PCCN Markham

Prostate Cancer Canada Network

Newsletter

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NEXT MEETING

Tuesday, December 11 2018 - 7:30PM

St. Andrews Presbyterian Church – Main St Markham

Rose Room - DOWNSTAIRS

(Free Parking off George St)

Group 'Round Table' Discussion
Survivors ask questions, share concerns
moderated by your peers
Why not bring a few seasonal treats to share

IN THIS ISSUE ...

The November Cooking Class was a great hit! Thanks to everyone who attended!

A couple of quotes.....

"I Thought I was a good cook but I learned a lot"

"Wow, Dijon mustard is an emulsifier helping sauces thicken up"

We will consider this or similar activity again

MERRY CHRISTMAS & HAPPY HOLIDAYS!!!!

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Prostate cancer: Scientists reveal new way to target stubborn cells

Published Thursday 25 October 2018 by Monica Beyer Fact checked by Jasmin Collier

A new compound that targets hard-to-treat prostate cancer cells may pave the way for a new, more successful treatment in the future, a new study reports.

Researchers find a new compound that is more able to target stubborn prostate cancer cells.

The study, which is now published in *Nature Communications*, notes that this particular compound targets areas that lead to the multiplication of prostate cancer cells.

The researchers, at the New York University (NYU) School of Medicine in New York City, created a compound called cyclic peptoids.

Cyclic peptoids specifically seek targets that current prostate cancer treatments cannot.

The scientists were able to develop a compound that reduced prostate cancer cell growth (in cultures) by 95 percent, when compared with untreated cells.

How the treatment differs from current drugs

Current prostate cancer treatments target hormonal signals that encourage the growth of prostate cancer.

People who take these type of medications, known as anti-androgen drugs, often experience a recurrence of cancer growth within months.

This has led to more research in hopes of developing new treatments that can work with these "undruggable" targets.

That's where Dr. Susan Logan, an associate professor in the Department of Urology from the NYU School of Medicine, and study co-author Prof. Kent Kirshenbaum, also from the NYU School of Medicine, come in.

"Rather than continue making compounds that are just like older drugs, the focus of our work has been to rethink the definition of what a drug-like molecule can be," notes Dr. Logan.

Their report highlights how their compound blocked cancer growth by hampering the interaction between proteins that turn on the genes that make cells multiply.

This gene activity helps the prostate grow during a person's early development, but it does not continue to trigger cell production later in adulthood — that is, unless there are changes that reactive them, which can lead to prostate cancer.

https://www.medicalnewstoday.com/articles/323442.php

Surgery & combination therapy optimizes results in aggressive prostate cancer management

On **Nov 19, 2018** Boston, MA —

Men presenting with aggressive prostate cancer – Gleason Score of 9 or 10 – comprise most of those who will die from prostate cancer worldwide, and despite surgical removal of the prostate (radical prostatectomy), their cancer will recur more than 80 percent of the time.

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In a new multinational study of 639 men with a Gleason Score of 9 or 10, researchers at Brigham and Women's Hospital investigated how treatment with surgery plus the appropriate use of post-operative, low-dose radiation and hormone therapy, before cancer recurrence, fared as an option for these men. They found that death from prostate cancer within five years following this option or the standard option of high dose radiation and hormone therapy was less than 10 percent likely as compared to 22 percent with surgery alone. Results published today in *JAMA Oncology* suggest post-operative radiation and hormone therapy, before cancer recurrence, as a new prostate cancer treatment option for men with a Gleason Score of 9 or 10.

"In many cases when cancer recurs, radiation and hormone therapy are recommended, but our findings indicate that the best survival outcomes can be achieved by implementing these therapies directly after surgery and not waiting for the cancer to recur," said Anthony Victor D'Amico, MD, PhD, chief, Genitourinary Radiation Oncology at the Brigham. "While more than 75 percent of men in this study had risk factors for recurrence following surgery for which radiation and hormone therapy could have been recommended, only one-third received those treatments."

