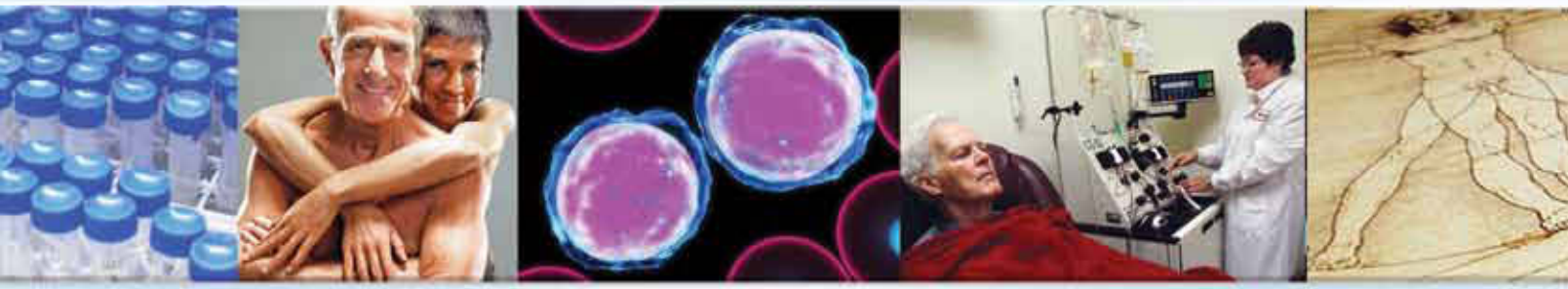
PROVENGE UPDATE



Common Questions for an Uncommon Treatment

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It has been a while since science has generated something unique for prostate cancer treatment. But the immunotherapy PROVENGE® is just that – unique. This uniqueness has proven both promising and puzzling; encouraging and educational. PCRI would like to address some current questions and concerns about this treatment option, as part of our ongoing effort to educate and empower prostate cancer patients, families and advocates.

In our May 2010 issue, we reported on the FDA's approval of PROVENGE (sipuleucel-T). Since then, PCRI has experienced PROVENGE from almost every perspective - the physician, the patient, and the Helpline caller. As always, PCRI hopes to offer clarity where there may be confusion.

Dendreon often uses the following terms to describe PROVENGE:

autologous	cellular	immunotherapy
comes from you	made of cells	treatment that helps the immune system fight disease

PROVENGE is unique because:

It does *not* kill cancer cells. Instead, this treatment is designed to retrain, or "turn on" your own immune system cells that were originally designed to kill cancer, but have failed for some reason. Thus, PROVENGE is called an immunotherapy.

It is made starting with a process called leukapheresis (or apheresis), which is unlike any other prostate cancer treatment procedure. Leukapheresis involves the removal of a small number of a patient's immune cells from their blood over the course of 2-4 hours on a specialized machine called a cell separator.

It is given as three infusions over one treatment cycle, usually about a month long, and is then finished for good. Provenge is not a treatment that is reconsidered or repeated.

It has few side effects, especially compared to other prostate cancer treatments for men with metastatic or hormone refractory disease.

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These unusual aspects of PROVENGE have created new questions for patients and their advocates:

Can I get treatment with PROVENGE? Eligibility

The FDA approved PROVENGE in the United States for men who meet the following criteria:

1. castrate resistant (hormone refractory)
2. metastatic
3. little to no cancer symptoms (mainly pain).

If you fit all three of these criteria, then you may be eligible for PROVENGE, and it is something you should be researching personally to discuss with your physician(s). The most common administering physicians are medical oncologists and urologists.

Some patients who do not fit the FDA's criteria for Provenge may still obtain access through ongoing clinical trials. Since **trial information is constantly changing,** this option requires some dedicated research.

Just because a treatment is on the market and is FDA-approved, does not necessarily mean all clinical trials cease. In some circumstances, a pharmaceutical company may need or desire additional data, which requires further research. A trial may be created to provide that data, which can simultaneously create opportunities for patients to obtain treatment.

