

Targeted Radionuclide Therapy and Prostate Cancer

What is prostate cancer?

Prostate cancer is the most commonly diagnosed cancer among men in the United States, other than skin cancer. According to the American Cancer Society, approximately 238,000 new cases of prostate cancer are diagnosed, and more than 29,000 men die from the disease annually in the United States.

Imaging plays an important role in diagnosing and staging prostate cancer—as well as monitoring patients for recurrent disease (for more information on imaging, see the Molecular Imaging and Prostate Cancer Fact Sheet). Radionuclide therapies have long been used to alleviate pain in patients with metastatic prostate cancer—or cancer that has spread to the bone—and new therapeutic agents are under development as well.

What is targeted radionuclide therapy and how does it work?

Targeted radionuclide therapy (also called molecular radiotherapy) involves a radioactive drug called a radiopharmaceutical that targets cancer cells. Radiopharmaceuticals typically consist of a radioactive atom (also known as a radionuclide) combined with a cell-targeting molecule that seeks and destroys cancer cells. Some radionuclides have the ability to target specific cells on their own.

When injected into the patient's bloodstream, the radiopharmaceutical travels to and delivers radiation directly to or near disease sites. This treatment is known as 'targeted' radionuclide therapy because it damages cancer cells while limiting radiation exposure to healthy tissue. This type of therapy offers promise as a vehicle for personalized treatment of cancer because it can be tailored to the molecular properties of a specific tumor.

Targeted radionuclide therapy is currently used to treat certain cancers, including metastatic prostate cancer. However, researchers are developing and testing new targeted radionuclide therapies to treat a variety of other cancers.

About prostate cancer

The prostate gland, located just below the bladder and in front of the rectum, is part of the male reproductive system. It is about the size of a walnut and surrounds the urethra (the tube that empties urine from the bladder). The prostate gland makes fluid that is part of the semen.

Prostate cancer occurs when certain cells within the prostate gland grow in an uncontrolled, abnormal manner. Some tumors grow slowly while others grow at a more rapid pace. When localized, or confined to the prostate gland, prostate cancer may be cured.

Prostate cancer that spreads outside the prostate gland may initially grow into nearby tissues or lymph nodes. When prostate cancer spreads to distant sites within the body (or metastasizes), it most commonly involves the bones of the pelvis and spine. When the cancer spreads into the bone, it can cause pain, fractures and other complications that significantly impair a man's health. Preventing or slowing the spread of prostate cancer to the bones is a major goal of treatment.

There are many treatment options for men with prostate cancer, including surgery to remove the prostate gland, radiation therapy, chemotherapy, hormonal therapy, and immunotherapy. Male sex hormones (called



androgens) that circulate in the bloodstream can cause prostate cancer to grow. A common form of prostate cancer treatment reduces the level of androgens or blocks them from working. Despite such treatments, some prostate cancer continues to grow. This state is referred to as castration-resistant prostate cancer (CRPC). CRPC is often associated with cancers that have spread to the bone, called bone metastases. Treatment for men with CRPC is often aimed at controlling or relieving bone pain.

Molecular radiotherapy for metastatic prostate cancer

The following molecular radiotherapies are currently used to relieve pain and/or treat castration-resistant prostate cancer that has spread to the bone:

- strontium-89 chloride (Metastron®)
- samarium-153 (Quadramet®)
- radium-223 dichloride (Xofigo®)

Both strontium-89 and radium-223 are radionuclides that target areas of increased bone turnover and are directly injected into the bloodstream. Samarium-153 must be combined with a molecule that targets bone prior to being injected into the bloodstream.

Men undergoing targeted radionuclide radiotherapy often receive several injections, each separated by a period of weeks. Research has shown that this course of therapy is effective in relieving pain. Side effects of the therapy include myelosuppression, a condition in which red blood cell, white blood cell and platelet production decreases. Molecular radiotherapy is sometimes combined with chemotherapy.

Radium-223 (Xofigo), the newest radiopharmaceutical to be approved by the United States Food and Drug Administration, is unique because of the type of radiation it emits. Unlike strontium-89 and samarium-153, which emit beta particles, radium-223 emits alpha particles. Alpha particles deposit a higher amount of energy over a shorter distance than beta particles. Xofigo is especially promising because in addition to providing pain palliation, studies have shown that it can also extend overall survival in patients.

Is molecular radiotherapy covered by insurance?

Medicare and most insurance companies cover the cost of targeted radionuclide therapy. Check with your insurance company for specific information on your plan.

What new molecular radiotherapies are being developed?

As the fields of molecular biology and genomics advance, tumor properties and pathways are being revealed, providing new cancer-specific targets for molecular therapies. For example, scientists have identified a molecular mechanism called CXCR4 that is involved in prostate cancer cell migration and invasion. Researchers are working on developing anti-CXCR4 antibodies that can impair these mechanisms.

Scientists are also working on new molecular therapies that will further personalize treatment plans based on specific biochemical markers found in the patient and the characteristics of his disease. In addition, new studies are evaluating combination therapies, such as the use of molecular radiotherapy together with the immunotherapy known as sipuleucel-T (Provenge®), to more effectively treat prostate cancer.



Finally, molecular radiotherapies are playing a role in the emerging field of theranostics. Research has revealed markers for prostate cancer, including cell surface proteins, cell receptors, enzymes, and peptides that can be used both to image disease and as targets for therapy. In theranostics, imaging probes such as the radiotracers used in PET scanning are paired with cancer-destroying agents. Following delivery of these therapeutic agents, imaging can be performed to study and measure the effectiveness of the therapy.

The protein prostate-specific membrane anti-gen (PSMA) is a biomarker for prostate cancer because it is expressed by virtually all forms of the disease, especially metastatic and castrate-resistant cancers. Researchers are studying the use of a PSMA-targeting molecule labeled with a radionuclide as a means of both imaging and treating prostate cancer. Research is also under-way to study imaging and molecular radiotherapy with a bombesin derivative that targets gastrin-releasing peptide receptors (GRPr) expressed by prostate cancer cells and bone metastases.

Is radionuclide therapy safe?

Many medical procedures have side effects and risks; the same is true of radionuclide therapy. Used in the right way for the right patient at the right time, nuclear medicine is very safe—the benefits of the procedure very far outweigh the potential risks.

About SNMMI

The Society of Nuclear Medicine (SNMMI) is an international scientific and medical organization dedicated to raising public awareness about nuclear and molecular imaging and therapy and how they can help provide patients with the best health care possible. With more than 18,000 members, SNMMI has been a leader in unifying, advancing and optimizing nuclear medicine and molecular imaging since 1954.

The material presented in this pamphlet is for informational purposes only and is not intended as a substitute for discussions between you and your physician. Be sure to consult with your physician or the nuclear medicine department where the treatment will be performed if you want more information about this or other nuclear medicine procedures.

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Society of Nuclear Medicine and Molecular Imaging
1850 Samuel Morse Drive
Reston, VA 20190
www.snmami.org
www.discovermi.org