A prior study showed that the risk of death is much higher when surgery alone is performed, compared to the risk following the standard treatment option of high dose radiation and hormone therapy. D'Amico points out that the lack of use of radiation and hormone therapy following surgery for men with Gleason Score 9 or 10 prostate cancer is largely due to concern about overtreatment. "However, overtreatment in this population with aggressive and advanced prostate cancer is very unlikely given that prostate cancer will recur in at least 80 percent of these men within five years of surgery and require radiation or hormone therapy at that time," D'Amico said.

Researchers note additional study is needed to determine whether treating these men with post-operative low-dose radiation and hormone therapy before cancer recurrence can produce the low prostate cancer death observed in the study. Given that no randomized trials are available to answer this question specifically for men with Gleason Score 9 or 10 prostate cancer, this is the only evidence to date supporting this new treatment option.

The authors declare no conflicts of interest or relevant funding sources.

https://scienmag.com/surgery-combination-therapy-optimizes-results-in-aggressive-prostate-cancer-management-2/

Low-Risk Prostate Cancer: Don't rush to get treatment

If you are diagnosed with low-risk prostate cancer, you should discuss treatments and quality-of-life issues with your cancer care team.

Prostate cancer is often treated by urologists and/or radiation oncologists.

Common treatments are surgery and radiation. However, there is another approach to learn about. It's called "active surveillance." It's for men with low-risk prostate cancer.

In active surveillance, your team watches your condition closely. If tests show that it's getting worse, you will get treatment. Discuss active surveillance with your team. Here's why:

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Treatment isn't always needed.

Many men with low-risk prostate cancer are treated immediately, with surgery or radiation. Treatment is not necessary for many patients and it can cause sexual, urinary, and bowel problems.

Often, prostate cancer is low-risk.

Many prostate cancers are found with a prostate-specific antigen (PSA) blood test. Often these cancers are low-risk. This means:

- The tumour is small.
- It is contained within the prostate.
- The PSA blood test is not very high (less than 10).

For most men with low-risk prostate cancer, the tumour is probably growing so slowly that it will not become life-threatening. Usually a man with low-risk prostate cancer passes away of something else, even if he doesn't get treatment for prostate cancer.

Active surveillance may help your quality of life.

With this approach, you have regular checkups, including a PSA test and rectal exam. You'll get a prostate biopsy if needed. You can start treatment at any time if the cancer starts to grow.

Active surveillance is a good choice for many men with low-risk prostate cancer, because they can avoid the side effects of treatment. This is an especially important choice if you are older or in poor health.

Treatment can have side effects.

Side effects from surgery or radiation may include:

- Impotence—not getting erections that are firm enough for intercourse.
- Leaking urine. There may be complete loss of bladder control, but this is less common.
- Frequent, urgent, bloody, or painful bowel movements.

When should you get immediate treatment for prostate cancer?

If your cancer is advanced or higher-risk, you will probably need treatment right away. Signs of higher-risk cancer include:

- PSA value that is quite high or rapidly rising.
- Test results show that the tumour is outside the prostate gland. Or the tumour is growing rapidly and is likely to spread outside the gland.
- Gleason score is high-risk.

Ask your team if your cancer shows any of these signs. If so, active surveillance may not be a good choice.

Talk to your cancer (oncology) care team.

Your team is an important source of advice. Some men may benefit from having a low-risk tumour treated right away, even if they might have side effects. Discuss your treatment options and quality-of-life issues with your team.

Choosing a treatment for prostate cancer:

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Most men with low-risk prostate cancer have time to think about their choices. These tips may help you reach a decision.

Review your health history. Give your cancer care team your full personal and family medical histories. Ask how your age and general health could affect treatment. Ask if you have any condition that might increase the risks of treatment, for example, conditions such as diabetes, heart problems, or bowel disease might increase your risk of sexual, urinary, or bowel problems.

Think about your values. Discuss these questions with your spouse or partner:

- Do I want to get rid of my cancer, even if I might have sexual or urinary problems?
- Which side effects would upset me most?
- Would I be okay with active surveillance, even if I am worried and have to see a health care provider more often?