There are currently three PROVENGE trials recruiting patients listed on the web at www.CLINICALTRIALS.gov. One of these may be of interest to men who are **not** metastatic and **not** on hormone therapy. Patients should research these trials and discuss them with a physician.

Sequencing of Sipuleucel-T and ADT in Men With Non-metastatic Prostate Cancer: *(Phase 2; no placebo)*

- Initial Basic (eligibility) Criteria:
- Prior "primary therapy" for prostate cancer
- PSA rising
- PSADT < = 12 months
- No metastases
- No ADT within last 6 months
- No prior ADT for more than 6 months duration
- No Xgeva or radiation within 6 months
- No Leukine or chemo within 3 months

For further criteria, locations, and contact information, visit www.CLINICALTRIALS.gov. Please note that this information is current as of the publication of this article, but is subject to change.

Availability

To date, PROVENGE is available only in the United States. Though not yet available in all 50 states, most states do have administering physicians. The PROVENGE website (www.provenge.com) has a user-friendly site locator, which allows patients to "Find a PROVENGE Provider" by entering their zip code.

PROVENGE sites include both large and small institutions; and both academic and community settings. Dr. Mark Scholz, Medical Director of Prostate Oncology Specialists in California and PCRI co-founder, was one of the first doctors to offer PROVENGE to his prostate cancer patients. "I want my patients to be focused on fighting cancer with the best tools available to us – and PROVENGE is a major advancement in that fight," he said.

For future availability in other countries, continue to monitor www.DENDREON.com and www.PROVENGE.com.

Affordability

The national Medicare system officially ruled in June 2011 that PROVENGE will be covered for men with Medicare who meet FDA criteria (mentioned above). Patients with private insurance should read their own policy carefully and discuss coverage with their insurance company. Many private insurance companies follow Medicare guidelines. You can contact Dendreon ON Call to speak with a case manager regarding questions related to your insurance coverage at (877) 336-3736.

For patients who are able to access PROVENGE through a clinical trial, treatment may be provided free of charge. Patients should always ask about the costs involved in a clinical trial.

For patients who are considered underinsured (i.e. need help with deductible costs, co-pays, or other co-insurance and travel costs), do not have insurance, or have exhausted all claims and appeals with their insurance provider, Dendreon has created a **Patient Assistance program.** This program is currently active, and more information can be found by calling **(877) 336-3736.**

How Do I Know if PROVENGE is right for my cancer?

As mentioned, a patient must meet specific criteria to be considered for PROVENGE treatment and reimbursement. Additionally, it is always important to weigh risks and benefits when making a treatment decision. Here are some issues unique to PROVENGE that should be considered and discussed with your physician(s):

Since the entire treatment process takes approximately one month to complete, and an immediate cancer response is not always apparent, the discussion on whether to pursue Provenge should include consideration of the time necessary to complete treatment. In other words, if your cancer is progressing rapidly, does it really make sense to undergo PROVENGE at this time? Would it be less risky to get the cancer under control with another treatment before investing approximately one month's time to undergo PROVENGE treatment? This discussion should take place with your physician(s), and is unique to PROVENGE since it is an immunotherapy which does not elicit immediate cell kill.

I'm planning on PROVENGE treatment soon – what do I need to know?

How are your veins?

