

Low-Dose Prostate Drug Can Match Standard Dose, Cut Costs

Giving patients with metastatic castration-resistant prostate cancer (CRPC) just one quarter of the normal dose of abiraterone acetate (AA) (Zytiga, Janssen) with food achieves at least as great a reduction in prostate-specific antigen (PSA) levels as the standard dose without food, the results of a prospective, randomized trial reveal.

AA, which is a standard of care in CRPC, was administered under fasting conditions at a dose of 1000 mg during

its pivotal trials, despite early clinical studies that showed that drug exposure was significantly increased when the drug was administered with food.

The study included 72 patients with CRPC. The results show that after 12 weeks, giving a quarter dose of AA with a low-fat meal was not only noninferior to the standard dose without food in terms of reducing PSA levels but also that the duration of response was comparable, all at a lower plasma concentration.

The research was published online March 28 in the Journal of Clinical Oncology and was first presented at the 2017 Genitourinary Cancers Symposium.

The team writes: "The pharmacoeconomic implications of this study's findings are compelling.

"AA has an approximate retail cost of \$10,000 per month. With a median time receiving treatment of 16.5

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Medical Advisors

Paul Daeninck M.D.
Medical Oncologist

Darrel Drachenberg
M.D. Urologist

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Radiation Oncologist

Thanks!



The Manitoba Prostate Cancer Support Group offers support to prostate cancer patients but does not recommend any particular treatment modalities, medications or physicians ; such decisions should be made in consultation with your doctor.

MPCSG – active since 1992.

Next Meeting:

Wednesday, May. 16 ,2018

Speaker: Dr. Paul Daeninck

Title: "Questions and answers about prostate cancer symptoms"

Location: The First Unitarian Universalist Church of Winnipeg, 603 Wellington Crescent

Time: 7 – 9 pm.

(First hour for general discussion; second hour for expert guest speaker)

Free Admission Everyone Welcome

Plenty of free parking



Thought of The Day

Evening news is where they begin with 'Good evening' and then proceed to tell you why it isn't.

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months in metastatic CRPC, the per-patient cost savings with the LOW dosing would exceed \$100,000," they say.

They add: "Given the prevalent paradigm of developing drugs with large food effects under fasting conditions, there are multiple other opportunities to lower drug costs by administration with food."

Lead author Russell Z. Szmulewitz, MD, assistant professor of medicine at the University of Chicago, in Illinois, told Medscape Medical News, "Our trial provides crucial but not definitive data to support low-dose abiraterone with food."

Szmulewitz believes this use is appropriate for some patients. "I do not think that physicians should use it indiscriminately without a more robust trial with clinically validated endpoints," he said. "However, for cases in which patients have cost issues, it is now reasonable for physicians to discuss the option with those patients, which is what I do in my practice."

A larger clinical trial in castration-sensitive metastatic prostate cancer is in the planning stages.

Janssen Says Stick to the Labeling
In the current trial, the team randomly assigned 72 patients with progressive CRPC to receive either low-dose AA (250 mg with a low-fat meal) or standard AA (1000 mg during fasting) along with prednisone 5 mg twice daily.

The patients, who were from seven institutions in the United States and Singapore, were well balanced and typical of a standard CRPC population. The median age was around 73 years, and the patients' ECOG (Eastern Cooperative Oncology Group) status

was 0 or 1. The only difference was that there were more African Americans in the low-dose AA group, at 31% vs 14% in the standard arm.

PSA levels were assessed monthly. Every 12 weeks, testosterone/dehydroepiandrosterone sulfate (DHEA-S) levels were determined, and disease burden was assessed radiographically. Drug concentrations were calculated from plasma samples.



There was a greater reduction in PSA levels from baseline to week 12 with low-dose AA, at a mean log change of -1.59 vs -1.19 in the standard dose group. These findings established the noninferiority of low-dose AA on predefined criteria.

At 12 weeks, three (9%) standard-dose AA patients experienced primary PSA progression, vs one (3%) patient in the low-dose AA group.

