

New Therapies in Advanced Prostate Cancer – By Dr. Roanne Segal

Approximately 26,500 new cases of Prostate Cancer are diagnosed annually in Canada with the majority of those presenting with early stage disease. With early screening, diagnostic measures and improved surgical and radiation techniques, the majority of these men are cured of their disease.

Unfortunately some men will have their cancer return and about 4,000 men die of the disease annually. Upon initial relapse the majority of the cancer cells are sensitive to and the disease is driven by the presence of the male hormone, testosterone. We call this stage of the cancer Hormone Sensitive Prostate Cancer (HSPC). What follows then is that control of disease or the cancer is through lowering of the male hormone levels or hormonal deprivation. We call this treatment, Androgen Deprivation Therapy or Androgen Suppression Therapy (ADT/AST). In this way, the cancer cells are starved of their fuel and they cease to grow. With this therapy, most men can enjoy a prolonged period of disease control; generally speaking 24-48 months. In some it may be significantly longer and can be up to 10 years.

Unfortunately, not all cancer cells remain sensitive to this treatment and with time they can mutate (change), or find other ways or sources of testosterone which lead to a resurgence or growth of the prostate cancer. This phase of the illness is called metastatic Castrate Resistant Prostate Cancer (mCRPC) and until recently carried a rather grave prognosis. In the last two years, significant advances have been made in this particular stage of the illness with the result that men are now not only living longer but with a very significant improvement in their quality of life. Many men do not realize that these new treatments can change their lives.

Based on the current standard of care, the first-line treatment for symptomatic mCRPC is chemotherapy with Taxotere[®] (docetaxel). As with any form of chemotherapy there are multiple side effects including nausea, low blood counts, nerve damage (neuropathy) and even the possibility of new or worsening diabetes. Only about 30% of men treated will respond and their disease will come back under control.

The duration of this control, despite all the side effects, is only about 3.5 months. Furthermore, many men, because of their other previous health conditions, are not even considered to be candidates for this therapy. In other words, most of the time, we had little else to offer other than symptomatic or palliative care.

Thankfully, this is changing.

New treatments for prostate cancer

Over the past two years there have been a number of new therapies for men with advanced mCRPC.

Provenge[®] (*Sipuleucel-T*), Provenge is a vaccine therapy, and was the first of the options discovered for men with mCRPC. This therapy takes the patient's own cells, and uses them to turn on his own prostate cancer. This results in a direct attack on that patient's prostate cancer. While this sounds perfect, the results of this approach show only a 4-month survival benefit. Furthermore this treatment only seems to work in a particular group of men with very favorable type of prostate cancer. It is well tolerated with few side effects; very costly and not available in Canada.

Jevtana[®] (*Cabazitaxel*) is the second of the therapies that was found to be effective in this group of patients. It is an intravenous chemotherapeutic agent, similar to Taxotere. Like the vaccine, there is a 4-month survival benefit. However, the side effects have proven to be a significant challenge, and many men cannot tolerate the treatment. In general, this therapy should only be considered in the younger, healthy gentleman and be administered in a center with knowledge and expertise in both the disease and this treatment.

Xtandi[®] (*MDV3100 or enzalutamide*) is the first of two new oral treatments. It is a very promising drug that binds the hormone-receptor on prostate cancer cells, ultimately 'turning off' the genes needed for the growth of cancer. Patient trials showed significantly higher survival rates, tumor shrinkage and favorable

toxicity profile in men who were taking the therapy. Currently, this medication is only available through special access programs to those patients who have progressed on docetaxel.

Finally Zytiga® (abiraterone) is the second of the new oral therapies. It works by blocking enzymes that drive testosterone production, starving the cancer of the signals needed for growth. This therapy has offered patients a 4-month survival benefit in clinical trials and is very well-tolerated. To date, Zytiga® has only been approved for use in patients who have received prior chemotherapy with docetaxel. Results of a recent clinical trial have shown promise in more general or earlier use, but this has not yet been approved.

Zytiga® “has given me life. I am able to participate with my family, my friends, with my grandchildren, with my children.” – Ron Grant

Ron Grant’s story

Ron Grant, who has metastatic prostate cancer, has taken a number of different therapies over the years, including surgery, ADT, chemotherapy and radiation. But these only provided him with temporary improvements. In 2010, he started treatment with Zytiga®, with excellent results. Aside from his PSA levels returning to normal, he has also resumed a very active lifestyle and is spending more time enjoying all the things in life that he used to.

“I have had a super summer. Maybe one of the best summers, in terms of being active and no pain, in 3 or 4 years,” says Ron Grant when describing his recent vacation to Eastern Canada. “My quality of life this summer has been better than it’s been in at least 2 or 3 years.” Ron goes on to explain how he now travels to watch his grandsons play hockey in different parts of the province and how he looks forward to spending quality time with family. Ron says that Zytiga® “has given me life. I am able to participate with

my family, my friends, with my grandchildren, with my children. A lot of the restrictions are lifted. I don't have to go travel for chemo every 3 weeks. You're not tied to a string."

"My family isn't as worried all the time any more. For a while, it was affecting my wife more than it was affecting me." – Ron Grant

New clinical trials are currently being conducted for both MDV3100 and abiraterone in prostate cancer patients who have never been on chemotherapy. If these treatments show benefit in these patients, regulatory bodies may eventually approve, and fund, their use in earlier stages of the disease.

Despite all the challenges, we are clearly on the verge of a very exciting time in the treatment of advanced prostate cancer, with many new and promising medications being pursued by pharmaceutical research companies. So it becomes critical that you take a proactive role in managing your health. Do the research, talk to friends and other patients, go online and then follow up with your healthcare provider to see which therapies are right for you.

The Author

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