The apheresis process is conducted on a machine that utilizes larger needles, similar to blood donation equipment. If your veins are not suitable for larger needles, your doctor may recommend a temporary "Central Venous Catheter". This catheter is different than a port, or a PICC line. Dendreon recommends your physician evaluate what is best for you about one week before the first scheduled leukapheresis procedure. 3

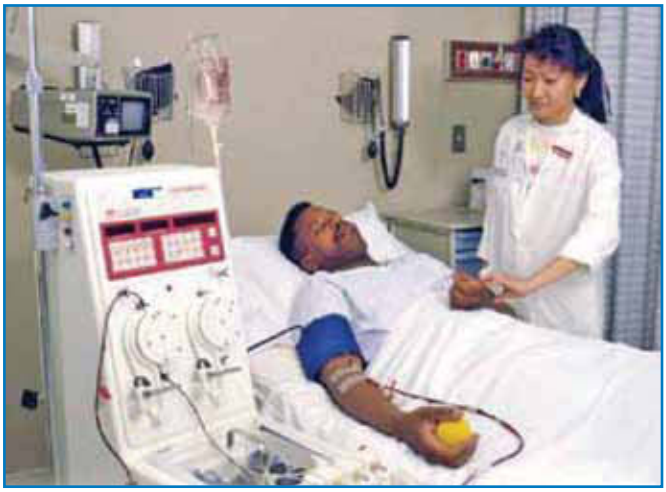
If your physician recommends a catheter, some simple maintenance is involved both at the incision site, and in the lines themselves. This is common, and is done to prevent infection and any blockage in the catheter lines. Make sure you ask both the apheresis center and your physician's nurses about this catheter maintenance schedule.

It should be noted that the majority of men in the PROVENGE clinical trials did NOT need a central vein catheter for apheresis.

Do I need a driver for apheresis?

Since the apheresis process can take 2-4 hours, it is recommended that you have someone who can drive you home after each procedure. Some men experience temporary citrate toxicity, tingling including tingling around the mouth, and fatigue. Please see the full Prescribing Information found at www.PROVENGE.com for more information.

Most pheresis centers have dedicated nurses who are attentive and experienced with the procedure. Many centers also have television or DVD player available to pass the time. You may wish to inquire about this in advance, or bring your own DVD player to keep yourself occupied.



I've heard of some PROVENGE samples being rejected. What should I do if this happens?

In some rare cases, a PROVENGE sample, which is delivered back to the physician's office, may not pass all the quality control regimens required. This can be for a variety of reasons. But since this product is so individualized, quality control procedures are paramount, and one more unique aspect of PROVENGE.

The approval or rejection of a PROVENGE infusion usually takes place by direct communication between Dendreon and the physician's office, on the day of scheduled treatment.

If, for some reason, your PROVENGE treatment does not pass all inspections and is rejected, the leukapheresis process will need to be repeated, and the PROVENGE treatment recreated. This may *(Continued on page 16)*

initially create concern for a patient, but there is no reason to believe it will affect the effectiveness of PROVENGE treatment. In fact, in controlled clinical trials, PROVENGE was administered in a great variety of schedules. Though the current regimen involves 2 weeks in between treatments, the dosing intervals in trials ranged from 1 to 15 weeks. [10]

Does PROVENGE interact with any other drugs?

Because PROVENGE is an immunotherapy made for your own white blood cells, it is unlike other synthetic drugs and their metabolization. No studies of drug interactions have been performed, and there are currently no known contraindications. [4]

Dendreon does state that PROVENGE immunotherapy should not be given with any other drugs that are designed to suppress the immune system. The most common of these would be steroid medications (hydrocortisone, prednisone, dexamethasone, etc.). This raises an important question for men who are on either ketoconazole with hydrocortisone or Zytiga with prednisone.

Although the steroid medications given with ketoconazole (Nizoral) and Zytiga (abiraterone) are meant to be steroid replacement, not immunosuppressive, this should be discussed with your treating physician. It is critical to note that steroid medications should not be stopped "cold turkey," as this can be dangerous. Oral hydrocortisone, prednisone, and other steroid medications should be stopped gradually by titrating the dosage down. Again, this should be discussed with your treating physician(s).