The absolute PSA response rate at 12 weeks was 58% in the low-dose arm and 50% in the standard-dose arm. The duration of response was comparable, at a median progression-free survival of 8.6 months in both arms.

The low-dose intervention yielded changes in androgen levels that were similar to the standard dose; at the end of the study, DHEA-S concentrations were 10.2 µg/dL and 9.1 µg/dL, respectively.

The team found that the maximum plasma concentrations of AA were

higher in the standard-dose group than in the low-dose group (P = .012).

Approached for comment, Daniel M. Geynisman, MD, assistant professor in the Department of Hematology/Oncology, Fox Chase Cancer Center, Philadelphia, Pennsylvania, told Medscape Medical News that the study was "important" and "well-designed."

He said: "Abiraterone is an extremely commonly used drug in men with metastatic prostate cancer, and it is a very expensive drug, costing thousands of dollars a month."

The investigators revealed that "exposure of the drug can be increased significantly if it's given, instead of on an empty stomach as it's normally prescribed and approved, but rather with food," Geynisman said.

The low-dose treatment is now "an important option" for some clinicians and their patients, who will have "seemingly with very similar results."

In circumstances "where cost and access to drugs are an issue...paying for 25% of the drug is a huge deal," he added.

Geynisman also noted caveats: the trial was small, and the endpoint of PSA levels at 3 months is not standard.

He explained: "You look for things like progression-free survival or radiologic progression or overall survival. This is sort of an intermediary endpoint. It's not as hard of an endpoint as the others, and so one could question whether or not they've really proven noninferiority.

"But at the same time we know that PSA is great surrogate for all the other endpoints in prostate cancer, and so it's reasonable to assume that it is," he added.

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The new results will not change practice widely, although they will give clinicians "some wiggle room," he said.

Crucially, Geynisman warned that although it is possible that a similar food effect could be seen for other oncology drugs, it is not a given.

He said that, instead, it's going to be "drug dependent, and you have to take it on a case-by-case basis.

"I certainly wouldn't use these results to translate that to any other medication in oncology," he said.

Geynisman added, however, that in

general, the study "does open the door to the question of how drugs get approved and how they are evaluated."

In a statement, Janssen said that AA should be taken, in accordance with the prescribing information, "on an empty stomach."

It warns that taking AA with food "may cause more of the medicine to be absorbed by the body than is needed and this may cause side effects." It noted that "the use of food as a way to increase bioavailability in patients with cancer could present problems and risks."

The company said that "given the

variation in the content and composition of meals, the recommendation is to take [AA] exactly as described in the prescribing information."

The research received institutional funding from OncoTherapy Science and Dicerna. The original article contains a complete listing of the authors' relevant financial relationships.

J Clin Oncol. Published online March 28, 2018.

Liam Davenport April 18, 2018

<https://www.medscape.com/viewarticle/895350>

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CancerCare Manitoba Gala Fundraiser for Men's Health

This event ("***A Gold-Plated Evening***") was held on Wednesday April 4, 2018 at the RBC Convention Center in Winnipeg, from 6 pm to later than 10 pm. There were approximately 800 to 1000 attendees, with representatives from a broad spectrum of Winnipeg's, and indeed Manitoba's, "Who's Who".

The presenting sponsor of this year's event was *The Paul Albrechtsen Foundation, Inc.*, along with a large number of other major donors. Event tickets, augmented by a lively auction of a variety of items, contributed significantly to the fundraising efforts. This is a Manitoba event and all the funds raised are used to support the cancer care community in this province. Our support group (MPCSG) was represented

by two members of the board of directors.

