Prostatepedia[1]

[1]expert insight + advice

Immunotherapy

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In this issue....

In this issue we get an update on immunotherapy for prostate cancer. As a reader, you may note that we frequently return to this topic and you may well wonder why? After all, my primary interest has always been on the pharmacology of cancer drugs. The answer is that I have long believed that the goal of treatment should be a long-term complete remission. It has long been evident that this would be difficult to achieve with cancer drugs alone.

By complete remission, we mean that no cancer is visible by any scanning modality and the PSA is undetectable. Note, this does not mean the patient is cancer-free, just that the cancer has been reduced to a microscopic scale and is no longer growing. Why not have "cure" as a goal? As it turns out, "cure" is hard to define in any way that is clinically useful. The best definition I have seen is that it is a complete remission that lasts until the patient dies of something else. In which case, the patient is not "cured" until he has died. Until then, he is in a durable complete remission. Thus, as long as we are dealing with a living patient, a durable complete remission is the best we can hope for.

In prostate cancer, major progress has been made in reducing the amount of cancer in men with metastatic disease, including the frequency of complete remissions. Similarly, the duration of disease control has continued to improve. However, we are far from being able to place a significant proportion of patients into a durable complete remission. In laboratory models of cancer treatment, various immunotherapeutic approaches improve the effectiveness of radiation therapy as well as many drugs. So, it is plausible that immunotherapy may be much more effective in combination than it is as a solo treatment.

Once a patient is in complete remission, the next issue is how to make that remission durable? In other words, how do we keep microscopic residual disease from growing. This area of research is called "cancer dormancy". In this field, ongoing immune attack on the cancer has proved one of the more consistent successful approaches to maintaining cancer dormancy.

In summary, our continued interest in immunotherapy is based upon the possibility that it might increase the odds of a remission as well as make remissions more durable.

Charles E. Myers, Jr., MD P1

Contents:

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Contributors:

Editorial + Billing Offices
274 Redwood Shores, #739
Redwood City, CA 94065
(800) 975 6238

Administrative Offices
PO Box 655, Earlysville, VA 22936

C. Drake MD, PhD
Immunotherapy Today

Dr. Charles G. Drake is the Director of Genitourinary Oncology, Co-Director of the Cancer Immunotherapy Program, and Associate Director for Clinical Research at the Herbert Irving Comprehensive Cancer Center, New York-Presbyterian/ Columbia University Medical Center.

He spoke with *Prostatepedia* about the current state of affairs for immunotherapy for prostate cancer and what he anticipates happening in 2021.

What is the state of immunotherapy for prostate cancer in 2020? Are there any new developments over the last year that you'd like to call attention to?

Dr. Charles G. Drake: There are several novel approaches to immunotherapy in early phase trials in the clinic right now. One that we're particularly excited about at Columbia involves a series of agents called "bi-specific antibodies." These drugs are aimed at addressing one of the main obstacles to immunotherapy for prostate cancer—that is, there are not a lot of immune cells in prostate cancer to start with.

Another way to say this is that prostate cancers are "cold" tumors, as opposed to other cancers that are chock-full of immune cells, like melanoma. These drugs have two arms, one arm grabs on to tumors, usually through a handle on the tumor called prostate-specific membrane antigen (PSMA). The other arm of the bi-specific is designed to drag immune cells called T cells into the tumor.

What is especially exciting about this is that not only do the immune-cell attracting arms grab the cells and drag them into the tumor, that grabbing activates the T cells so that they're ready to kill the tumor. These are early trials, mostly Phase I, and are aimed at patients with late stage disease, but if they're safe and have activity, we hope to move them into earlier stages of the disease over time. If patients are looking for trials of bi-specifics, they can look on www.clinicaltrials.gov for the companies who are developing them, namely Amgen, Regneron, Janssen, Harpoon, and others.

Are there any new and enrolling immunotherapy clinical trials that you've got your eye on?

