatigue
- Back pain
- Diarrhea
- Hot flashes
- Peripheral edema (swelling in the hands and feet)
- Musculoskeletal pain
- Headache
- Upper respiratory infection
- Muscular weakness
- Dizziness
- Insomnia
- Lower respiratory infection
- Spinal cord compression
- Hematuria
- Paresthesia

Listening to the feedback on the advanced prostate cancer online support group fatigue seem to be the side effect experienced by most of the men taking the drug. They report an overwhelming fatigue that will often interfere with day-to-day life.
Prior to the approval of docetaxel as chemotherapy an agent to combat advanced prostate cancer the go to drug was mitoxantrone plus prednisone. Mitoxantrone plus prednisone reduces pain and improves the quality of life in men with advanced, hormone-refractory prostate cancer. It operates by interfering with the cancer cells ability to grow and spread, but it does not extend life. It remains today as a standby "end of life" treatment for men with advanced prostate cancer because of its ability to improve the quality of life.

**Caution** - A serious, but uncommon side effect of mitoxantrone can be interference with the pumping action of the heart. You can tolerate only up to a certain amount of mitoxantrone during your lifetime. This "lifetime maximum dose" may be lower if you have heart disease risk factors such as having received radiation to the chest, advancing age, and/or use of other heart-toxic drugs. Your doctor should check your heart function before you take any mitoxantrone and should monitor your heart health periodically during your treatment.
Complementary and Alternative Therapies

Complementary, or “integrative,” and alternative therapies are not the same thing and should not be confused with each other. Complementary therapies are therapies intended to “go along with, hand in hand” with the traditional therapies we use to treat prostate cancer. Sometimes they are designed to enhance the underlying therapy, but usually they are used to mitigate the negative side effects of traditional therapies. They are supportive measures that enhance your well being by controlling symptoms. Their benefits are usually supported by clinical studies.

For example some of the complementary therapies are used to help control nausea and vomiting are:

- Acupuncture
- Acupressure
- Hypnosis
- Muscle relaxation with guided imagery
- Chewing on some pieces of ginger or suck ice chips during the infusion
- Using Anti-seasickness (acupressure) wristbands (available in many drug stores)
- Marijuana may soothe nausea. A synthetic version of the active ingredient in it, THC, is in the prescription drug, Marinol (dronabinol).
- Chi-Gong and Tai chi

Using marijuana may help relieve the nausea and pain. However, its use raises serious issues in states where its purchase or use is illegal, regardless of its possible benefits to cancer patients. There may be safety issues as well. Unless the marijuana is grown and prepared in a pharmaceutically controlled environment, there may be contaminants such as mold or fungus. If your immune system has been compromised (which chemotherapy will do) you might not be able to fight infections induced by contaminated marijuana.

Memorial Sloane Kettering Medical Center (MSKCC) in New York City has excellent resources on complementary therapy (they refer to it as "Integrative Medicine) online. Go to: http://www.mskcc.org/cancer-care/integrative-medicine/about-herbs-botanicals-other-products

Alternative therapies, on the other hand, promise cures, are often invasive, harmful, and costly. They have not been subjected to the rigors of clinical trials and always lack evidence to back their claims. In short, they are simply voodoo medicine, marketed too often to desperate patients eager for a cure. The real problem is that they delay the use of proven treatments, which allows the cancer to continue to progress while ineffective alternative “cures” are being used.
Remember: as with everything in life, if it sounds too good to be true, then it probably is not true. “On the fringe” fashionable treatments, especially special diets, come in and out of vogue all the time. None of them cures cancer. Contrary to popular rumor, no person or company has found a way to cure cancer but is keeping it off the market so they can sell more expensive traditional drugs or treatments.
What Is Disease Progression?

The process of prostate cancer metastasizing from the prostate gland to other parts of the body is called “disease progression.” Disease progression also includes the emergence of new metastases, as well as the growth (enlarging) of existing metastases. Disease progression is measured by evidence seen on scans and on PSA progression.

Other than for Provenge, disease progression is one measure of treatment failure.

Exactly how prostate cancer spreads is not yet well characterized. It is often thought to spread either through the vascular system or through the lymphatic system. It may use both. The end result of the spread is development of tumors in other parts of the body, both near and distant from the location of the prostate gland. Bones are the most common sites for metastases to develop, but prostate cancer can also spread to soft tissue organs.

What Are Circulating Tumor Cells?

One new area we will be hearing more about is how cancer cells move though the body. These are called circulating tumor cells, or CTCs. Measuring the numbers of these circulating cancer cells, and characterizing them may provide a picture of both the aggressiveness of the cancer, as well as prognostic information (http://advancedprostatecancer.net/?p=4469, http://advancedprostatecancer.net/?p=4394 and http://advancedprostatecancer.net/?p=4256) In turn, CTCs may become a method to initiate more effective treatment in real time. The working hypothesis is that the more CTCs there are, the more aggressive the cancer is. Accordingly, if a treatment is working, we should see a decrease in the number of CTCs.

We expect to see an explosion of new research in this area. The majority of current research is still involved in finding better ways to find and identify these cells in the blood and validate their ability to inform us about disease progression and treatment effectiveness. There is also active development underway to find more efficient and less costly methods to measure CTCs in the blood.

The really exciting future of this research will also include the ability to characterize these cells in order to evaluate the drug’s potential effectiveness on an individual, personal level. (http://advancedprostatecancer.net/?p=4490) This will enable precise targeting of the proper drug, as well as evaluate actual efficacy when there are no other existing biomarkers (http://advancedprostatecancer.net/?p=4128).

What Are Bone Metastases?

Bone metastases are tumors that have spread from the original cancer site in the prostate gland to the bones. The most common bone sites for them to develop are in the pelvis, spine, thighs and ribs. However, they can develop in any bone anywhere in your body. Bone metastases can become extremely
Normal bone is constantly being remodeled, or reabsorbed and then reformed. Simply put, bone is broken down into its basic parts and then re-built. Prostate cancer disrupts the balance between the osteoclast cells that break down or reabsorb the old bone and the osteoblast cells that create new bone. When the balance is disrupted, tumors develop that can cause fractures, spinal compression, severe pain, weakness, numbness and difficulty urinating. Bone metastases can also cause hypercalcemia, which is abnormally high levels of calcium in the blood causing constipation; nausea; pain; poor appetite; vomiting; kidney problems with flank pain; frequent thirst; frequent urination and kidney stones.

Detecting Bone Metastases

Since bone metastases symptoms vary from man to man, it is important to correctly distinguish bone metastases from other conditions such as arthritis. If you experience bone pain it is important to tell your doctor. X-rays can diagnose bone metastases best, but bone scans, CT scans, PET scans, MRIs and blood tests can also contribute to an accurate diagnosis.

If bone metastases go without treatment, a man with castrate resistant prostate cancer is likely to experience approximately 1.5 skeletal related events (SREs) annually (Citation: Saad F, Gleason DM, Murray R, et al., J Natl Cancer Inst. 2002;94:1451-1468) with a median time to the first SRE of 10.6 months (Citation: Saad F, Gleason DM, Murray R, et al., J Natl Cancer Inst. 2002;94:1458-1469).

Early detection of bone metastases allows more effective treatment to delay bone pain and other complications.

Bone Metastases need to be treated not only because they can cause severe pain, but because they also cause bones to weaken and fracture. Uncontrolled progression of bones metastases can completely disable a man. Bone metastases can cause spinal cord compression that can lead to paralysis, even death. Additionally, bone metastases can invade bone marrow hampering the generation of new red blood cells.

Preventing and Treating Bone Metastases

There are a number of different treatments that will affect bone metastases, including chemotherapy, hormonal therapy (ADT), radiation therapy, and bisphosphonates. All these therapies can slow progression and growth of bone metastases.

Both radiation therapy and bisphosphonates are designed to target bone metastases.

- **External Beam Radiation Therapy (EBRT)** can be aimed at sites of painful bone metastases (spot radiation). EBRT relieves pain in the majority of men and is most useful for treatment when there are only one or two sites causing pain. When there are more than one or
Radiopharmaceuticals, are a systemic treatment that has been recently approved by the FDA. These drugs are administered by intravenous infusion (IV).