The theme this year was focused on "men's health" which includes colorectal and lung cancer along with prostate cancer (only the latter is unique to men). Funds raised this year are specifically intended to help enable the acquisition and implementation, in Winnipeg, of MRI fusion biopsy technology for diagnosis and staging of prostate cancers. The two highlight formalities of the evening were presentations by Dr. Sri Navaratnam, President and CEO of CancerCare Manitoba, and a "fireside chat" involving Dr. Jeff Saranchuk (Medical Director of the Prostate Centre) and Mr. Doug Harvey (a prostate cancer patient). Both presentations were informative and entertaining and

served to convey a positive message about the current status of cancer care in Manitoba, as well as projecting an optimistic outlook for what the future holds.

The presentations were well received by the audience. This evening served to reveal the breadth and depth of the community support and involvement in the fight against cancer and to ensure that Manitobans can receive excellent cancer treatment right here in our home province. This helps place in perspective the role of our own support group, which is that we are but one part of a much larger effort meeting the needs of prostate cancer patients.

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Diagnosed With Metastatic Castration-Resistant Prostate Cancer: What's Next?

If you have metastatic castration-resistant prostate cancer, the hormone therapy you've been taking is no longer controlling the disease as it should. Here's what you should know.

It's a somewhat long and confusing name, but the term metastatic castration-resistant prostate cancer (mCRPC) refers to a cancer that has spread (metastasized) beyond your prostate gland and for which hormone therapy is no longer effective in stopping or slowing the disease.

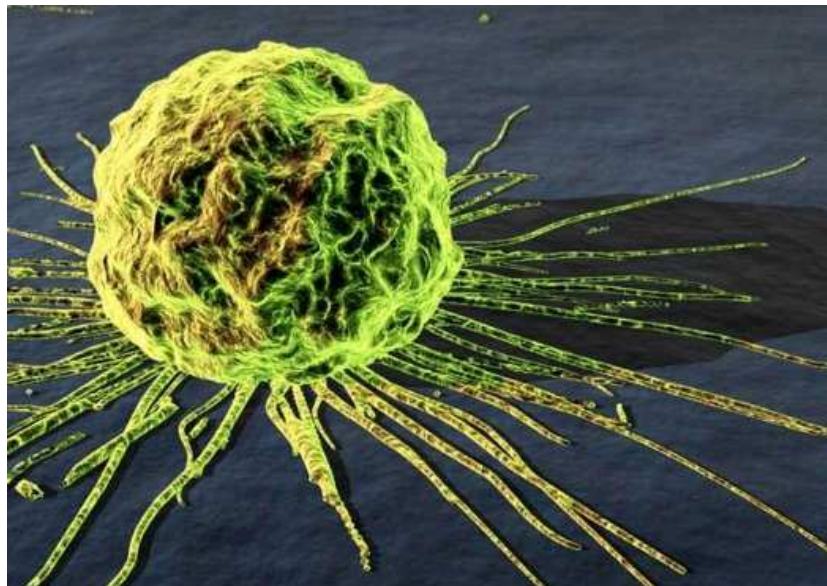
This type of prostate cancer can be very hard to cure, even when doctors catch it early. "This cancer escapes control," says oncologist Michael S. Cookson, MD, a professor and the chairman of the department of urology at the University of Oklahoma College of Medicine in Oklahoma City. "It's like a car that keeps moving even though you're pushing on the brakes in the form of hormone therapy."

It's common for hormone therapy, known as androgen deprivation therapy (ADT), to stop working after a few years. ADT works by blocking testosterone from stimulating the cancer to keep growing. The term "castration resistant" refers to a cancer that is no longer responding to this type of therapy.

According to the American Society of Clinical Oncology (ASCO), many men with prostate cancer eventually develop mCRPC. It's hard to pin down exact numbers — in part, because newer, more sensitive imaging technologies are now able to find cancer cells that

couldn't be found before, explains Scott T. Tagawa, MD, a medical oncologist at Weill Medicine and New York-Presbyterian Hospital in New York City.

"Our scans are getting better," says Dr. Tagawa. "When we just had X-rays, we missed small things. Then we got MRIs and CT scans, and we still missed some things. But now that we have more specific PET scans, we can see things we couldn't see before."