Dr. Drake: There are at least six large Phase III trials of anti-death protein 1 (PD-1) drugs that have recently opened. None of these trials test immunotherapy by itself; they all combine anti-PD-1 with another therapy. For example, there are trials trying to make chemotherapy work better and/ or last longer; these compare chemotherapy Taxotere (docetaxel) to chemotherapy plus anti-PD-1. Both Keytruda (pembrolizumab) and Opdivo (nivolumab) are being tested that way. Similar trials combine immunotherapy with a switch in hormonal therapy from Zytiga (abiraterone) to Xtandi (enzalutamide). There's even a cutting-edge trail (I'm biased because I'm one of the principal investigators) that adds immunotherapy to combined hormonal therapy Lupron [leuprolide] + Xtandi [enzalutamide]) for newly diagnosed metastatic disease.

Moving immunotherapy early on in the treatment paradigm might be more effective because there are fewer cancer cells to deal with and less overall suppression. At Columbia, we've even got a "triple-whammy" trial that combines hormonal therapy, chemotherapy, *and* immunotherapy for men with newly diagnosed metastatic disease. That trial, PRIME-CUT, is a small, 20-patient, signal-seeking study, but we're hopeful that aggressively using three effective therapies all at once can lead to deep and durable responses in treated patients.

Are there any immunotherapy clinical trials about to report out that you've got your eyes on?

Dr. Drake: Those large Phase III trials will take a while to enroll and complete, so I'm not sure if anything will be coming out on the sooner side. There was an interesting report at American Society of Clinical Oncology Genitourinary Cancers Symposium (ASCO-GU) of an innovative combination approach; here, two drugs that were relatively ineffective on their own were combined to yield a 33% rate of objective responses in men with soft tissue disease. The two drugs used were Cabometyx (cabozantinib), a tyrosine kinase inhibitor that's approved for kidney cancer, and anti-programmed deathligand 1 (PD-L1) called Tecentriq (atezolizumab).

Both of those drugs failed in Phase III trials in prostate cancer—on their own. But together, they seem to have activity, which is an example of the principle of synergy, i.e., when one plus one equals more than two. A single-armed study of that combination is being expanded to enroll approximately 130 patients total, and the sponsor (Exelixis) has announced that if the results are promising, they would consider going to the FDA for approval based on a single-armed study. Since single-armed approvals are virtually unheard of in prostate cancer, that would be surprising, but it will be interesting to see what the data look like. That trial is for men who have progressed on next-gen hormonal therapies like Zytiga (abiraterone) or Xtandi (enzalutamide), but who have not had chemotherapy yet. Patients can look it up on www.clinicaltrials.gov if they're interested.

Looking ahead to 2021: are there any clinical trials that you'd like to see happen that are not yet underway?

Dr. Drake: We're involved in a study of another novel immunotherapy that works by blocking the A2A receptor, which is heavily expressed in the prostate cancer micro-environment and which turns off multiple kinds of immune cells. Blocking A2A by itself has shown some activity in terms of shrinking prostate cancers, but now we're enrolling into a trial that combines the A2A blocker (AZ4635) with other immune drugs like the PD-L1 blocker Imfinzi (durvalumab).

What we're excited about is a triple combination that combines two different A2A targets with anti-PD-L1, another triple-whammy. This is not far off; we hope to open the triple arm in the next couple of months.

Any final thoughts for patients reading this?

Dr. Drake: If patients are interested in immune therapy for prostate cancer, the best way to get that is on a clinical trial. They should ask their doctors about trials available to them and might also consider looking on www.clinicaltrials.gov. While some of the trials mentioned above are large, randomized Phase III studies available at many sites, some of the more cutting-edge trials are small, and only available at a few academic centers. If they're interested in those smaller trials, a second opinion at a referral center makes sense. It's important to keep in mind thought that some of those studies are a real commitment in terms of travel and time. Still, all of the drugs and regimens we now use routinely were developed through carefully conducted trials and if patients want the latest in treatment that's something worth considering. Pp1

Emmanuel Antonarakis, MD
Immunotherapy in 2020

Dr. Emmanuel Antonarakis is a Professor of Oncology and Urology at the Johns Hopkins University Sidney Kimmel Comprehensive Cancer Center.