Radiopharmaceutical drugs usually relieve pain from bone metastases. They travel throughout the skeleton and are able to directly target the metastases in the bone so they are most effective for men with a number of different and diffuse painful bone metastases.

The newest radiopharmaceutical approved for bone metastases caused by prostate cancer is Radium (RA) 223 dichloride (Trade name: Xofigo®).

The FDA approved Xofigo in May of 2013. In a clinical trial of 809 men with castration-resistant prostate cancer that had spread to their bones, but not to other organs, the men who received RA 223 lived an average of 14 months compared to just over 11 months for men who received a placebo injection. They also reported significant palliative benefit (pain relief).

Radiopharmaceuticals have shown themselves to be very effective in relieving severe pain.

Radium 223 is a systematic treatment mimics calcium that binds with minerals in the bone to deliver radiation directly to the bone tumors while limiting the damage to the surrounding normal tissues. Since it is systemic it can be used to treat multiple bone metastases in different parts of the body.

Radium 223 is administered once a month as an IV injection into a vein. The IV infusion should be slow, lasting at least more than one minute. The dosage is variable depending upon the body weight of the man. The dosage level 50 kBq/kg body weight or 1.35 microcurie/kg body weight. The larger the man, the more radium 223 required.

The most common side effects of Radium 223 are:

- Nausea
- Diarrhea
- Vomiting
- Swelling of the leg, ankle, or foot (edema).
- Anemia
- Lymphocytopenia
- Leukopenia
- Thrombocytopenia
- Neutropenia

RA 223 is a breakthrough treatment. At this time a full treatment protocol consists of six treatments. The next question to be faced is, can it be used multiple times? In the best-case situation this is a question that will need to be answered by additional clinical trials. Alternatively,
there is an excellent chance that we will have an answer to this question by reviewing the clinical practices of our doctors as they search for the optimum treatment protocols. Although the current literature states that only six doses are considered safe, this is not to say that additional doses would necessarily be unsafe.

Unlike other drugs used in the treatment of men with advanced prostate cancer, the body does not metabolize RA 223; it decays naturally and is expelled. During the first week after the injection 63% is excreted in the fecal matter. Cleaning your toilet bowl is important and should be done while limiting contact with the water in the toilet. Not discussed, but equally important, is to take care that after moving your bowels you clean yourself thoroughly and don’t allow anyone to have a chance contact with the used toilet paper. Proper hygiene practice includes:

- Flush the toilet several times after each use;
- Wipe up and flush any spilled fecal matter;
- Wash your hands after using or cleaning a toilet;
- Wash soiled clothes and bed linens separately from other laundry.

Prior to the approval of RA 223 other useful radiopharmaceuticals were available and which still may be used. RA 223 is a superior treatment because it does not have a long-range (distance) effect on surrounding healthy cells, while older radiopharmaceuticals spread beyond the tumor location. Additionally, RA 223 is the only treatment in this class that has demonstrated any survival advantage.

Other radiopharmaceuticals include Strontium-89 (Metastron) and Samarium-153 (Quadramet), which specifically target bone lesions. As well, there are two other radioactive isotopes, rhenium 86 and rhenium 188, which have been utilized less frequently to treat bone metastasis caused by prostate cancer.

Prior to the approval of Radium 223, Metastron (strontium-89) had been the most common radiopharmaceutical for treating men with prostate cancer that has metastasized to the bone. Men with advanced prostate cancer who are responding to chemotherapy appear to have a better chance of survival if bone metastases are treated with strontium-89 every six weeks in conjunction with a chemotherapy drug.

Dosages of radiopharmaceuticals vary with the individual and the type of treatment. Dosages of radioactive materials are expressed in units called millicuries.

Strontium 89 is injected into a vein. The usual dosage is 4 millicuries, depending on age, body size, and blood cell counts. Repeated doses may be required.

Samarium 153 is also injected slowly into a vein. The usual dosage of samarium 153 is 1 millicurie per kg (0.45 millicurie per lb) of body weight. Repeated doses may be necessary. Because samarium 153 may accumulate in the bladder, it is important to drink plenty of liquid prior to treatment and to urinate often after treatment.

Strontium-89 and samarium 153 may temporarily lower the number of white blood cells, which you need to fight infections. The number of blood platelets, which are important for proper blood
Strontium-89 and samarium 153 are excreted in the urine. To prevent radioactive contamination, you should follow special measures for one week after receiving strontium-89 and for 12 hours after receiving samarium 153:

- Use a toilet rather than a urinal;
- Flush the toilet several times after each use;
- Wipe up and flush any spilled urine or blood;
- Wash your hands after using or cleaning a toilet;
- Wash soiled clothes and bed linens separately from other laundry.

If you suffer with bladder control problems you must take special measures following treatment to prevent contamination with radioactive urine. Speak to your doctor about this prior to treatment.

While there are no warnings regarding radiation exposure to people around you, if you are involved with a child, a pregnant woman or other vulnerable individual, you might want to speak with your doctor about any particular risk.

Flush of the skin and transient increased bone pain are among the common side effects of strontium-89.

Signs of infection due to low white blood cell counts after treatment with strontium-89 and samarium 153 are fever, chills, cough or hoarseness, lower back or side pain, painful or difficult urination. Be sure to see a doctor if these symptoms persist.

Signs of low platelet count after treatment with strontium-89 and samarium 153 include, bleeding or bruising, black, tar-like stools, blood in urine or stools and tiny red spots on the skin.

Radiation therapy or other anticancer drugs may amplify the harmful effects of strontium 89 and samarium 153 on the bone marrow. Medicines containing calcium may prevent strontium 89 from being absorbed by bone tissue. Bisphosphonates may also prevent samarium 153 from working effectively.

**Bisphosphonates**

Bisphosphonates are drugs that prevent bone from breaking down or becoming reabsorbed. There are two FDA approved drugs in this class, zoledronic Acid (Zometa) and denosumab (Xgeva).

Zoledronic acid (Zometa) is the most commonly used bisphosphonate in men with advanced prostate cancer. Zometa not only reduces the risk of developing bone complications, it also controls existing bone metastases. Zometa is prescribed for men with castrate resistant prostate cancer after ADT fails. This should not be confused with taking oral bisphosphonates to maintain bone mineral density (BMD).
Stay well hydrated while getting your infusion.

Zometa is administered by infusion (IV). Be sure that you are well hydrated by drinking a lot of water prior to the infusion (and during it). Make sure that the infusion staff member monitors your electrolytes during the treatment course. A small number of men experience incapacitating bone, joint and/or muscle pain. If you do, discontinue the bisphosphonate treatment. In order to minimize potential side effects, ask your doctor to time your initial infusion rate to not less than one hour, and then not less than 30 minutes for each subsequent infusion.

Denosumab (Xgeva), approved by the FDA in November 2010, is the newest of the bisphosphonates, and is a human monoclonal antibody for the treatment of osteoporosis, treatment-induced bone loss (i.e. by ADT), and bone metastases in men with castrate resistant non-metastatic prostate cancer.

Compared to Zometa, Xgeva has been shown to delay the onset of bone problems, including bone metastases. It also has been shown to reduce pain and improve the a man’s quality of life (www.advancedprostatecancer.net/?p=4509). It is delivered monthly via injection. (Citation: XGEVA Delays The Onset Of Bone Metastases In Men With Non-Metastatic Castrate Resistant Prostate Cancer http://advancedprostatecancer.net/?p=2910)

According to a Johns Hopkins alert there is a growing body of evidence that has linked the extended use of bisphosphonate therapy to an increasing risk of an uncommon and very serious fracture in the thighbone (femur). (http://www.johnshopkinshealthalerts.com/alerts/osteoporosis/Bisphosphonates-for-Osteoporosis_6795-1.html?s=W1R_140125_001&st=email).

Long-term bisphosphonate use creates a significant increase in the risk of dangerous and unusual fractures.

In a 2011 long-term study of bisphosphonate use published in the Journal of the American Medical Association (JAMA), "Researchers found that older women who had used bisphosphonates for at least five years had a 24 percent lower risk of developing fractures in the hip and spine than their counterparts on bisphosphonate therapy for less than five years. It went on to caution that long-term users were more likely to develop fractures in the thighbone just below the hip (subtrochanteric) and further down the straight part (femoral shaft) of the thighbone—areas where fractures are not typically seen in people with osteoporosis.” Speak with your doctor regarding this risk.