Find out all of your treatment options. Ask your health care providers about each choice, including benefits and side effects. Some health care provider only suggest the option they know best. Typically:

- A radiation oncologist can discuss active surveillance and radiation treatment.
- A urologist can discuss active surveillance and surgery.

Talk about your choices with these physicians and your family health care provider.

https://choosingwiselycanada.org/low-risk-prostate-cancer/

New dual action cancer killing virus

19 Nov 2018

Scientists have equipped a virus that kills carcinoma cells with a protein so it can also target and kill adjacent cells that are tricked into shielding the cancer from the immune system.

It is the first time that cancer-associated fibroblasts within solid tumours - healthy cells that are tricked into protecting the cancer from the immune system and supplying it with growth factors and nutrients - have been specifically targeted in this way.

The researchers, who were primarily funded by the Medical Research Council (MRC) and Cancer Research UK, say that if further safety testing is successful, the dual-action virus - which they have tested in human cancer samples and in mice - could be tested in humans with carcinomas as early as next year.

Currently, any therapy that kills the 'tricked' fibroblast cells may also kill fibroblasts throughout the body - for example in the bone marrow and skin - causing toxicity.

In this study, published in the journal *Cancer Research*, the researchers used a virus called enadenotucirev, which is already in clinical trials for treating carcinomas.

It has been bred to infect only cancer cells, leaving healthy cells alone.

They added genetic instructions into the virus that caused infected cancer cells to produce a protein called a bispecific T-cell engager.

The protein was designed to bind to two types of cells and stick them together.

In this case, one end was targeted to bind to fibroblasts.

The other end specifically stuck to T cells - a type of immune cell that is responsible for killing defective cells. This triggered the T cells to kill the attached fibroblasts.

Dr Joshua Freedman, from the Department of Oncology at the University of Oxford, who was first author on the study said: "We hijacked the virus's machinery so the T-cell engager would be made only in infected cancer cells and nowhere else in the body. The T-cell engager molecule is so powerful that it can activate immune cells inside the tumour, which are being suppressed by the cancer, to attack the fibroblasts."

Dr Kerry Fisher, from the Department of Oncology at the University of Oxford, who led the research said: "Even when most of the cancer cells in a carcinoma are killed, fibroblasts can protect the residual cancer cells and help them to recover and flourish. Until now, there has not been any way to kill both cancer cells and the fibroblasts protecting them at the same time, without harming the rest of the body.

"Our new technique to simultaneously target the fibroblasts while killing cancer cells with the virus could be an important step towards reducing immune system suppression within carcinomas and should kick-start the normal immune process.

"These viruses are already undergoing trials in people, so we hope our modified virus will be moving towards clinical trials as early as next year to find out if it is safe and effective in people with cancer."

The scientists successfully tested the therapy on fresh human cancer samples collected from consenting patients, including solid prostate cancer tumours which reflect the complex make-up of real tumours.

They also tested the virus on samples of healthy human bone marrow and found it did not cause toxicity or inappropriate T cell activation.

Dr Nathan Richardson, head of molecular and cellular medicine at the MRC said: "Immunotherapy is emerging as an exciting new approach to treating cancers. This innovative viral delivery system, which targets both the cancer and surrounding protective tissue, could improve outcomes for patients whose cancers are resistant to current treatments. Further clinical studies will be crucial to determine that the stimulation of the patient's immune system does not produce unintended consequences".

Dr Michelle Lockley, Cancer Research UK's expert on immunotherapy, said: "Using the power of the body's own immune system to tackle cancer is a growing area of research. This work in human tumour samples is encouraging, but can be complicated - one of the biggest challenges of immunotherapies is predicting how well they will work with the patient's immune system, and understanding what the side effects could be. The next stage will be using clinical trials to test whether this is both a safe and effective way to treat the disease in people."

The virus targets carcinomas, which are the most common type of cancer and start in cells in the skin or in tissues that line or cover internal organs, such as the pancreas, colon, lungs, breasts, ovaries and prostate.