Prostatepedia spoke with him recently about the current state of immunotherapy for prostate cancer.

What's the state of immunotherapy for prostate cancer in 2020? Have there been any new developments over the last year?

Dr. Emmanuel Antonarakis: The new developments for prostate cancer, with respect to immunotherapy, have to do with programmed cell death protein 1 (PD-1) or programmed death-ligand 1 (PD-L1) inhibitors. We already have Provenge (sipuleucel-T), but there haven't been that many major advances with that immunotherapy since 2010. The most well-studied PD-1 inhibitor is Keytruda (pembrolizumab), which is the PD-1 inhibitor from Merck. The current trials suggest that there's a 5-10% response rate of metastatic prostate cancer to Keytruda (pembrolizumab) in the overall patient population.

PD-1 inhibitors in prostate cancer have efficacy in a minority of patients, but they are probably not broadly successful on their own. There are a number of combination strategies being pursued.

In the case of Keytruda (pembrolizumab), there are three randomized Phase III trials testing some unique combinations. One study is looking at Xtandi (enzalutamide) with or without Keytruda (pembrolizumab) in men with metastatic prostate cancer.

There's a second randomized Phase III study of Taxotere (docetaxel) chemotherapy with or without Keytruda (pembrolizumab).

A third Phase III study is testing the combination of Keytruda (pembrolizumab) plus Lynparza (olaparib), a poly ADP ribose polymerase (PARP) inhibitor, versus either Xtandi (enzalutamide) or Zytiga (abiraterone) in patients who have previously received one or the other but not both of these hormone agents.

There's a reasonable chance that at least one of those Phase III studies will be successful. The one that I'm most excited about is called Keylynk-010, the one combining Keytruda (pembrolizumab) and Lynparza (olaparib). We suspect that patients that have DNA repair mutations, such as BRCA2, might be more susceptible to immunotherapy treatment. We also know that those patients respond favorably to PARP inhibitors like Lynparza (olaparib). The goal of this study is to see whether the combination of those two drugs could expand the PARP inhibitor indication beyond those patients that have a DNA repair mutation. That study is a molecularly-unselected trial, which means that patients do not have to have a DNA repair gene mutation to enroll. If they do, they're still eligible, but they are not required to have a mutation to participate.

At Johns Hopkins, we are doing some interesting and novel things to try to make PD-1 inhibitors work better. One of the most exciting things that we're doing, which is unique to Johns Hopkins, is using a paradoxical approach for the treatment of metastatic prostate cancer. We call this treatment bipolar androgen therapy, or "BAT" for short. BAT uses supraphysiological doses of testosterone, also called high-dose testosterone, as a treatment for castration-resistant prostate cancer. Previously, we published that one-third of castrate-resistant prostate

cancer patients who receive high-dose testosterone benefit from that treatment.

We've also shown that high-dose testosterone can stimulate anti-tumor immune responses. In particular, we have shown that BAT stimulates a pathway called STING (stimulator of interferon genes). We are now doing a study where we give patients with metastatic prostate cancer BAT followed by treatment with Opdivo (nivolumab), which is the PD-1 inhibitor from Bristol-Meyers Squibb. We are seeing quite unprecedented results that seem to be much greater than what we would expect with either agent used alone. The combination of high-dose testosterone plus Opdivo (nivolumab) is something that we are eagerly pursuing as we speak.

Do you have a clinical trial for testing this that patients could enter?

Dr. Antonarakis: We do. The trial is called "COMBAT" (COMBination of Bipolar Androgen Therapy with Nivolumab) and is currently ongoing. The patients all have to have castration-resistant prostate cancer. It's otherwise quite open-ended. We require a mandatory soft tissue biopsy at baseline since we want to learn more about the immunological mechanisms that explain how these drugs work. If a patient has only bone disease and they're not eligible for a biopsy, then they cannot participate unfortunately. Other than that, it's for a relatively broad population of metastatic castration-resistant prostate cancer patients.