Osteonecrosis of the Jaw (ONJ)

Osteonecrosis of the Jaw (ONJ) is a disfiguring and disabling condition where the jawbones suffer literal bone death through infection and rotting. ONJ is a well-known side effect of all the bisphosphonates, both Zometa and Xgeva. However, its reputation far exceeds its actual impact, as only a very small number of men ever develop ONJ. However, there is nothing wrong about taking precautions to prevent the possibility of developing ONJ. These would include a comprehensive dental examination and completion of all needed dental work before starting any bisphosphonate treatment protocol. While receiving treatment, maintaining excellent oral hygiene is vital. Try to avoid all invasive dental procedures such as tooth removal, and make sure that your dental professionals know that you are taking bisphosphonates whenever you have any treatment. Just stopping bisphosphonates prior to any dental work does not lower your risk, as these drugs remain in your
The risks of developing ONJ are statistically the same whether you take Zometa or Xgeva. Overall, 2% of cancer patients treated with Xgeva developed jaw necrosis, not significantly different from the 1.45% incidence with Zometa.
Soft Tissue Metastases (Visceral Metastases)

Although less common than bone metastases in prostate cancer, the presence of visceral (soft tissue) metastases is adversely prognostic in men with metastatic castration-resistant prostate cancer (mCRPC). The prognostic outlook regarding the specific location of the visceral metastasis is unclear.

In the TAX 327 phase III trial, men receiving docetaxel or mitoxantrone every 3 weeks or weekly with prednisone, were analyzed retrospectively to study the impact of the specific site of visceral metastasis on overall survival (OS).

The men were assessed for OS based on the site of metastases: liver with or without other sites, lung with or without bone or lymph nodes, bone plus lymph nodes, bone only, and lymph nodes only. Men with liver metastases with or without other metastases had shorter median OS (10.0 month; 95% confidence interval) than men with lung metastases, with or without bone or nodal metastases (median OS: 14.4 month; 95% confidence interval).

Men with lymph node-only disease had the best median OS (26.7 month; 95% confidence interval), followed by men with bone-only metastases (median OS: 19.0 month; 95% confidence interval) and bone-plus-node disease (median OS: 15.7 month; 95% confidence interval). (The Prognostic Importance of Metastatic Site in Men with Metastatic Castration-resistant Prostate Cancer, Pond, Sonpavde,Wit,Eisenberger,Tannock and Armstrong; Published Online PII: S0302-2838(13)01011-7 DOI: 10.1016/j.eururo.2013.09.024)

When to Use A Treatment & What Drugs Should Be Combined?

The recent approval of six new drugs for the treatment of prostate cancer (Xgeva, Provenge, Zytiga, Xtandi, Xofigo and Jevtana) raises an important question regarding the proper sequence and timing of treatments, as well as the efficacy of combined treatments in order to maximize overall survival.

An example is a small phase I trial which combined docetaxel (Taxotere) and prednisone with different dose levels of Ketoconazole (Keto). This trial enrolled 42 men with metastatic, castrate resistant prostate cancer (mCRPC). They were treated with docetaxel and prednisone (D+P) three of every four weeks plus a daily dose of Keto. The researchers studied a variety of different Keto doses and docetaxel plus prednisone (D+P). They found that by combining the therapies, PSA levels were lowered by 50 percent in 62% of the men and that 28% of the men with soft tissue metastases had a partial response to therapy.

They also found that the median overall survival of the men was 22.8 months, but by altering the timing of the treatments they found that there was a significantly greater survival in men who were D+P naïve than in men who had already been previously treated with D+P (36.8 vs 10.3 months). There was a correlation between Keto and D+P clearance (the time it takes for your body to rid itself of the drugs). Keto increased docetaxel exposure 2.6-fold at a Keto dose of 1,200 mg daily, 1.6-fold with 800 mg daily, and 1.3- to 1.5-fold with 600 mg daily.
The trial concluded that a combination regimen using 600 mg Keto daily was well tolerated and that the maximum tolerated dose of D+P in combination with Keto was 32 mg/m2. They also suggested that this combination has significant anti-tumor activity in men with castrate resistant prostate cancer. (Citation: J Urol. 2010 Jun;183(6):2219-26; A phase I clinical study of high dose ketoconazole plus weekly docetaxel for metastatic castration resistant prostate cancer.; Figg WD, Woo 5, Zhu W, Chen X, Ajiboye AS, Steinberg SM, Price DK, Wright II, Pames HL, Arlen PM, Gulley JL, Dahut WL. -PMID: 20399458)

In terms of combining Provenge with other CRPC treatments, its manufacturer, Dendreon, is now running new clinical trials designed to evaluate the use of Provenge at different times during prostate cancer disease progression and with different drug combinations like ADT, Yervoy and Zytiga.

All these studies deal with the all-important question of how to combine and how to sequence treatments in disease process. How we properly order and combine treatments to maximize our survival remains a great and as yet unanswered question. (http://advancedprostatecancer.net/?p=1677)
Combating Edema: Fluid Retention

Edema is the abnormal collection of fluid beneath the skin, and was formerly known as dropsy or hydropsy. Edema produces swelling that can become very painful. It is one issue that many of us might have to deal with but that unfortunately receives very little attention from the medical community.

Some people refer to edema as fluid retention. It’s not uncommon to see the fluid building up in legs, arms, feet, hands, lungs, face, heart, and/or abdomen. Your physician or nurse should check your ankles at each visit to test for swelling.

Edema that remains unchecked can become severe enough to cause damage to your kidneys, heart and lungs.

Edema can be aggravated by general changes in your body caused by your prostate cancer and its treatment. Poor nutrition, as well as some of prostate cancer medications, can also cause edema. Docetaxel, corticosteroids (prednisone, methylprednisolone, or hydrocortisone that are prescribed to accompany many of drugs); anabolic steroids (fluoxymesterone, testosterone, methyltestosterone); and non-steroidal anti-inflammatory agents (ibuprofen, indomethacin, naproxen, rofecoxib, celecoxib) and thalidomide, can all cause edema.

Edema comes from either leaking fluid from your blood vessels or when your body generates more fluid than your lymphatic system is able to remove. The removal of or damage to the lymph nodes from treatment together with the cancer itself can be responsible for the lymph system being unable to function adequately, leading to the development of the edema.

Edema can be very serious. If you experience any of the following contact your doctor immediately:

• Wheezing, shortness of breath, or trouble breathing;
• Chest pain or tightness;
• Swelling or weight gain so that your clothes do not fit;
• Rapid weight gain, such as gaining more than 5 pounds in a single day;
• Urinating smaller amounts than usual or not passing any urine;

Whenever you are sitting or lying down, using pillows or cushions to raise your feet and legs above your heart is a primary counterstrategy to edema. If you have severe edema, lie down and rest for several hours each day with your legs elevated. You can also limit your risk of developing edema by:

• Modifying your diet to eliminate salt (as an alternative to salt use pepper, lemon or other herbs);
• Avoiding foods that always overuse salt in their preparation;
• Find someone who can give you a lymphatic drainage massage;
• Wear elastic compression stockings during the daytime. You can purchase these at medical supply stores and pharmacies. They are sized so your first pair should be bought from a medical supply store where they can measure you for the proper fit (wear a pair of shorts to get measured). Compression stockings help push fluid back into your system. Normal stockings
or pantyhose do not work. Sometimes it may be hard to put these stockings on. Try using a pair of kitchen type rubber gloves to grab the sides of the stockings to pull them up. To take them off just peel them back from the top to the toe.

- Walking is important, and when you are sitting wiggle your toes and ankles often.
- Your doctor may prescribe medication (diuretics) to treat your edema. Diuretics will increase the amount of water you pass in your urine. Follow the directions carefully. Check with your cardiologist to see if diuretics are ok for you.

Restaurant food, especially fast food, is always full of large amounts of unnecessary salt: an edema creator.

Sometimes edema builds up in the abdomen and constricts breathing. In this situation a treatment called pericentesis is performed. If this condition develops you will need to have the fluid aspirated (removed) with a needle to allow you to breathe comfortably.