This means "that the same man who was non-metastatic before is now metastatic, because we have more sensitive scans [and can find incredibly small tumors]," Tagawa says. And finding cancer sooner means treating it sooner.

New Treatment Options

For most men with mCRPC, there's a lot to be hopeful about. Over the course of the past decade, several new treatments have been introduced, says Dr. Cookson, that can extend life expectancy and improve quality of life.

Since 2004, various new drugs have been approved, with each addition

designed to suppress testosterone in new ways, according to the Harvard Medical School.

While there have been a lot of promising developments, treatment guidelines still recommend that most people stay on ADT while adding on newer therapies, such as:

- **Docetaxel** A type of chemotherapy, this was the first approved therapy to prolong survival for men with metastatic CRPC.
- **Cabazitaxel** This newer type of chemotherapy, given along with prednisone, is an option when docetaxel is ineffective.
- **Sipuleucel-T** This treatment processes your immune cells outside of the body to essentially turn them into a vaccine, then the processed cells are returned to your body during treatments several times a week. It's primarily for men who have few or no cancer symptoms.

- **Hormone therapies** like abiraterone and enzalutamide This new generation of hormone therapies for mCRPC targets male hormones in different ways than do traditional hormone therapies. Both of these drugs, which are given in the form of pills, have been shown to lengthen survival.
- **Xofigo (radium-223 dichloride)** With this treatment, you're given an infusion of radioactive material that attacks the cancer cells within bones.

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The Role of a Multidisciplinary Care Team in Treatment

Keep in mind that the optimal treatment strategy for mCRPC is different for each person — and that it’s a complicated disease to treat. That’s why it’s important to assemble a team of doctors and specialists to keep your treatment — and you — on track.

Your team should include an experienced urologist, advises Cookson, as well oncologists who are comfortable with the newer treatments and know how to use them.

A study published in July 2015 in the Journal of Urology agrees, finding that with so many new treatments coming on board, doctors have to juggle a lot of factors when figuring out your best next steps — from what kind of symptoms you have to your personal preferences, as well as any other health conditions that may have to be taken into account when coming up with a treatment strategy.

It’s also important for your care team to review the medicines you’ve already taken for prostate cancer, and plan the sequence of the medicines you’ll take

next. Getting the order right is important because certain drugs can make subsequent treatments more, or less, effective.

Your care team should also watch you closely to determine whether you have any resistance to any medicines, so that they can make changes quickly if necessary.

Ideally, your care team should possess “expertise in distinct domains of cancer care,” such as imaging, chemotherapy, radiation, and surgery, according to a study published in the Annals of Oncology in August 2015.

You’ll also want key specialists to talk to each other about your treatment options before you start a new therapy — to determine exactly how your cancer is progressing, and to interpret results from imaging tests. Your care team should come up with an individualized treatment plan that considers the different benefits and risks, as well as the costs, of all your options; it should also include any clinical trials you should consider.

Quality of Life With mCRPC

According to a review published in the British Medical Journal in October

2016, you may not experience pain or other symptoms at this stage of cancer, or you may experience many. It’s different for everyone. So along with treating the cancer itself, be sure to talk to your doctors about any symptoms and side effects you’re experiencing in order so that the right ways to alleviate them can be found. You should also ask your care team about options for palliative care.

Because it can be very stressful to have advanced prostate cancer, and tough to talk about what it all means for your future, the ASCO urges men to have an open and honest conversation with their care team. Discuss what you’re worried about, and what’s important to you. There are many ways to look for and get emotional support.

By Jennifer Warner 4/9/2018

Medically Reviewed by Rosalyn Carson-DeWitt, MD

Additional reporting by Andrea Peirce

<https://www.everydayhealth.com/hs/advanced-prostate-cancer-what-is-crpc/>

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In Memoriam *James Anthony Leddy* 1935-2018

Long term survivor with prostate cancer. Active member of Board of Directors of MPCSG for many years. Died unexpectedly from causes unrelated to his cancer. He will be missed.