The other unique thing we're doing at Johns Hopkins is to question whether we may have been targeting the wrong immune checkpoints in prostate cancer. PD-1 and cytotoxic T-lymphocyte-associated antigen 4 (CTLA-4) are two checkpoints that are expressed in many cancer types. In prostate cases however, both PD-1 and CTLA-4 are only expressed by the minority of advanced prostate cancers. On the other hand, there is another checkpoint that is called B7-H3 (CD276), which used to be called PD-L3. B7-H3 is highly expressed on both localized and advanced prostate cancers. Fortunately, there is an antibody that inhibits B7-H3, called enoblituzumab, and we have decided to test this in the first-ever prostate cancer trial. We are doing this at Johns Hopkins.

We decided to learn more about enoblituzumab's mechanism of action and immunologic effects by using it in men who have non-metastatic localized prostate cancer who are candidates for radical prostatectomy. It's a pre-prostatectomy neoadjuvant trial, where we give six doses of intravenous enoblituzumab on a weekly schedule prior to prostatectomy. The goal of that study is two-fold. First, we want to see if we can increase cure rates from the prostatectomy because many of these patients are indeed curable. Second, we want to use the radical prostatectomy tissue to examine immunological responses in the prostate gland and in the prostate tumor that is surgically removed at the time of prostatectomy, as well as anti-tumor immunity in the peripheral circulation.

This study, unfortunately, has recently closed to enrollment. We enrolled 32 patients, and we are eagerly awaiting the results. The preliminary data, which have been presented only in abstract form, appear promising. We believe that this neoadjuvant trial has given us enough hope to justify using enoblituzumab in advanced metastatic castration-resistant prostate cancer. We are designing several trials in that population now, but those trials are not yet open.

Do you have a projected date for when they might open?

Dr. Antonarakis: Perhaps 6 to 12 months from now.

There are some other exciting things that are going on in the field that are not necessarily happening here at Johns Hopkins. One is chimeric antigen receptor (CAR)-T cells, which are engineered T cells designed to target and kill any cell expressing prostate-specific membrane antigen (PSMA). There are several ongoing clinical trials to test these. The one that I have been involved with is the PSMA CAR-T cell from Poseida (https://poseida.com/).

The other type of molecule is called a bispecific T cell engager (BiTE). There are a number of companies, the most notable one being Amgen, developing a PSMA-specific BiTE. One end of the antibody binds to a cluster of differentiation 3 (CD3), a T cell receptor, and the other binds to PSMA. It brings CD3 + T cells in proximity to PSMA-expressing cancer cells. The T cells can then mount an anti-tumor response against PSMA-expressing prostate cancer cells. All these trials are new and opened in the past year. We also just came back from the American Society of Clinical Oncology Genitourinary Cancers Symposium (ASCO GU 2020). There, we presented a randomized Phase II study of Provenge (sipuleucel-T) alone versus a combination of Provenge (sipuleucel-T) plus Xofigo (radium-223). The first author was Dr. Catherine

Marshall. The study was a positive trial. It was a 32-patient study, and 16 patients were randomized to receive Provenge (sipuleucel-T) alone while the other 16 patients were randomized to receive Xofigo (radium-223) plus concurrent Provenge (sipuleucel-T). Five of the 16 patients in the combination group had a prostate-specific antigen (PSA) 50% or greater reduction. In the Provenge (sipuleucel-T) alone, there was a 0% PSA reduction. That was initially exciting.