Dealing with Constipation

Constipation is an unfortunate experience for many of us. Beyond discomfort, it can become painful, as the normal toxins produced by the body are retained. To deal adequately with constipation it is important to be consistent in your care and recognize its symptoms.

Because of the adverse effects of ADT, many men are taking calcium and Vitamin D. Both can create constipation. (http://www.easy-immune-health.com/vitamin-d-and-constipation.html and http://www.everydayhealth.com/health-questions/vitamin-d/does-vitamin-d3-cause-constipation).

There are many ways to deal with constipation, including:

- Increase the fiber in your diet, including fruits, nuts and fiber cereal.
- Drink plenty of water throughout the day and add prune juice as well as dried fruit to the daily regimen.
- Try drinking two to three cups of warm water in the morning.
- If you need more help, add Magnesium Citrate together with Vitamin B6. Begin with 250 mg of Magnesium and 50 mg of B6. Be sure to continue to drink a lot of water as well as prune juice.
- Try over the counter or prescription stool softeners and laxatives.
- Many of the men on the advanced prostate cancer on-line support group suggest drinking a “cocktail” brew of a stool softener, a laxative, milk of magnesia, prune juice and coffee (One of the men at the advanced prostate cancer support group commented that he doesn't know how bad it tastes or if it even tastes bad at all because the chemotherapy had already killed his taste buds.
- Many of us will ultimately resort to an occasional fleet enema. They are inexpensive and highly effective. But they are also habit forming.
• If you do become constipated make sure that your doctor knows and is informed as to what you are doing to combat it.

• Increase your exercise level.

The late John Arnold (former member of the online advanced prostate cancer support group) shared a recipe he obtained from a hospice nurse who cared for him. He described the concoction fondly as the “Brown Bomber” and claimed that it worked like a charm:

• Every day take two “Senna Plus” tablets four times: two upon waking, two with lunch, two with supper, and two at bedtime.

• Whenever two or more days pass without a respectable bowel movement drink along with your normal morning coffee, a mixture of 4 tablespoons of milk of magnesia, 4 tablespoons of coffee, 4 tablespoons of prune juice.

John claimed that when you stirred it all up it didn’t taste bad at all. He reported that by the second evening he always had a good bowel movement, adding that he would take a second dose on the second day as well if he hadn’t had a movement on the first day. He also said that the nurse told him that whenever he had a bowel movement not to repeat the milk of magnesia, coffee, and juice mixture again for two days without a good movement. He indicated that his treatment worked well and would often carry him for five days before needing to repeat the treatment. During these five interim days he kept on taking the “Senna Plus” as well as occasionally drinking some prune juice.

Dealing with Weight Loss and Appetite

Dealing with the loss of appetite and related weight loss often becomes a problem as we journey through treatments. Many treatments depress appetite, or the nausea becomes so overwhelming it’s impossible to eat. A common recommendation seen in the general press is to use high caloric food supplements such as Boost and Ensure. This can help, but they’re expensive and will not be covered by insurance. Members of the online Malecare Advanced Prostate Cancer Support group have made the following suggestions:

• Carnation Instant Breakfast Drink (chocolate, vanilla and strawberry) together with ice cream provides a delicious high protein drink. Brenda froze this drink so her husband could eat it like an ice.

• Someone recommended the generic version of V8 juice with additional spices added. He said that while he was on chemotherapy it had sufficient “bite” to break through the tastelessness of food.

• Another individual recommended Blue Cheese: a wedge a day kept the doctor away! It is tangy and tasteful.

Here are some recipes from the Advanced Prostate Cancer online support group:

• From Bobbie: Breakfast Shake
  2/3 cup whole milk
  ½ cup fruit
2-3 tablespoons quick oats
4 ice cubes
2-3 tablespoons of sugar or honey
2-3 tablespoons of wheat germ

Place the milk and oats in a blender and let sit for 5 minutes. Blend until smooth. Add remaining ingredients and blend again. Add additional sugar and fruit to your taste.

• From Bobbie: Protein Fruit Drink
  1 mango, peeled and diced
  6 strawberries
  1 cup water or milk
  sugar to taste
  ¼ cup cooked and cooled beans (garbanzo, pinto, navy etc.)

  Puree and enjoy with a squeeze of lime if desired.

• From the Block Center Integrative Cancer Care in Chicago: High Energy Shake (1225 calories)
  8 oz. soy milk
  1 cup fruit
  ½ banana
  1 large scoop whey protein
  2 tsp L-Glutamine powder
  1 Tablespoon Almond Butter
  1 Tablespoon Sesame Oil (or other good oil like olive)
  ½ cup soy ice cream or ¾ cup firm, non-GMO tofu
  ¼ tsp cinnamon powder
  dash agave nectar or maple syrup

  Blend for thirty seconds in a high-speed blender.
Swallowing Pills

One man’s wife on the advanced prostate cancer online support group reported that her husband had difficulty swallowing pills the size, texture, and taste of Zytiga. He has found that swallowing them with carbonated water while holding his chin up allows him to successfully down the pills. Some drugs like Zytiga will have their absorption increased by crushing. Do not crush your pills to make them easier to swallow unless your doctor has approved of this practice.

Financial Help: Getting Required Medications and Treatments

Treating advanced prostate cancer can quickly become very expensive, especially for those of us without medical insurance, high co-pays and little savings or income.

The first step is to talk to your doctor and ask if there are any programs they are aware of which can help you pay your bills. Ask if the physician can give you drug samples. Many doctors are constantly receiving free samples from the drug companies and will usually pass them on to you if you ask. Ask for a referral to the social work department at the hospital for information regarding organizations that provide financial aid for cancer patients.

The next step is to Google the name of the drug to locate the pharmaceutical company’s web page. Most of the major pharmaceutical companies have patient assistance programs. Call the phone number listed for the company’s Patient Assistance Program and discuss your situation with their representative. Some Pharmaceutical Patient Assistance numbers for the drugs used to treat advanced prostate cancer are:

- Dendreon / Provenge 877-336-3736
- Amgen / Xgeva 888-657-8371
- Novartis / Zometa 800-277-2254
- Janssen / Zytiga 885-998-4421
- Astellas / Xtandi 855-898-2634
- Sanofi / Jevtana 888-847-4877
- Sanofi / Taxotere 888-847-4877
- Bayer / Xofigo 855-696-3446

You may also wish to contact the following organizations to see if you qualify for assistance:

- The Partnerships for Prescription Assistance can greatly reduce the cost of certain prescription medications, including many that are typically used in the treatment of advanced prostate cancer. They can be reached at: 1-888-477-2669 or at www.pparx.org.

- The Cancer Financial Assistance Coalition (CFAC) is a group of national organizations that provide financial help to patients. CFAC educates patients and providers about existing resources through a searchable database of financial resources. To find out more, go to http://www.cancerfac.org/
• The Health Well Foundation is a 501(c)(3) non-profit organization established in 2003 that is committed to addressing the needs of individuals with insurance who cannot afford their co-payments, coinsurance, and premiums for important medical treatments. To find out more about the Health Well Foundation, go to: http://healthwellfoundation.org/.

• Chronic Disease Fund (877-968-7233) helps underinsured patients with a chronic disease obtain medication.

• NeedyMeds.com is an information source about companies that offer patient assistance programs. These programs help those who cannot afford medications to obtain them at no or low cost through the manufacturer.

Local service or voluntary organizations such as Catholic Charities, Jewish Social Services, the Lions Club, Lutheran Social Services, the Salvation Army, as well as others may be able to offer financial assistance. Some of these organizations offer grants to help cover the cost of treatment and other expenses, while others provide assistance with specific services or products, such as travel or medications.

A social worker or the local telephone directory should provide a list of organizations. Many hospitals and clinics also maintain a list of service organizations in the community. You should also use Internet search engines to find compassionate care and drug assistance programs.

General assistance programs providing food, housing, and other services may also be available from the county or city Department of Social Services (check online or the local telephone directory for contact information).

For direct financial assistance, you may contact your city’s Department of Social Services.

Community-based groups, such as local churches, synagogues, mosques, and lodges may also provide assistance for people with cancer, sometimes even if the person is not a member of that particular organization or religion. Some hospitals also have private funds available for patients in need.