RIP

Prostate Cancer Presentations

The Manitoba Prostate Cancer Support Group uses a number of methods to provide the general public with information on prostate cancer. One such method is making “power point presentations” to any organization, company or group interested in learning about the disease.

The support group started this practice shortly after the support group’s incorporation in 1992. The presentations began by the support group founder, Norm Oman. Tom Boomer recalls attending a presentation by Norm Oman in the fall of 2008 at the Masons Temple on Kimberly Ave. in Winnipeg. The presentations were carried on by Tom Boomer and Len Bueckert when both were on the board of the support group. They did many presentations to Manitoba Hydro employees in the Winnipeg, Dorsey Substation and at Lac du Bonnet as well to other groups in the Winnipeg, Selkirk, Headingly, and at various rural communities as far west as Swan Lake and Neepawa, Manitoba.

To date the power point presentation, that Tom and Len adapted using Norm Oman’s original presentation, is used with minor changes that reflect the statics and conditions of today. The presentations, which take approximately 45-60 minutes, include the following:

- ◆ Power Point Presentation
- ◆ Discussion
- ◆ Question & answer
- ◆ Handouts

Examples of presentations made in 2017 & 2018 include the following with attendance in brackets:

- February 1- Community Health Group on Grant (35)
- October 5-Air Canada Retirees (90)
- November 11- Afro-Caribbean Association (35)
- January 3- CN Pensioner’s Association of Manitoba (67)
- January 25-Transcona Sizzling Seniors Lunch and Learn (17)

Part of the support group mission is to spread awareness of prostate cancer and encourage males 40 years and older to be checked for prostate cancer. The presentations are very effective in meeting this part of the support group’s mission. Most presentation attendees are introduced to prostate cancer for the first time and providing this information and raising awareness could make a difference in whether they or their significant other gets checked early. Early detection saves lives.

The support group board requests your assistance in making the community at large aware that the support group will, at no cost, make a presentation on prostate cancer to any group that so requests. When you have a contact who would like a presentation refer them (or do it on their behalf) to Patrick Feschuk at lizpat@shaw.ca or at 204-654-3898, or contact one of the other members of the support group board.

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Potential Lines of Attack Against Prostate Cancer

Researchers from The University of East Anglia (UEA) have contributed to the world's largest study into genes that drive prostate cancer – identifying 80 molecular weaknesses that could be targeted by drugs to treat the disease.

The Cancer Genetics Team at Norwich Medical School, UEA, led by Prof Colin Cooper and Dr. Dan Brewer, have played an active role in this research, performing mathematical analyses, providing scientific insight and helping to lead the study.

Around a quarter of the gene mutations identified involve the targets of existing drugs that are either licensed or in clinical trials – suggesting that these could offer promise for further study as new approaches to treatment.

And the landmark research also opened

up 60 new potential lines of attack against prostate cancer for future investigation, as well as identifying many new genes associated with the development of the disease.

Around 34 institutions from across the UK and internationally, analysed tumour genetics of nearly a thousand patients with prostate cancer, alongside a wealth of drug data.

The study is published in the journal Nature Genetics, and was largely funded by Cancer Research UK.

The researchers obtained genetic information from the tumours of 112 men with prostate cancer and pooled it with data from other studies, together analysing samples from 930 prostate cancer patients.

They combined detailed genetic analysis with the latest Big Data approaches to identify large numbers of genetic changes that underlie the development and spread of prostate cancer. They then took this genetic information and drew up a map of the network of associated proteins.

Using canSAR, a comprehensive database for cancer drug discovery, they found that 80 of the proteins in the network were possible drug targets.

Some 11 of these were targeted by existing licensed drugs and seven by drugs in clinical trials, while 62 were identified as potential targets to explore.

While further research is needed

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before the potential new targets could be explored in clinical trials, the new study has opened up many potential ways of targeting the disease.