Source: Medical Research Council

https://ecancer.org/news/15135-new-dual-action-cancer-killing-virus.php

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Salvage Prostatectomy May Benefit Some Prostate Cancer Patients

Jody A. Charnow, Editor November 13, 2018

Study of men who underwent salvage radical prostatectomy for radiorecurrent prostate cancer found a 10-year rate of biochemical progression-free survival of 33%.

Salvage radical prostatectomy (SRP) may benefit carefully selected patients with recurrent prostate cancer (PCa) following radiotherapy, researchers concluded.

The findings from their multi-institutional prospective study of 41 men who underwent open SRP for radiorecurrent PCa compare favorably with previous research suggesting that patients who respond best to SRP are those with lower PSA values and lower-grade disease prior to radiation treatment, and a prolonged post-radiotherapy PSA nadir, James L. Mohler, MD, of Roswell Park Comprehensive Cancer Center in Buffalo, New York, and colleagues reported in *Prostate Cancer and Prostatic Diseases*.

The 41 men were enrolled from 1997 to 2006 as part of the Cancer and Leukemia Group B (CALGB) 9687 trial. The group, which had a median age of 64 years at SRP, included 24 men who underwent external beam radiation therapy, 11 who had brachytherapy, and 6 who received both. The median time from radiation therapy to SRP was 64 months. With respect to pathologic staging, 44%, 54% and 3% had pT2, pT3, and pT4 disease, respectively. Of the 41 men, 17% and 12% had positive surgical margins and positive pelvic lymph nodes, respectively.

In other findings, 17 (45%) of 38 evaluable patients had urinary incontinence (defined as use of 3 or more pads per day) prior to SRP, with 88% reporting urinary incontinence at 6 months, 85% at 12 months, and 63% at 24 months following SRP. At a median follow-up of 91 months, the 2-, 5-, and 10-year rates of biochemical progression-free survival were 51%, 39%, and 33% respectively, according to Dr Mohler's team. The overall survival rates at those time points were 100%, 89%, and 52%, respectively.

The men had a median pre-radiation therapy PSA level of 5.5 ng/mL and most had a pre-treatment Gleason score of 7 or less. The median duration of post-radiotherapy PSA nadir was 30 months and the median time between radiation and SRP was more than 5 years.

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Dr Mohler and his colleagues noted that 25% to 35% of men with clinically localized PCa receive radiation therapy as definitive treatment, and the cancer recurs despite improvements in patient selection, delivery techniques, and use of concomitant systemic therapy. They pointed out that radiation therapy for PCa has changed since the study started enrolling patients. Most of the cohort did not have intensity-modulated radiation therapy or high-dose radiation therapy, which today are considered standard of care. In addition, 75% of patients with known pre-radiation clinical staging had palpable disease. "As a result, the enrolled patients do not represent a current population of radiation patients and therefore the enrolled patients should be expected to have worse outcomes after both radiation and SRP," they wrote.

The study had other limitations, as well. Their cohort was younger than the average age of failure after initiation treatment of PCa, and it was too small for post-hoc multivariable analysis to determine who was at greater risk of treatment failure.

Despite the limitations, the authors wrote, strengths of the study include its prospective and multi-institutional design with long-term oncologic outcomes. Most recent published series, they pointed out, have been retrospective, single-institution studies with shorter follow-up.

Reference

Mohler JL, Halabi S, Ryan ST, et al. Management of recurrent prostate cancer after radiotherapy: long-term results from CALGB 9687 (Alliance), a prospective, multi-institutional salvage prostatectomy series. *Prostate Cancer Prostatic Dis*. 2018; published online ahead of print.