What was even more exciting was that the radiographic progression-free survival (PFS) in the control group, Provenge (sipuleucel-T) alone, was only three months. In the combination group, the PFS was nine months. It looked like there was a tripling of PFS by adding the Xofigo (radium-223) to the Provenge (sipuleucel-T). (https://www.youtube.com/watch?v=mzOk5VO3r38)

Based on these promising results, we are now in discussions with both Bayer, who makes Xofigo (radium-223), and Dendreon, who makes Provenge (sipuleucel-T), to design a larger Phase II study, or even a Phase III study, to prove the efficacy of the combination and to potentially lead to expanding the label of both drugs. Both companies are interested in moving forward with that type of design. If the stars align, that study should be open about one year from now. Pp

Andrew J. Armstrong, MD ScM FACP
Immunotherapy Trial

Dr. Andrew J. Armstrong is Professor of Medicine and Surgery and Associate Professor in Pharmacology and Cancer Biology at the Duke Cancer Institute.

Prostatepedia spoke with him recently about his clinical trial looking at deathligand 1 (PD-L1) inhibitors for men with neuroendocrine prostate cancer.

What motivated you to start your clinical trial?

Dr. Andrew Armstrong: There are two main classifications of patients with metastatic prostate cancer. There are the patients who have typical adenocarcinomas of the prostate that commonly produce prostate-specific antigen (PSA) and are initially androgen receptor-dependent and responsive to hormonal therapies. Adenocarcinoma refers to cancers that arise from the glandular structures of the prostate, and this morphology or appearance is retained frequently in this most common subtype of prostate cancer. Most of our approved drugs have been studied and are effective for these patients, for example, Xtandi (enzalutamide), Zytiga (abiraterone), all the androgen receptor (AR) inhibitors, the taxanes, Provenge (sipuleucel-T), and Xofigo (radium-223). This subtype makes up over 97% of prostate cancers at diagnosis.

Then there are patients with a less common but important and more aggressive subtype called neuroendocrine prostate cancer (NEPC). Another term for this is small-cell prostate cancer or anaplastic or aggressive-variant prostate cancer, and these types of cancers do not make as much PSA and are less androgen receptor-dependent. These tumors tend to have many more mutations in them, particularly in critical tumor suppressors such as TP53, RB1, and PTEN, similar to small cell lung cancers, and have a histologic appearance more similar to small cell lung cancers than typical prostate cancer. These cancers tend to spread to organs like the liver or lungs rather than bone, and can make other markers besides PSA such as CEA and chromogranin-A, and have other features of aggressive disease. These NEPC or NEPC-like prostate cancers typically do not respond to hormonal therapy or AR inhibitors, or emerge later in the setting of resistance to these hormonal therapies, and do not respond well to taxane chemotherapy, Provenge (sipuleucel-T), or Xofigo (radium-223). So these men have an unmet need for better therapies.

About 1 – 2% of men with prostate cancer have NEPC/pure small cell histology at diagnosis, but recent studies show that about 20% of men with metastatic castration resistant prostate cancer (mCRPC) who have progressed on first line hormonal therapies will have this NEPC variant on biopsy. Thus, this aggressive variant prostate cancer is an emerging threat and is being increasingly recognized by clinicians, pathologists, and through tumor-based genetic testing.

There have been recent approvals of programmed cell death protein 1 (PD-1) inhibitors in patients with small-cell lung cancer based on important durable objective responses in a subset (10-20%) of these patients, and even higher when combined with chemotherapy. The rationale for our study is that, genetically, small-cell prostate cancer is similar to small-cell lung cancer, moreso than it is to prostate adenocarcinoma, where the response rate to PD-1 inhibitors alone is quite low at around 6%. This may be related to the higher tumor mutational burden in these NEPC tumors, making them more recognizable to the immune system, and we have also found higher (PD-L1) expression in these tumors.

Because of a lack of response to these other therapies, we have proposed and are running a first-in-prostate trial of a PD-L1 inhibitor for these patients.

This is the first trial that has tested the activity of PD-1 pathway blockade in a dedicated clinical trial for these patients. The PD-L1 inhibitor that we are using is called Bavencio (avelumab), which is made by Pfizer. Bavencio (avelumab) is FDA approved in kidney cancer, Merkel Cell carcinoma, and bladder cancer. It's an active drug, just like the other PD-1 and PD-L1 inhibitors, and agents targeting this pathway are quite active as single agents and approved in over a dozen cancer types now. This is an investigator-initiated clinical trial that's open at Duke University right now.