PROVENGE and leukapheresis have not been studied with concurrent chemotherapy. Concurrent use of chemotherapy with PROVENGE may alter either its effectiveness or its safety. In trials, chemotherapy has been used before PROVENGE and after PROVENGE, but not during. Prior use of chemotherapy is not required for PROVENGE treatment. [5] [6]

Zometa – In PROVENGE trials, 48 percent of men were also on Zometa. There were no recommendations to stop Zometa, and no known contraindications. [5]

I had PROVENGE. How do I know if I responded?

This is the foremost question patients and physicians face.

Again, since immunotherapy is not designed to kill cancer cells directly, but rather train your own immune system to kill the cancer cells, the cancer response can have a different appearance. This is an area of science and research that we will all watch develop over time. However, we do know the following:

PSA response – Some patients have reported PSA responses, but many have shown no initial PSA response. Increases in PSA doubling time have been documented in small studies, [1] but it is also important to note that immediate PSA response is uncommon, and usually not expected. It is understandable that the nature of retriggering the immune system may take time. A phase 2 study with PROVENGE suggested a significant difference in immune system reactivity after PROVENGE compared to placebo at 8weeks. [2] Again, this is a developing area of science and research that we should continue to monitor.

Circulating Tumor Cells – The CTC blood test was not used or measured during PROVENGE trials, so it is unknown if measuring CTCs is helpful in monitoring response.

Survival – Raw statistical data from scientific studies can be challenging to explain, or even interpret for an individual. We know that median overall survival significantly increased in PROVENGE trials. A median survival improvement of 4.1 months with PROVENGE compared to placebo . We also know that at the end of three years, the proportion of patients who were alive in the PROVENGE group in the largest Phase 3 trial was 50% percent higher (32%) than the proportion of patients alive in the placebo group (22%). [4] [5]

It can also be helpful to understand that other drugs for hormone refractory prostate cancer have been FDA approved with similar or smaller survival benefit. For example, Zytiga (abiraterone acetate), which was FDA-approved in 2011, showed a 3.9 month benefit in overall survival. [7] And the chemotherapy Taxotere (docetaxel), FDA approved for prostate cancer in 2004, produced an overall survival benefit of 2.4 months. [8]

A "memory". In PROVENGE studies evidence of a remaining effect in the immune system has been shown, meaning it continues to work in your body after the treatment is complete. Sometimes this is called memory. [9]

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Your next treatment – Since immediate PSA response may not be observed after PROVENGE, and some studies have documented a memory effect in the immune system, it may be reasonable to plan and discuss your next treatment strategy after PROVENGE. One study has documented an improved survival if PROVENGE was given before Taxotere compared to giving Taxotere alone. 3 Again, this is an area of research that we will watch develop over time, but there is evidence that planning your next treatment is reasonable and even prudent.

Patient Experiences

Discussions between patients on their experiences with PROVENGE, such as the one that Frank LaBarba has given us, are necessary in navigating any new treatment. PCRI has created a new online community, called the Blue Community (www.PCRIBC.org), where men and their families can connect, discuss, and post their experiences. The discussion on PROVENGE would be welcome and extremely beneficial to others. Visit the forums on www.PCRIBC.org today.

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Meet Madhu Rajaraman, PCRI Senior Writer-Editor

Madhu Rajaraman, 24, moved to Los Angeles from central New Jersey in October to join PCRI as Senior Writer-Editor. Ms. Rajaraman is responsible for developing PCRI's editorial and communications content, including the quarterly *Insights* newsletter, web content updates, social media and the brand-new PCRI Blue Community.

Before joining PCRI, she worked as a reporter for the News21 initiative on the future of journalism, the Maryland Capital News Service, the Association of Public Health Laboratories and the American Journalism Review. Ms. Rajaraman holds a dual bachelor's degree in English and psychology from Rutgers University and a master's degree in multimedia journalism from the University of Maryland. In her spare time, she enjoys photography, music, and going to the beach. She resides in Culver City, California.

Please contact Ms. Rajaraman at madhu.rajaraman@gmail.com to submit comments, suggestions and submissions for PCRI's publications and social media efforts.