For example, the research raised the possibility that BRAF and ATM proteins could be targeted in prostate cancer – and research is already under way in these areas.

The team also established a timeline of genetic changes in prostate cancer, which could in future improve ways to spot the disease – as current methods of diagnosis, such as PSA testing, are unreliable.

The timeline could also help predict the way prostate cancer evolves in individual patients, which might allow treatment to be adapted to combat drug resistance.

Joint project lead, Professor Colin Cooper, Chair of Cancer Genetics at Norwich Medical School, UEA, said:

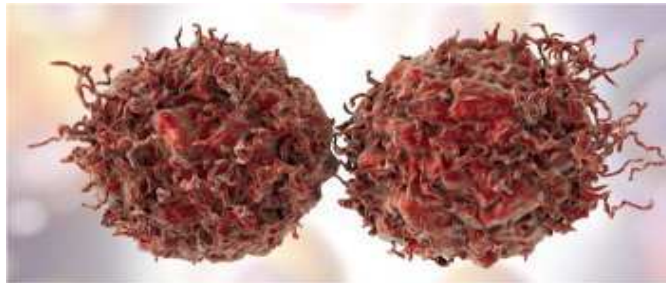
"The treatment of prostate cancer represents a significant global health problem, so it was great that experts from UEA were able to play a leading role in this pioneering research.

"The study provides an important step towards personalising treatment for men with prostate cancer. We have

identified many pathways by which this cancer develops, for which new drugs can be used to disrupt those pathways and potentially improve treatment."

Study leader Professor Ros Eeles, Professor of Oncogenetics at The Institute of Cancer Research, London, said:

"Our study applied cutting-edge techniques in Big Data analysis to unlock a wealth of new information about prostate cancer and possible ways to combat the disease.



"One of the challenges we face in cancer research is the complexity of the disease and the sheer number of ways we could potentially treat it – but our study will help focus our efforts on the areas that offer most promise for patient benefit."

Study co-author Professor Paul Workman, Chief Executive of The Institute of Cancer Research, London, said:

"This study has uncovered a remarkably large number of new genes that drive the development of prostate cancer, and given us vital information about how to exploit the biology of the disease to find potential new treatments.

"We hope our findings will stimulate a wave of new research into the genetic changes and potential drug targets we have identified, with the aim that patients should benefit as soon as possible."

Dr. Justine Alford from Cancer Research UK, said:

"A major hurdle to making further progress against prostate cancer is the lack of ways to accurately predict how a person's disease will progress, making it challenging to know which treatment is best for each patient. By greatly enhancing our understanding of the genetics behind the disease, this research edges us closer towards that goal. If confirmed by further research, in the future this knowledge could help doctors better tailor treatments to an individual's cancer, and hopefully see more people survive their disease."

April 17, 2018, University of East Anglia
<https://medicalxpress.com/news/2018-04-potential-lines-prostate-cancer.html>

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BOARD VOLUNTEERS WANTED

As a result of undertaking several new initiatives / activities we require volunteer Board members to assist in general volunteering, advertising, fund raising, public meetings, special events, planning and all other activities that provide awareness and support to our members and the general public. The only qualification is a willingness to help. Please contact any Board member listed on the last page for further details and to volunteer.

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FUTURE MEETINGS 2018

20 June

Speaker: Dr. Jason Ediger, Ph.D. C. Psych.
 Title: "What about when bad things really do happen?" *Coping with the worry and uncertainty of prostate cancer*

18 July

Speaker: Dr. David Dawe
 Title: "Advances in treating hormone resistant prostate cancer"

 All meetings (except September) will be held at :
 The First Unitarian Universalist Church of Winnipeg,
 603 Wellington Crescent

All meetings are 7 – 9 pm.
 (First hour for general discussion;
 second hour for expert guest speaker)

Everyone Welcome Plenty of free parking

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- Irek Iskat — membership
- Patrick Treacy — speakers

For general information please contact Jos Borsa at number listed above

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Bottom Line Computer Services
 publication

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