The purpose of our Phase II trial is to test the preliminary clinical activity of this agent, which is an immunotherapy. It's an immune checkpoint inhibitor in men who have this form of aggressive variant prostate cancer.

Can you walk us through the trial step by step?

Dr. Armstrong: Eligibility is the most important first consideration. There are two main criteria for enrollment. You are eligible if you have tissue that says you have NEPC or small-cell prostate cancer based on a biopsy. We are also interested in studying patients that have typical adenocarcinoma of the prostate, the more common type, but that have clinical features that suggest they're more like NEPC. We call this anaplastic criteria or aggressive criteria, where they have a large amount of cancer but little PSA, or they have a high lactate

dehydrogenase (LDH). Serum LDH is a marker that's associated with aggressive disease. Having liver metastases is an additional criteria that would permit eligibility if the biopsy does not show small cell features.

There are several additional criteria. For those patients with typical adenocarcinoma of the prostate, patients should have already had drugs like Zytiga (abiraterone) or Xtandi (enzalutamide) and chemotherapy since they will have wanted to have tried the standard-of-care options. Then, if they progress, they can consider the trial as an experimental treatment once standard options have been tried. If a patient has pure small cell prostate cancer, prior hormonal therapy is not required, but platinum-based chemotherapy is required since this is the current standard of care in this setting.

There are two ways for patients with prostate cancer to get small-cell prostate cancer or NEPC. One is right off the bat. We call that de novo small cell when it occurs at diagnosis. The other type, which is more common, is for a patient to start off with more typical prostate cancer and then for that cancer to be transformed later into NEPC. The cancer evolves. It adapts to hormonal therapy, and the cells that emerge from hormonal therapy lead to a third of patients who have this form of NEPC. We have written this trial to permit both types of patients to be eligible, either de novo or transformed after hormonal treatment.

Is there any difference in how men respond to different therapies if they end up with NEPC in different ways?

Dr. Armstrong: It's possible that in patients that have transformed NEPC that different cancers may coexist with each other. Many studies have shown that you can have regular prostate cancer and neuroendocrine prostate cancer in the same patient. It's like a hybrid cancer.

It's possible that those patients may benefit from combined approaches. For example, if they're developing resistance with this emerging, transformed NEPC, they can continue on the Xtandi (enzalutamide) on this trial, and we will give the PD-L1 inhibitor concurrently. That allows patients to have both of their cancers treated simultaneously. The idea is to follow on the successes seen with lung cancer where you're seeing durable responses. The data from this trial is not yet public and we are looking for just a few more patients to complete this study in 2020. We are excited to see patients respond and benefit and be able to understand the basis for these responses to build upon this study going forward.

What can patients expect to happen step by step during the trial?

Dr. Armstrong: The clinical trial is open only at Duke University. Patients have to come repeatedly to Duke, so it's probably difficult for patients to travel long distances. The patient is treated with an infusion every two weeks. It takes a few hours to complete. They get scans every eight weeks to see if it's working. If it's working, they stay on the study. If it's not, they come off. That's how we know it's working, by imaging their cancer to see if the tumors shrink. It's a fairly intensive study, so most of our patients come from within a few hours away. Side effects of immune therapies

can include immune activation and inflammation of different organs like the colon or lung or skin, and we carefully manage patients who develop these immune side effects.

The first step is to meet with our team at Duke and hear about the risks and benefits of this study and whether it makes sense for you. We have over 20 active studies open at Duke right now, so if this study does not fit your cancer, we likely have many other options for you.

Are there any fees for participation that patients should be aware of?

Dr. Armstrong: The treatment itself is provided by the study, so there's no cost for the treatment. There are some research studies that are being done, including blood tests and access to tumor tissue. None of that costs patients anything. Standard of care tests like regular routine labs and physical exams and imaging are billed to insurance, so there's no additional cost. Parking is covered. We do not pay patients to participate.

Is there anything else that you want to add about this trial?