Sometimes getting treatments or special services will require travel. This means that you and your caregiver may end up being saddled with additional costs for transportation, lodging, and food. There are also programs that can help defray these additional costs. These include:

• Air Care Alliance (888-260-9707) offers a central listing of free transportation services provided by volunteer pilots and charitable aviation groups.

• Air Charity Network (877-621-7177) coordinates free air transportation for people in need.

• Angel Flight Samaritans (800-296-1217) provides long-distance travel for people with cancer and their families in need of travel assistance.

• The Corporate Angel Network (866-328-1313) arranges free air transportation for people with cancer traveling to treatment using empty seats on corporate jets.

• Joe’s House (877-563-7468) is a nonprofit organization providing a nationwide online service that helps cancer patients and their families find lodging near treatment centers: joeshouse.org

• The National Patient Travel Helpline (800-296-1217) provides information about charitable, long-
distance medical air transportation and provides referrals to appropriate sources.

- The National Association of Hospital Hospitality Houses (800-542-9730) is an association of more than 150 nonprofit organizations that provide lodging and support services to families and their loved ones who are receiving medical treatment away from home.

If you served in the US military during the period of the Vietnam War and were in country or on a ship on the waters near Vietnam, the Veterans’ Administration will automatically cover your costs for prostate cancer treatment. Those men with advanced prostate cancer will probably also receive disability payments.
Dealing with Pain

Unfortunately, advanced prostate cancer usually becomes very painful. Bones may break. Soft tissue gets pushed aside by growing metastases, causing increased pain and eventual organ failure.

There are medications that may be used to fight pain related to prostate cancer.

- Aspirin, acetaminophen, and ibuprofen ranging to the opioids such as morphine (including a morphine pump) can provide relief. Many of us will use Fentanyl patches, Dilaudid and methadone for breakout pain. If you have trouble keeping a pain patch adhered to your skin or you want to go swimming, try wrapping a stretch athletic tape that is available at many drug stores over the patch.

- Steroids reduce inflammation and dampen the body's painful reaction to the presence of prostate cancer in the bones.

- Bisphosphonates reduce bone pain, strengthen the bones, and possibly help to prevent fractures. They are often prescribed to people who have osteoporosis and are also used to lessen bone pain from cancer.

- Radiation therapy can be used to treat pain that is confined to a certain area by reducing the cancer tumor. For example, pain in the bones of the pelvis due to prostate cancer can often be treated with focal radiation.

- Radiopharmaceuticals use radioactive elements to reduce bone pain. Certain radiopharmaceuticals are specially designed to collect predominantly in the bones after being injected into the body. Once in the bones, the radiation emitted from the radiopharmaceutical works to kill cancer cells and relieve pain. However, they may attack bone marrow as well.

- While not studied as thoroughly, complementary treatments such as acupuncture, yoga, tai chi, meditation, and massage and herbal therapies have also been shown to help some people deal with pain.

If, after trying different medications, you are still experiencing pain, talk to your physician about seeing a specialist in oncology pain management. There are no points awarded for enduring pain, and life is too short to suffer pain.

None of us should have to worry about pain. If a doctor tells you that you are at risk for becoming an addict, then ask whom are they protecting? Tell them to get their priorities straight.

Stan, who is a member of the Malecare online Advanced Prostate Cancer Support Group, has also been a bedside hospice volunteer for 8 years. He posted a comment to another member, who is in hospice care and had raised a concern about moving to a morphine pump to better control his pain. Stan said:

“I've cared for people who were on the pump and it was a god-send. One thing I constantly encounter is a reluctance to take morphine until the pain becomes unbearable. It’s a much better approach to use morphine JUST as the pain begins and definitely before it becomes intolerable. As the pain progresses, you'll just need to assume that you'll have to up the dosage.” He also added that, “If you wait, it takes more morphine to get the pain under control and it takes longer to control”.
Depression

We all are subject to developing depression. However, it is important to understand that there are everyday types of depression, which is different than what is referred to as clinical depression.

Everyday types of depression are caused by bumps in the road of life. Over time, we can learn to accept these problems or take steps to resolve them, and are able to set the depression aside.

Clinical depression is a medical condition that becomes part of your consciousness, obstructs your ability to function, and requires the attention of a practitioner. If you find your world darkened by feelings of depression; if you withdraw from social encounters; if you lack any energy or will, or just don't get pleasure in anything anymore; if you are eating too much or too little, or getting too little sleep or can't sleep at all, or stay in bed all day; if you feel fatigued; or if you believe you are experiencing a complete personality change, you may be suffering from clinical depression.

A cancer diagnosis, especially of advanced prostate cancer, is significant in and of itself. For many of us, especially as we navigate the treatment process, clinical depression comes with the territory. But it can be managed.

If you find that you are becoming clinically depressed:

- Seek the help of a trained clinician – a nurse practitioner, social worker, psychologist or psychiatrist, one who works with oncology patients. Counseling can:
  - Help you develop ways to cope with your diagnosis.
  - Understand the meaning and implications of your diagnosis.
  - Help you make better treatment choices.
  - Help you manage your feelings.
  - Help you develop better communication skills with your families, friends and healthcare providers.
  - Manage your symptoms, drug side effects, pain and fatigue.
  - Deal with some of the financial burdens you face.
  - Deal with workplace issues resulting from your cancer or its treatments.
  - Understand and devise coping mechanisms to resolve sexuality and relational issues created by the cancer and its treatments.
  - Develop strategies to enter the post-treatment world.

- There are a number of different ways to find an appropriate clinician:
  - Ask your oncologist or the clinical nurse about counseling services available at your hospital or cancer treatment center.
• Ask your oncologist or clinical nurse for referrals to clinicians and counseling services in your community.

• Contact your health insurance company for a list of therapists or clinicians covered under your plan.

• Find out if your employer has an employee assistance program (EAP) that provides counseling services.

• Check with your prostate cancer brothers from a support group for recommendations of mental health clinicians trained and experienced in treating men with prostate cancer.

• Call your state or local association of social workers, psychologists or psychiatrists for a referral.

Another significant way to deal with both everyday and clinical depression is to exercise regularly. Studies have shown that exercise not only enhances physical health, but is also an excellent way to combat depression. Going to the gym is great, but not necessary. Above all, walk, walk, and then walk some more.

Exercise

Reduce stress in your life. There is some evidence that the stress hormone cortisol encourages the growth of cancer cells. Higher and prolonged levels of cortisol in the bloodstream (such as that associated with chronic stress) have been shown to have deleterious effects, including: impaired cognitive performance; suppressed thyroid function; blood sugar imbalances, including hyperglycemia; decreased bone density; loss of muscle tissue; elevated blood pressure; lowered immunity and inflammatory responses in the body; slowed wound healing; increased abdominal fat, which is associated with more significant health problems than fat deposited in other areas of the body; heart attacks and strokes; the development of metabolic syndrome (elevated levels of "bad" cholesterol (LDL) and lower levels of "good" cholesterol (HDL), leading to even greater health problems!

Reduce stress

Get a pet! Pets are known to improve the quality of life and our physical health. There have been many studies that show that the physical stroking of a pet lowers our blood pressure and increases the levels of (good) mood related hormones serotonin and dopamine.

Get a pet.

When I was having trouble walking my family gave me a dog, Charlie. I now walk Charlie several times a day, getting much needed exercise besides having a constant companion and a great friend.

Use medication if needed.
If the depression – or anxiety -- is severe, you might benefit from antidepressive or antianxiety medications. See a psychiatrist or nurse practitioner for assessment and treatment. A psychiatrist is a medical doctor specifically trained in psychiatry; a psychiatric nurse practitioner is a graduate level nurse with advanced training in psychiatric medication. There is no shame in using medication to lift your mood.

To read more about cancer and depression go to the NCCN web site at:

The Role of Sleep

A 2003 study published in the journal, *Brain, Behavior and Immunity*, showed a relationship between how well you sleep and how effectively you fight cancer. After analyzing previous studies, Stanford University psychiatrist David Spiegel, MD and colleague Sandra Sephton, MD stated that sleep problems alter the balance of at least two hormones that influence cancer cells.

One of these hormones is cortisol, the stress hormone that helps to regulate your immune system. Cortisol levels typically peak at dawn, after hours of sleep, and decline throughout the day.