NOTABLE

Management of Metastatic Prostate Cancer in Frail/Elderly Patients

Elizabeth R. Kessler, MD Nov 15, 2018

Prostate Cancer, Oncology Journal

Elizabeth R. Kessler, MD

TABLE 1 **Adverse Effects of Androgen Deprivation Therapy**

Domain	Metabolic/Body Composition	Sexual Health	Mood and Central Nervous System
Symptoms	• Loss of lean body mass • Increase in fat mass • Loss of bone mineral density • Altered lipid profile • Reduced insulin sensitivity	• Erectile dysfunction • Change of hair pattern • Gonadal atrophy • Loss of libido	• Hot flashes • Altered sleep patterns • Fatigue • Change in concentration

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Table 1. Adverse Effects of Androgen Deprivation Therapy

TABLE 2 **Comparison of Populations Treated With Abiraterone and Docetaxel in the Hormone-Sensitive Setting**

Study	Study Population	Drug	HR for Death	Median Age (range)	ECOG Performance Status	Grade 3–5 Toxicities (Rx vs ADT)
LATITUDE (N = 1,199)	100% metastatic	Abiraterone	0.62	68 (33–92)	0–2	63% vs 48%
STAMPEDE (N = 1,917)	• 28% node-negative • 20% node-positive • 52% metastatic	Abiraterone	0.63	67 (39–85)	0–2	47% vs 33%
CHAARTED (N = 790)	100% metastatic	Docetaxel	0.61	64 (36–91)	0–2	30% vs NR
STAMPEDE (N = 2,962)	• 24% node-negative • 15% node-positive • 61% metastatic	Docetaxel	0.76	65 (40–84)	0–1	52% vs 32%

ADT = androgen deprivation therapy; ECOG = Eastern Cooperative Oncology Group; HR = hazard ratio; NR = not reported; Rx = treatment.

Table 2. Comparison of Populations Treated With Abiraterone and Docetaxel in the Hormone-Sensitive Setting

Abstract / Synopsis:

As the world population ages, we can expect to care for an increasing number of older cancer patients. Prostate cancer is inherently a condition that affects patients of advanced age. In caring for these patients who have advanced prostate cancer, it is important to first assess the health status of the patient and his goals of care. As this is established, likely through a geriatric assessment, this will inform how to modify or mold the treatment plan to fit a patient's needs and vulnerabilities. These vulnerabilities may surface as patients undergo treatment such as androgen deprivation therapy—the backbone of systemic therapy for advanced disease. Androgen deprivation therapy leads to long-term adverse effects; therefore, providers should carefully consider its use and proactively manage toxicity. It is important to assess patients before starting treatment and to adjust the choice of therapy, or supportive services, in order to maximize benefit and minimize potential harms.

Introduction

Prostate cancer is predominantly a disease of the elderly, with peak incidence occurring at just over 70 years old.[1] Given the breadth of prostate cancer and its therapies, this article focuses on advanced hormone-sensitive disease only. This population is increasing as longevity rates rise and more patients present with advanced disease.[2] Most patients with prostate cancer are over the age of 65 years, and are thus considered part of the cancer population of older adults for which there are specific guidelines on care.

Geriatric Assessment

As in any older patient with cancer, one must first define the patient's general health and fitness with a geriatric assessment. Screening tools, such as the G8, are readily accessible, validated, and referenced in the National Comprehensive Cancer Network Older Adult Oncology guidelines.[3] Screening allows for

consideration of how the overall health status of a patient may influence treatment tolerance. Any major findings may lead to a more complete geriatric assessment, which can be performed in conjunction with a geriatric health provider. This approach allows for the identification of patients in whom treatment could cause significant toxicity, or patients who may tolerate therapy if given with additional supportive interventions. By defining a patient's geriatric health and fitness, the oncology team can adjust the care plan or work with supportive care providers to intervene for areas of vulnerability, such as medication adjustment or mobility therapy.

As part of these initial steps, it is also vital to assess the patient's goals of therapy and overall priorities. If the patient is not able to participate in these discussions due to cognitive dysfunction, then physicians must speak with the medical decision maker in order to best align care with the patient's values. The diagnosis of prostate cancer might not be more impactful for some patients than that of a chronic condition. Patients with advanced prostate cancer may still have an estimated life expectancy of 4 to 6 years, and as such, understanding how this diagnosis fits into his overall health picture is paramount. For example, an 83-year-old man in excellent health may have an average life expectancy of 8 to 9 years, while a 73-year-old man in poor overall health may have the same life expectancy. Thus, the initial approach to the care of an older patient with metastatic hormone-sensitive prostate cancer should include an estimate of the patient's age-matched life expectancy with an adjustment for health status, and how this compares with prognosis due to cancer.