Dr. Armstrong: Right now, the patients with prostate cancer that we know respond to these therapies are patients that have certain mutations, like mismatch repair deficiencies. We call that microsatellite instability (MSI)-high prostate cancer. Those patients respond well to these therapies. What we're trying to establish with this study is if there are other subsets of men with prostate cancer that could benefit from PD-1-based therapy. PD-1-based therapy is showing great activity in many cancer types, including kidney cancer, lung cancer, head and neck cancer, and bladder cancer. There are 12 to 15 other cancers that are seeing great outcomes with this class of immunotherapy.

The responses to PD-1 inhibitors alone in typical prostate adenocarcinoma is quite low, however, outside of these MSI-high tumors, which could be because we aren't treating the right subset of patients. Typical prostate cancer has few mutations that make it foreign to the immune system and recognizable by these therapies, so we think small-cell prostate cancer may be more likely to benefit.

We're already planning steps beyond this trial, where we will combine chemotherapy with immune checkpoint blockade or other immunotherapies. A recent trial demonstrated that Jevtana (cabazitaxel) plus Paraplatin (carboplatin) is highly active in these patients, and building off of this backbone with immunotherapy could benefit patients.

Twenty to thirty percent of all patients with aggressive metastatic prostate cancer tend to fit this type of scenario and could benefit from these approaches.

We hope to present the results of this paper within the next 6 to 12 months as we write new studies. Duke is part of a clinical trial network called the Department of Defense Clinical Trials Consortium, which allows us to quickly do trials with hundreds of patients to test new concepts and new compounds in order to identify those that are most likely to be successful moving forward. Pp1

For more information....

Contact Dr. Andrew Armstrong at andrew.armstrong@duke.edu or see https://clinicaltrials.gov/ct2/show/NCT03179410?term=PICK+NEPC&draw=2&rank=1 to find out more and how to enroll.

Mark Litwin, MD
California's IMPACT Program

Dr. Mark Litwin, Chair of the Department of Urology at the University of California, Los Angeles, co-founded California's innovative IMPACT program, which offers prostate cancer care for low-income, uninsured men.

He spoke with *Prostatepedia* about the program and its innovative approach.

How did the IMPACT program start?

Dr. Mark Litwin: IMPACT. which stands for Improving Access, Counseling, and Treatment for Californians with Prostate Cancer, started in 2001 in California. Under the Gray Davis administration, the state had some discretionary funds and decided to put money into prostate cancer. They wanted to create a program that would provide prostate cancer care for low-income, uninsured men. In particular, they wanted University of California physicians to take the lead on it because of the organizational infrastructure already in place throughout the state.

I had a series of meetings with what is now called the California Department of Health Care Services to create the program, which included a limited amount of statutory language. It was already written into the budget for that year. The Davis administration wanted the program to provide prostate cancer care for men at or below 200% of the federal poverty level, which defined low-income, and who were either uninsured or underinsured. The rest was left to us.

Because I have a background in urology, urologic oncology, and public health, I was in a position to put together a program. I sat down with my counterparts at the other University of California urology and radiation oncology units in San Diego, Irvine, Los Angeles, Davis, and San Francisco.

The program was put together with a combination of medical and nursing models. I worked closely with two nurse-scientist colleagues in particular to create this program, which covers medical care for men with prostate cancer who are indigent and uninsured and also provides them with patient empowerment, patient communication, and patient education. These are issues that physicians don't often focus on but are central in nursing. The program combines medical care, education, and empowerment to engage patients in their own health care as it relates to prostate cancer.

The funds were significant, which allowed us to create a program that included everything from outreach and education to diagnosis to counseling, like urological counseling for patients and families, nutritional counseling for dietary interventions, and counseling to try to get patients healthier in general. It also includes all the usual treatments for prostate cancer, from surgery, radiation, and chemotherapy to brachytherapy. Clinical trials are another element, as well as hospice care for patients at the end of life. It is A-to-Z care.