Female night shift workers, who have higher rates of breast cancer than women who sleep normal hours, are more likely to have a "shifted cortisol rhythm," in which their cortisol levels peak during the afternoon. At least two studies have shown those women typically die earlier from breast cancer than the general population. People who wake up repeatedly during the night are also more likely to have abnormal cortisol patterns.

The other hormone affected by sleep is melatonin that may have antioxidant properties that help prevent damage to cells that can lead to cancer.

"There’s a definite hormonal pattern that is affected by sleep that in itself can predict a more rapid progression of cancer (David Spiegel, MD, Stanford University). The big problem for cancer patients is they take too much on themselves and don’t give enough time to help their bodies cope with the illness."

The night is scarier then the day is for most people. So, if you’re lying in bed and can’t sleep, turn on the light. It’s pointless to just lie in bed and not be able to sleep. If you can’t sleep, get up and do something; don’t just lie there staring at the ceiling. Try listening to an audiobook. I find that reading can be difficult because it’s difficult to concentrate, especially when I’m upset. An audiobook often solves this problem for me. Then, after awhile I go back to bed and fall asleep.

**I know that after every night comes the morning. I just have to figure out how to get to it and then enjoy it.**

On the flip side when I feel fatigued I don’t fight it because I know I’m not going to win. I just take a nap.
The Role of Stress

Stress can affect tumor growth and spread, but the precise biological mechanisms underlying these effects are not yet fully understood. It is possible that the effects of stress on the immune system may in turn affect the growth of some tumors (Citation: Andersen BL, Farrar WB, Golden-Kreutz D, et al. Stress and immune responses after surgical treatment for regional breast cancer. Journal of the National Cancer Institute 1998; 90(1):30-36).


Studies suggest an association of certain psychological factors with the growth or spread of cancer, such as feeling helpless or, conversely, suppressing negative emotions. (Citation: Garssen B. Psychological factors and cancer development: Evidence after 30 years of research. Clinical Psychology Review 2004; 24(3):315-338).

In general, stronger relationships have been found between psychological factors and cancer growth and spread than between psychological factors and initial development of cancer (Citation: Thaker PH, Han LY, Kamat AA, et al. Chronic stress promotes tumor growth and angiogenesis in a mouse model of ovarian carcinoma. Nature Medicine 2006; 12(8):939-944).

Ask yourself if it is possible to view your advanced stage prostate cancer as part of the human aging process. Not terribly desirable, but now perfectly normal for you—and now, part of your story.

Cancer is not your punishment. Cancer is a medical reality, albeit a very serious one. You can still control much of your destiny by empowering yourself to take control your medical care by choosing the most appropriate physicians and taking an active part in deciding on treatments. Also, continue to live your life to the fullest extent possible, whatever that may mean to you.

Seek and find others who share your diagnosis by joining support groups (face to face and online groups) and openly share your situation and your feelings. Trust your brothers, many of them have already walked the path ahead of you.

Other actions you can take to control stress include:

- See a social worker, psychologist or psychiatrist who works with cancer survivors.
- Learn to meditate.
- Practice deep breathing exercises and/or guided imagery.
- Take an exercise class, go swimming, ride a bicycle.
- Learn Yoga.

Most importantly, as we have said already many times: accept that life is the way it is today, yesterday no longer matters.
I keep enjoying life between my treatments.

Taking Control of Your Life

We all have things in our lives that make us sad and unhappy. Having cancer is one of these things. Now it is time to find the good and positive things in your life that make you happy and spend time with them.

This must be a very conscious decision.

Interrupt negative thoughts—your brain can only handle one thought at a time.

Simply put: I don’t care how old I am or what the other people think, I want to go to the bouncy castle and so, I am going to go now!
Hospital Admission and Discharges

Emergency room visits will probably become a part of your cancer and treatment experience. When this happens, there are potentially serious financial pitfalls for you to avoid. Sometimes a hospital keeps you there for a little while for observation, but doesn't formally admit you and doesn't assign you a diagnostic code. It doesn't matter how long this "little while" is, it could be a few hours, overnight, or even a longer period, but this is not an admission and you have not received a diagnostic code. If you are there only on "observation status," Medicare and most other private insurers will NOT pay. You could find yourself being handed a bill for $25,000 or more!

Make sure you have a diagnostic code.

Most states have regulations that require a written discharge plan before a patient is allowed to return home. Without this plan, and until you agree that the plan you receive is both safe and adequate, you should insist on remaining in the hospital. Do not buckle to pressure from the hospital staff until you are satisfied with the discharge plan. Remember to consider issues such as being sure your medication will be available, navigating stairs, help with bathing, and with other personal needs.

Friends and Family

Friends and families are important. But as you go through your cancer diagnosis and treatments, your interactions and involvement with them will change. Some people say that a cancer diagnosis lets them know who their real friends are and identifies those who are not really friends. To a certain extent this is true, but to some extent it’s not true.

When hearing you have cancer, people may feel awkward and often don’t know what to say, so they simply don’t say anything. Does this mean they’re not really your friends? That’s your decision to make. But there’s no question that some people will rise to the top, be ever-present, and be able to express their concern for you.

Even good people don’t always know what to say. Be a little forgiving.

Learning to ask for help is unfamiliar and often difficult for many of us. As we go through our treatments we are going to need help, so it’s important to just understand that there is nothing wrong in asking for help. Figure out what you are able to do for yourself, and then ask others to help with what you are unable to do by yourself.
We all want to feel loved and needed; it makes us feel good. If you ask a friend or family member to help they will feel needed and they will feel good for being asked. What is wrong with that?

Be as specific as you can in your request. It is hard to know what is helpful if you ask someone to just help out and you probably will not end up being helped. Asking someone to walk the dog at 3 p.m. or drive you to the doctor’s office at 11 a.m. will get you real, needed help and allow the other person to know they have provide you with a concrete and needed service.

**Need help? Ask for it.**

On the other side, even good friends may be able to offer specific help and say something like; “I’ll bring you and your family dinner on Thursday night.” Even though the statement, “Just let me know if I can help,” is very nice, it forces the decision back onto you. You may not know at that moment what kind of help you need—or even if you do, whether or not your friend is capable of carrying it out. When you’re dealing with cancer you already have plenty of decisions on your plate, and may lack the energy or will to handle one more. If the person is a real friend they will not be offended if you tell them you don’t know what help you need and ask them to offer specific help.

A constant complaint many cancer patients mention is that friends and family members all call at different times and want to know the same information. Questions such as, “How are you feeling?”, “What’s next?” and so on. This can become very difficult and wearing. Not only is dealing with the requests for information difficult for you, but it also becomes difficult for your caregivers. Fortunately, there are resources available that will keep everyone in the loop without putting a significant strain on you or your caregivers. Many people find that setting up a web presence relieves them of the constant burden of repeating the same information over and over.

Probably the simplest thing to do is for you or a caregiver to create a mailing list of the important friends and family members and send out a periodic update to them—either in writing or via email. Feel free to let people know how you wish to be contacted so that you don’t become overwhelmed. Let them know that you appreciate their concern, explain that you do not intend to offend them by controlling communication, and that you will let them know when and if you are up to receiving reply emails, phone calls, and/or visits. These updates can also be used to ask for specific help and assistance you might need.

**Surround yourself with positive people**

**Preparing For End of Life -Hospice Care**

For many people, death is something not talked about. But if you enter the end stage of advanced prostate cancer, hospice care needs to be considered. While hospice is by no means mandatory, it can be a godsend.

Stan, who is a member of the Malecare on-line Advanced Prostate Cancer Support Group and a
bedside hospice volunteer for 10 years, has insightful and useful comments pertaining to end of life.

Dealing with and accepting the end of life for those of us with prostate cancer can be very difficult. Sometimes the need to continue life is more for others than for ourselves. Often times, we feel that there are issues that need to be finished that will help our loved ones accept our inevitable death. This unwillingness to “let go” can be translated into refusing to stop life-sustaining medication, even though they may come with awful side effects and no quality of life.

Most of us would think that the final acceptance of the inevitable would be prompted by the overwhelming side effects of the medications. However, just as important may well be the fact that we find a way to bring closure between our family and us, and settle the outstanding issues that we may have with them. Things like asking for forgiveness, forgiving, expressing love and gratitude, assurance from loved ones that they were ready to go on with their lives, can help bring closure and comfort that would allow us to let go and move on.