With this preliminary evaluation pooling together the physiologic age of the patient and his ability to participate in care planning, as well as the general goals of such planning, disease biology should also be considered. The sites of metastatic disease, the presence or absence of symptoms, and the rate of disease progression inform the remainder of the care-planning discussion. Overall, patients may be assessed as fit, frail (problems that may be reversible), disabled (nonreversible problems that may be adapted), or so ill that only supportive care should be considered.

Hormone Therapy in Older Patients

The backbone of prostate cancer treatment is hormonal therapy, which aims to limit the activation of the androgen receptor (AR) with testosterone. This limitation of AR activation may occur through agents that decrease circulating testosterone, such as gonadotropin-releasing hormone (GnRH) agonists or antagonists. The use of these agents also decreases testosterone precursors and other off-target effects of testosterone. Agents such as nonsteroidal anti-androgens block AR activation and yet preserve circulating testosterone levels.

Providers must carefully consider the toxicities of androgen deprivation therapy (ADT) in a physiologically older population. These patients have less reserve to absorb additional imbalances or conditions that will impact their current steady state. In general, agents that result in a hypogonadal state can lead to toxicities within the following domains: metabolic and body composition; sexual health; and mood and central nervous system (CNS) symptoms (**Table 1**).

Metabolic and Body Composition

Patients may experience changes in metabolic parameters and body composition, such as bone mineral density loss and sarcopenic obesity.[4,5] These changes occur naturally through the aging process and are accelerated with the use of ADT. The risk of osteoporosis development is important to keep in mind because geriatric syndromes (such as fall risk, delirium, and incontinence) can predispose patients to osteoporotic fractures. Men who suffer an osteoporotic fracture have a higher mortality risk compared with women.[6,7] As such, preventing bone mineral density loss may in turn prevent a fracture and the associated morbidity and mortality risk of such an event. In order to modify this risk, all patients on ADT should take a daily vitamin D and calcium supplement and engage in weight-bearing exercise.

Older patients with prostate cancer who have been initiated on ADT should also undergo baseline bone mineral density testing and should strongly consider bone-modifying agents, as appropriate, to avoid the development of osteoporosis. Providers may also use the Fracture Risk Assessment Tool (FRAX) score, which estimates the 10-year risk of any fracture and specifically hip fractures based on multiple variables.[8] Men should be offered an additional bone-modifying treatment (ie, bisphosphonate therapy) if their FRAX scores include a 10-year risk of hip fracture ≥ 3% or a 10-year estimated risk of major osteoporotic fracture ≥ 20%. There are no data to support the use of bone-modifying agents in the treatment of prostate cancer; in the hormone-sensitive setting, these are primarily used as agents to prevent osteoporosis.

Soft-tissue body composition may also change as patients gain fat mass and lose muscle mass—known as sarcopenic obesity—on ADT. In community-dwelling older patients, sarcopenic obesity has been linked to increased risk of morbidity and mortality.[9] The loss of lean body mass impacts balance and mobility, such that these patients may be at increased risk of falls or trouble completing their activities of daily living. It has been noted that these body composition and balance changes can occur as early as 3 months after therapy begins.[10] In order to maintain functional independence, providers should strongly consider referral for prehabilitation or have a low threshold for referral to a cancer rehabilitation program. Patients highly value preservation of functional independence,[11] so proactively enlisting additional supportive care services is suggested in order to avoid declines while on therapy.