We designed the program to get care for patients in their own communities instead of having them enter so-called ivory tower health centers. This makes care accessible for patients. We worked hard to establish a program that provides good quality care along with good access to care. We have providers, doctors, hospitals, and therapists in all 58 counties of the state, though some counties have more resources than others.

We have offices throughout the state so patients can be seen, evaluated, and engaged with much closer to home. The program is now administered out of Los Angeles.

One of the things that makes the program unique is that every patient is assigned a nurse case manager based here in Los Angeles. The nurse case manager talks regularly with the patient and helps empower them to engage in the care that they need. It helps a lot with accessing care and navigating the complexities of the confusing health system that we have. Our nurse case managers are godsends and a special element of the program.

How do men apply?

Dr. Litwin: When we started the program, there wasn't a lot online. So we had outreach coordinators who went all throughout the state to various places, like unemployment offices and migrant health clinics, anywhere we might find individuals who needed access to the program. It was very hands on. Now, a lot of it is done online. Our website (california-impact.org) lists a phone number (800-409-8252) that connects patients to live enrollment coordinators who take down the patient's information to make sure they qualify for the program based on income and status.

For example, we may be able to determine if they are eligible for a more comprehensive insurance, like Medi-Cal, and didn't know it. If they are eligible for Medi-Cal, we'll help them apply for Medi-Cal, and that's ultimately better for the patient.

We determine through a series of questions that we ask that they're not eligible for Medicare, or Medi-Cal, or any other more comprehensive program. If they meet the income requirements, which is less than 200% of the federal poverty level for their household size in that year, then they get enrolled in the IMPACT program. They get sent a contract, which is an agreement that allows them to attest to the fact that they're providing us with accurate information, and then we tell them exactly what our services are. There's no cost to them at all because it's all funded by the state.

They are assigned to a nurse case manager who does initial intake, which involves a two-hour phone visit to help assess their needs, both in terms of prostate cancer and other social needs. If we're able to, we refer them to other programs to address those other needs. The nurse helps them figure out what type of doctor they need. Are they recently diagnosed? Do they need to see a radiation doctor and a surgeon? Were they diagnosed many years ago but lost their insurance? Do they need routine follow up, or do they have advanced disease, and they need a clinical trial? The nurse assesses the answers to these questions and others and works with one of our medical directors, a physician in a leadership position, to help them figure out what the patient needs.

If the patient lives in a major urban area, it's easier for us to get them to the doctor they need right away. If they live in a place like Modoc County, Del Norte County, Siskiyou County, or any one of the more rural places in the state, then it's trickier to get them access to care. We have systems set up all throughout the state to either provide care locally or to put them in a rideshare and get them to somewhere where they can get care.

A lot of readers are support group leaders or other key members of their community. What can they do to help get the word out?

Dr. Litwin: Send the link of our website to as many people as possible who might need it. We have tons of resources on the website that tell people how to reach us to see if they're eligible to enroll in the program. The website also includes a lot of resources that we've developed over the years, educational resources for every aspect of the prostate cancer experience. All of our resources are available in both English and Spanish. They're all available in written form, and many of them are available in audio form.

The hope is that anybody with prostate cancer who is looking for information about a particular aspect of care can access it. That might be anything from issues related to surgery or radiation, chemotherapy, catheters or urinary symptoms, or any other aspect of the prostate cancer experience. We always try to develop resources in a manner that is culturally competent. We want to be culturally sensitive to the particular needs of any patient group or subgroup that we serve. We also try to be sensitive to health literacy and to the fact that most educational materials that are developed in this country are aimed at a high sophistication level that many people don't totally understand, whether they're insured or not. Our materials are meant to be thoughtful and educational, but they are also written at a level that the average person can understand.

Anybody who wants flyers or information to post or hand out at health fairs or other venues can access them on the website for download. We're also happy to send them out to people. Pp!

For more information....

PACT Program
info@california-impact.org

274 Redwood Shores, #739
Redwood City, CA 94065
(800) 975 6238
info@prostatepedia.net
www.prostatepedia.net

Coming Up!

March:
Genomics