Bringing closure helps the survivors, their family and their friends.

For those who do go into hospice that’s not based in our home, there are things that can be done to ease the transition. We all have problem with changes, and when you are seriously ill you will have even more difficulty with change. Your family should bring your favorite items like pictures, flowers, trophies, etc., to your room. This will help provide comfort to you and to your family.

Deciding to go into hospice signals to a person and their family that the end of their life is nearing. As difficult as this process is, it could also be used as an opportunity to discuss end of life issues including finding ways to bring closure to the still open issues.

In response to a question about how much time one has left Stan said that’s difficult even for the most knowledgeable person to predict. However, there are phases that give an indication of “closer.”

“There may come a time when the ingestion of food and water becomes uncomfortable. Your body is saying it no longer can use it. Don’t force either, it does not extend life.

“There will be a shift in your sleep/wake patterns (more sleep--less awake).

“Your hospice team should have already given you a pamphlet on “what to expect” or a similar phrasing. In it will be a description of a number of physical changes to expect. These alerts will be helpful to your caregivers.

Dying means that your body systems begin to shut down. You may appear to be in a coma. It can last from days to a week or more. But even from a coma, you can regain consciousness, even momentarily, and talk about hearing everything that occurred at the bedside. Hearing may be one of the last senses to go. Tell your loved ones — now — that they should talk to you if you find yourself in a coma because you may very well still be hearing them. Remember, what is done from now until death can do much to ease your transition and reduce the severity and duration of your loved ones’ grief.”
Drugs On the Horizon

Following Taxotere’s approval seven years ago there were no new advanced prostate cancer drugs available until the recent approvals of Provenge and Zytiga in 2010 and 2011. The really great news is that there are many more potential new drugs in the FDA approval pipeline, or visible on the horizon.

• **XL184** ([http://advancedprostatecancer.net/?p=2162](http://advancedprostatecancer.net/?p=2162))

  XL184 is still in a very early testing stage, however it has been characterized as "very intriguing." In very early testing, 19 of 20 men in a phase I trial showed improvement in their scans. To the surprise of the investigators, for some of the men in the trial, their bone scans no longer showed any cancer despite prior scans that showed mets. Additionally, relief for some of the men was substantial enough that they were able to stop taking the narcotics they were using to control their bone pain caused by the bone metastases.

• **PROSTVAC-VF** ([http://advancedprostatecancer.net/?p=1529](http://advancedprostatecancer.net/?p=1529))

  Malecare is optimistic that the next prostate cancer vaccine to become available after Provenge will be Prostvac. A successful phase II trial of 125 men with metastatic prostate cancer demonstrated a survival advantage of 8.5 months, longer than that for Provenge. According to the development company, Bavarian Nordic, Prostvac, a therapeutic cancer vaccine, has received fast track status from the FDA. Additionally, the company has received Scientific Advice from the European Medicines Agency, and has successfully concluded the required "end of Phase II meeting" with the US Food and Drug Administration (FDA). Both European Medicines Agency and the FDA suggest there is a preliminary agreement to conduct a phase III clinical trial. As with the Provenge trial, the study will be placebo-controlled, using men with minimally symptomatic, castration-resistant metastatic prostate cancer after failure of surgery or radiotherapy.

  One significant difference between Provenge and Prostvac is in their treatment protocols.

  *Provenge* is a personalized treatment that requires that a man’s white blood cells to first be removed and shipped to a manufacturing plant where the cells are treated. After this treatment the processed cells are infused back into the patient’s bloodstream.

  *Prostvac* is an "off the shelf" product that is injected subcutaneously to induce a specific, targeted immune response that attacks prostate cancer cells. As with *Provenge*, side effects issues appear to be mild.

  At the Malecare web site, under our teleconferences ([www.malecare.org/teleconferences/](http://www.malecare.org/teleconferences/)) we have recorded an interview with Dr. Nicolas Vogelzang, who -beginning at minute 15:00- gives an
• **Cyclophosphamide (Cytoxan)** ([CP](http://advancedprostatecancer.net/?p=1620))

Cytoxan is another possible future second line chemotherapy for castrate resistant prostate cancer following the failure of taxotere.

Low-dose CP (50 mg/d) and dexamethasone (1 mg/d) were given in a metronomic manner (repetitive, alternating low doses designed to minimize toxicity and target the endothelium or tumor stroma, as opposed to targeting the tumor specifically) to 17 men. Treatment was continued until disease progression or intolerable side effects occurred.

Nine (9) men showed reduction in PSA (median 44.4%); four men had a greater than 50% response, and five men had a less than 50% PSA response. Eight men eventually experienced PSA progression. The overall survival was 24 months. Five men reported a decrease in bone pain after 4 weeks of treatment. Compared with side effects from Jevtana (cabazitaxel) the men did not report any grade 3 and 4 toxicities.

Further advantages of low-dose CP were its convenient oral administration, dosing schedule, low cost, and low-toxicity profile. These attributes in combination with immuno-regulatory and antiangiogenic potentials make Cyclophosphamideals a prime candidate for additional study for post chemotherapy use, and as a possible combination drug to be used with other treatment regimens.

(Citation: Med Oncol. 2010 Jun;27(2):569.; Nelius T, Klatte T, de Riese W, Haynes A, Filleur S. PMID: 19365737 [PubMed in process])

• **Sodium Clodronat**, ([http://advancedprostatecancer.net/?p=2033#more-2033](http://advancedprostatecancer.net/?p=2033#more-2033))

Sodium Clodronat is a bisphosphonate drug that has been shown to increase survival in patients with advanced prostate cancer but not with localized disease. It is not yet approved.
Clinical Trials

Clinical trials are essential for the development of new, safer, and more effective treatments. Trials have not only advanced our knowledge, they offer hope for the future for all men. Without trials we could not evaluate whether a new treatment works, if it is just “snake oil,” or even if it is even safe.

Participating in a trial can benefit you now and it will benefit others as well as yourself in the future.

I don’t care about research...I am in this clinical trial to get the latest treatment and the best chance I have of living longer

Clinical trials offer great hope, but they also present some risk. When deciding if you are willing to participate in a trial you must learn about the possible benefits and the possible risks to which you might be subjected.

There has been significant prior study of the investigation product before any drug or treatment makes it to a clinical trial on humans. There have been pre-clinical trials (bench science) and animal studies that lead up to the trial.

Before deciding to participate in a trial you should speak with your doctor as well as the clinical trial coordinator and ask;

• Is there strong evidence that this treatment could work for me?

• Is it a randomized trial?

• If it is randomized is there a chance I could get a placebo, or are all groups going to receive the investigation treatment?

• What are the risks and what are the benefits of my participating?

• If I do well on the investigation treatment will I be able to continue to receive it even after the trial has ended?

• If I receive the placebo will the trial protocol allow me to “crossover” and receive the investigational treatment if I so desire?

• What additional commitments will be required of me if I participate in the trial? Will there be additional tests or scans, doctor or hospital visits required? It’s important to make sure that you fully understand how much extra time and effort will be required from you.

• To what additional financial costs will I be obligated? Usually, the researchers will pay for the research costs, but you or your insurance company might remain responsible for your routine patient care costs. Check with and make sure that your insurance company will pay for these
When Should I Participate In A Trial?

There are appropriate trials for prostate cancer at all stages of disease progression. Many of us look to trials only when we feel there are no alternative treatments available to us. Trials are important at all stages and you should consider participating in one even if there are still treatment options open to you.

**Trials are a way to get cutting edge treatment before anyone else.**

What Are The Different Trial Phases?

Clinical trial research progresses in an orderly series of steps, called phases. The phasing of trials allows researchers to ask and answer questions in a manner that results in reliable information about the investigation drug or treatment, while also protecting the patient. Clinical trials are classified into one of three phases:

**Phase I trials:** These first studies in people evaluate how a new drug should be given (by mouth, injected into the blood, or injected into muscle), how often, and what dosage is safe. A phase I trial usually enrolls only a small number of patients, sometimes as few as a dozen.

**Phase II trials:** A phase II trial continues to test the safety of the new drug, and begins to evaluate how well it works. Phase II studies usually focus on a particular type of cancer.