Additionally, patients may experience metabolic consequences, such as decreased insulin sensitivity, elevated cholesterol levels, and hypertension, which contribute to an increased risk of metabolic syndrome and cardiovascular disease in this population. There are no consistent data linking ADT as a causal agent to cardiovascular disease and mortality. However, there are clear relationships between the metabolic changes that occur on ADT and their contribution to cardiovascular disease development.[12] Further analysis is likely needed to better understand different inflammatory responses to ADT. Prospective investigations have not shown a difference in cardiovascular event rates with GnRH agonists vs antagonists. However, a pooled retrospective analysis has shown a difference in the incidence of cardiovascular events between GnRH agonists and antagonists.[13] This warrants further investigation and could be considered in patients with a high risk of cardiovascular events who would benefit from systemic therapy.

Mood and CNS Effects

Other adverse reactions involve changes in mood, cognition, sleep patterns, and vasomotor skills.[14,15] The relationship between use of ADT and cognition requires clarification, but patients do report changes in emotion regulation and focus. These changes are significant in a population already at risk for cognitive decline, and they considerably impact a patient's ability to function independently. Patients may also experience labile mood and depressive symptoms that could alter quality of life.[16] In addition, use of ADT can contribute to sleep disturbances, in a population already affected by urgency and nocturia in conjunction with the aging-related changes to sleep patterns. This may worsen mood, focus, and function. There are supportive medications that can be used, but should be looked at with caution in an older population sensitive to medication changes. Avoidance of polypharmacy and consideration of altered metabolism of pharmacologic agents are basic tenants of geriatric medicine.

Alterations in the ADT Prescription

Large studies have supported the use of continuous ADT, as opposed to intermittent dosing, in the treatment of metastatic prostate cancer. However, follow-up meta-analyses have opened the door for use of intermittent ADT therapy,[17] which may improve quality of life and decrease the risk of resultant long-term toxicities for individual patients. Improved knowledge of these toxicities has caused providers to rightly consider the potential benefit and harms prior to prescribing ADT. ADT is a highly effective therapy and should not be ignored for patients who may benefit. In patients with limited life expectancy, in which quality of life is prioritized above longevity, consider the use of intermittent ADT. In addition, patients too frail to tolerate standard

testosterone-lowering treatment may undergo treatment with nonsteroidal anti-androgen monotherapy. This treatment is inferior to continuous ADT in terms of survival outcomes,[18] yet is active enough to potentially offer some short-term disease control or palliation of symptoms. In some patients, the risk of loss of muscle mass or potential cognitive changes on ADT may outweigh the potential benefit of therapy, and single-agent anti-androgen therapy might be considered. Other options include monthly dosing of ADT in order to monitor toxicity and to allow a quicker potential recovery of testosterone if treatment must be interrupted due to side effects. These decisions to alter the standard course of ADT should be carried out in conjunction with the patients and their supportive network. Considering patient priorities when discussing the potential risks and benefits of these approaches is necessary, as with any important medical decision.

Addition of Other Therapies in the Hormone-Sensitive Setting Docetaxel

As in many other malignancies, we have learned that combination therapy at the outset of treatment improves long-term disease control and survival outcomes. Both docetaxel and abiraterone acetate in the hormone-sensitive setting have demonstrated a survival benefit when added to standard ADT (**Table 2**). Based on these data, most providers should offer, or at least consider, additional therapies to treat patients at this stage. Certainly in a frail patient population, one must continue to assess the overall fitness of a patient. Any patient already thought of as fit should be offered unaltered therapy. Those found to be vulnerable or frail could be considered based on the ability to reverse at-risk conditions.

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Two large studies have evaluated the use of docetaxel and found a survival benefit in those with high-volume metastatic disease.[19,20] These studies enrolled patients in their mid-60s, representing a slightly younger, more fit population than a "real-world" patient. Templeton et al have investigated the use of docetaxel in a real-world setting[21] and found increased toxicities in comparison with the registry trials[19,20]; additional data suggest an increased incidence of febrile neutropenia if docetaxel is used prior to the development of castrate levels of testosterone.[21,22] In many cases, patients on clinical trials do not reflect the patient population we see in the clinic, especially in the case of older adults. In order to help navigate this, a geriatric screen and the use of a chemotherapy toxicity calculator, such as that validated by Hurria et al,[23] can provide useful information in estimating the potential for toxicity due to chemotherapy. Many older men with prostate cancer tolerate chemotherapy, but it is important to maximize pretreatment planning.