**Phase III trials:** These studies test a new drug, a new combination of drugs, or a new surgical procedure, in comparison with the current standard. A participant will usually be assigned to the standard group or the new group at random (called randomization). Phase III trials often enroll large numbers of people and may be conducted and coordinated at many doctors' offices, clinics, and cancer centers nationwide. They are also used to determine precise recommended dosages.

After a treatment has been approved and is being marketed, the drug's maker may study it further in a phase IV trial. The purpose of phase IV trials is to evaluate side effects, risks, and the benefits of the drug over a longer period of time and in a larger number of people than in phase III clinical trials. Thousands of people are involved in a phase IV trial. ([http://www.cancer.gov/clinicaltrials/education/what-is-a-clinical-trial](http://www.cancer.gov/clinicaltrials/education/what-is-a-clinical-trial))

You can read Malecare's frequently asked question guide about clinical trials at: [http://malecare.org/clinical-trials-faq/](http://malecare.org/clinical-trials-faq/)

We also recommend that you go to: [http://tinvurl.com/2cxtd8i](http://tinvurl.com/2cxtd8i) and register to receive clinical trial updates and announcements for trials that might wish to consider joining.
A Survival Advantage — Is It Worth It and What Does It Mean?

In order to obtain FDA approval, drugs must first go through a clinical trial that demonstrates a superior treatment result than the current standard of care. In some instances, the better result can simply be a demonstration that the investigational drug provides an advantage that is merely palliative (as Mitoxantrone is for advanced prostate cancer). But the best treatment result is increased length of survival. Survival, often expressed as “overall survival” is the gold standard of positive results; extending life is the goal.

I want to live longer, but I also want to enjoy my life...why can't these drugs focus on my quality of life?"

For example, the pivotal clinical trial for prostate cancer chemotherapy using taxotere showed that it provided a median of 2.5 months additional survival over the then-standard of care, Mitoxantrone.

Cabazitaxel (Jevtana), recently approved by the FDA to treat men who have failed chemotherapy with taxotere, provides a median of 2.4-month additional median survival time. Provenge adds a median survival extension of 8 months.

A median is not an average (which is the mean). One should not confuse the two. The “median” refers to the observation that half the men in the study survived longer and half experienced shorter survival time. No maximum survival times are considered in the evaluation. So, at least one half of the individuals in the clinical trial actually experienced an even longer survival advantage by taking the treatment. Don't let these survival medians often measured as a few months dissuade you from undertaking a treatment.

Recent debates about the value of these survival advantages have rocketed into the public awareness as the median survival advantages for all these drugs have been measured only in months, while all these treatments come with significant side effects and substantial additional economic costs. The big question is are these extra months of survival really worth the possible negative effects on your quality of life, and are they worth the economic burden they place on your family and on society in general?

Survival advantages are expressed as statistics, and statistics merely express general group trends. Statistics do not imply any guarantee, or even provide very helpful, information for an individual. The simplest way to explain this is recounting what my Statistics 101 teacher said on the first day of class;

“Ten women are in a room and one is pregnant.”

He then stated that from a statistical point of view it is possible to state that each woman is 10% pregnant.” We all know the physical absurdity of this statistically correct statement. Statistics are excellent in a large group trend analysis, but they are meaningless when it comes to understanding one's individual situation. Statistics do not provide any insight into what you can
Statistics are reinterpreted constantly, often to the detriment of understanding the potential upside of a particular drug or treatment for an individual. As noted above, survival statistics are expressed as a “median” survival time. One half of those participating in a trial lived longer than the median, and one half lived a shorter period than the median. The median does not take into account how long the men on the right side of the curve—the side that expresses a longer survival advantage—actually lived. Some, or perhaps many, are likely to still be alive after, perhaps long after, the numbers have been published.

Any one of us, actually one half of us, are going to be on the right side of the curve and live longer while the other half will have died. By participating in a trial or accepting a treatment, you have a 50% chance, therefore, of being in the group that responds better. And there’s absolutely nothing wrong with hoping you will be one of those men who lives longer—perhaps much longer.

In the protocol that most clinical trials follow, the median number often becomes blurred and contaminated. The studies that were conducted for Taxotere, Provenge and Cabazitaxel each allowed men in the placebo group to cross over to the treatment arm once they showed signs of disease progression. This means that men in the placebo group, who for statistical analysis purposes did not receive the investigational drug, were allowed to receive the actual treatment. Yet, their survival time was still calculated as if they remained in the placebo group and never actually received the investigational treatment, even though the drug may actually have extended their life.

So, are these treatments that measure median overall survival as just a matter of months’ worth it? They certainly provide hope, and they do offer the probability of life extension, possibly well beyond the statistical survival advantage. IN the end, it’s your decision. But when it comes to statistics always remember that statistics apply to a group, not to you as an individual.

Conclusion

None of us would willingly choose to live with advanced Reoccurring prostate cancer, but having this disease is not the end of the world, nor does it necessarily portend an early end to your life. There are numerous strategies and means with which to battle our disease while we continue to pursue a full and reasonably healthy life.

To accomplish this we each need to learn as much as possible about our disease, to take responsibility for our own health and for treatment decisions....Keep enjoying life.

“Not All Facts Are Knowledge” - T.S. Eliot

“Not All Knowledge Is Wisdom” - Bart Kamen, M.D., Ph.D.
It is your job to sort out the facts, the knowledge and most importantly, the wisdom

Appendix

Thoughts—From the Advanced Prostate Cancer Blog at:
www.advancedprostatecancer.net

* Happiness is taking pleasure in what you do have. It may also be a warm puppy, a kitten, reading a book, going to the racetrack or a baseball game. It doesn't matter what it is, just enjoy your pleasure.

* Set aside some time every day to ask two important questions;

1. What am I living for and how am I pursuing it?
2. What can I do or change and to make the world a better place?

* "Pain is part of being alive, and we need to learn that. Pain does not last forever, nor is it necessarily unbeatable, and we need to be taught that." — Rabbi Harold Kushner, popular speaker, author of numerous books, including When Bad Things Happen to Good People; and the officiant at my wedding.

* When the doctors told me that I had Reoccurring prostate cancer, they stamped on my forehead: "Expires ??/??/20??." I washed it off. Nobody can know when I would expire.

* I am not done with life. There are things I want to do and experience, places and people and more that I want to see, matters large and small that I want to be a part of, but I am also aware that I have been given notice, whether I like it or not. It is stamped on the front of my head for me and me alone to see, but I can and will keep it at the back of my mind for as long as possible

So, I will do as much as possible each and every day. I will embrace life and all that is good in my world. I also need, with the help of my physicians and my support network of family, friends, and colleagues, to work on extending that "Expired" date to its limit.

* I will not blame myself for my illness, and neither should you.

* Some mornings when I first wake up I feel like a normal, healthy man, with no thoughts of cancer, then the lightning bolt hits and I remember that I have it. I remember that I am likely to die because of this and there is only so much that I can do to forestall that destiny. But that doesn't matter; I am here today and very much alive.

*It comforts me somewhat that I am not alone; that I am one of a large community of men who
I take some encouragement from the fact that the vast network of medical researchers are actively pursuing better treatments and ultimately, a cure for what I have. Perhaps they will succeed in time to provide something that could radically improve my outlook.

Sometimes I just sink back into my mattress, pull the covers over my head and will myself back to sleep, in search of oblivion, or perhaps an uplifting dream.

* More often than not, I just decide to get up and get on with it, live my life, do something worthwhile and hopefully have some fun along the way.

* Many things are, we must accept, completely out of our control.

Other Thoughts:

The tragedy of life lies not in not reaching your goal. It lies in having no goal to reach. It is not a calamity to die with dreams unfulfilled. It is a calamity not to dream. It is not a disaster to be unable to attain your ideal, it is a disaster to have no ideal to reach for.

--Dr. Benjamin Elijah Mays 1894-1984

I cannot forget the many stories I hear about how people's positive attitude and positive thinking allows them to get through situations that seem to be hopeless. I believe if you expect to be sick and miserable, you will be sick and miserable. If you expect to do well your chances of doing well are much better; there is no guarantee, but why not shoot for the stars?

Outcome, at least with cancer treatment, has a lot to do with expectations. We have some control over whether we will become victims or victors. Stay positive. - Joel

- FOR ALL OF MY BROTHERS -