Abiraterone acetate and prednisone

Recent data support the use of abiraterone acetate for the treatment of metastatic hormone-sensitive prostate cancer.[24,25] This agent inhibits the adrenal production of androgens, and as such, further decreases available testosterone for AR activation. The use of abiraterone acetate has significantly improved overall survival, with tolerable side effects.[24,25] Abiraterone has been approved by the US Food and Drug Administration for the treatment of metastatic castration-resistant disease, and evaluation of the geriatric cohorts in a registry trial revealed excellent efficacy and tolerability.[26] This post-hoc analysis of fit patients in the chemotherapy-naive setting looked at differences in efficacy and toxicity among patients older (346 patients) and younger (736 patients) than 75 years old. Among the patients over 75 years old treated with abiraterone acetate plus prednisone, the survival benefit was similar compared with the younger group. Of note, the study enrolled patients with an Eastern Cooperative Oncology Group (ECOG) performance status score of 0 or 1 (a fairly fit population). One must recall that the ECOG score is fairly insensitive in older adults, and thus may overestimate their functional status and fitness for therapy.[27] The geriatric screen may help identify areas of disability not uncovered with the ECOG score.

The patients enrolled in the LATITUDE and STAMPEDE-abiraterone trials were generally older (median age, 67 years; range, up to 85 years in STAMPEDE), with ECOG scores of 0–2 compared with the CHAARTED and STAMPEDE-chemotherapy cohorts. Of note, patients being treated with abiraterone must take a low-dose corticosteroid to avoid mineralocorticoid excess, which results from alteration of adrenal function. In addition, patients may not have the means to pay for this costly agent, since older patients usually have a fixed income. Overall, there is little need for dose interruptions or reductions of abiraterone, and it should be considered for a broad group of older patients with newly diagnosed metastatic hormone-sensitive prostate cancer.

Summary

In summary, the first steps in care planning for older patients with prostate cancer are the most crucial. A thorough assessment of a patient's cognitive function, goals of therapy, and geriatric health through a geriatric assessment will guide decision making. The use of supportive therapy early after the initiation of ADT may decrease loss of functional independence and cognition. The treatment of advanced prostate cancer

is likely to continue to change with ongoing exploration of additional agents; these should be offered to fit older men, and considered in those with some vulnerabilities.

Financial Disclosure: *Dr. Kessler received study sponsorship for an investigator-initiated trial from Astellas.*

http://www.cancernetwork.com/prostate-cancer-frail/page/0/1

QUOTABLE

"It's not what's under the Christmas tree that matters but who's around it." – Charlie Brown, *A Charlie Brown Christmas*

"One of the most glorious messes in the world is the mess created in the living room on Christmas Day. Don't clean it up too quickly." – Andy Rooney

COOKING CLASS PICTURES!

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PCCN Markham

Prostate Cancer Support Group

Meets the 2nd Tuesday
Every month
September – June
St. Andrew's Presbyterian Church
143 Main St Markham

The Markham PCCN Prostate Support Group is generously supported by Dr John DiCostanzo, Astellas Pharma. PCCN, St. Andrews Presbyterian Church, and the Canadian Cancer Society.

The group is open to all; survivors, wives, partners, relatives and those in our community who are interested in knowing about prostate health. Drop by St Andrews Presbyterian Church 143 Main Street Markham at 7:30PM, the 2nd Tuesday every month from September to June. The information and opinions expressed in this publication are not endorsements or recommendations for any medical treatment, product, service or course of action by PCCN Markham its officers, advisors or editors of this newsletter.

Treatment should not be done in the place of standard, accepted treatment without the knowledge of the treating physician.

The majority of information in this newsletter was taken from various web sites with minimum editing. We have recognized the web sites and authors where possible.

PCCN Markham does not recommend treatment, modalities, medications or physicians. All information is, however, freely shared.

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We look forward to your feedback and thoughts. Please email suggestions to markhampccn@gmail.com

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